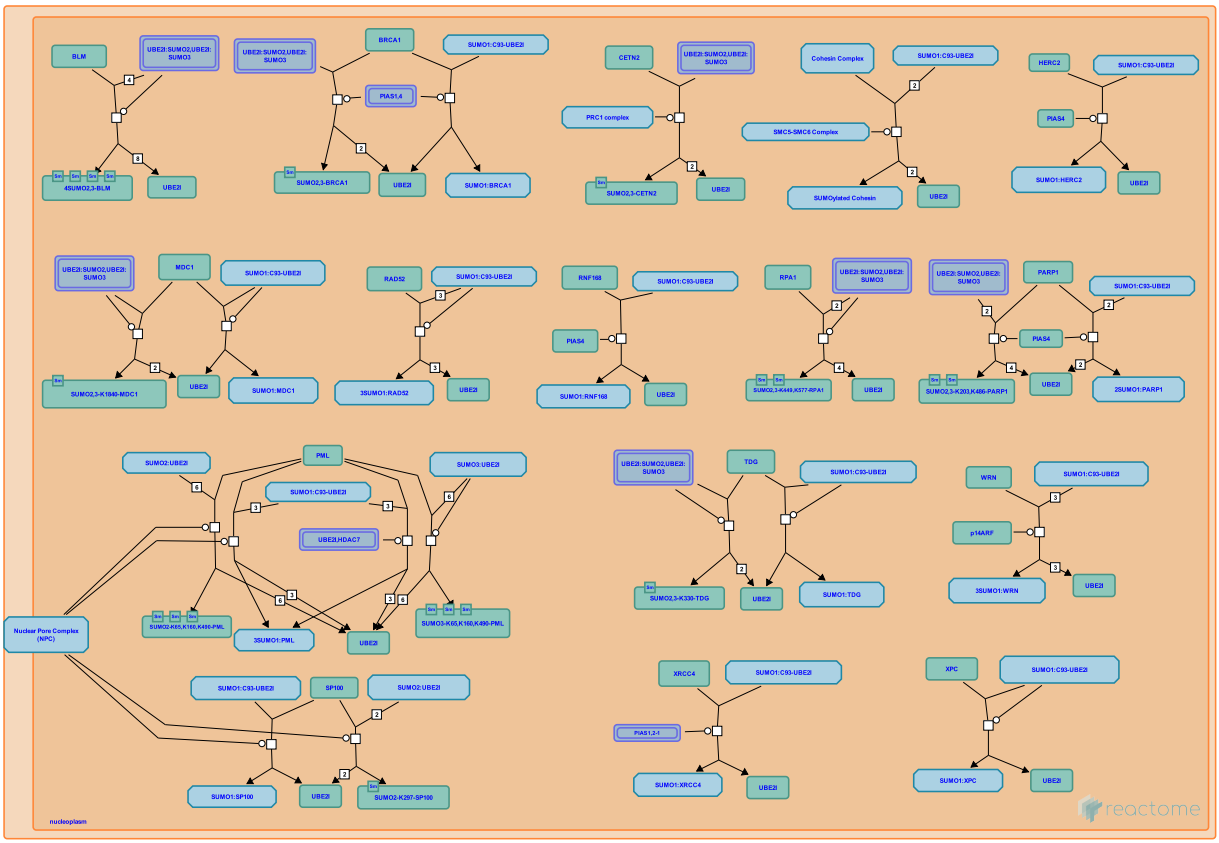
SUMOylation of DNA damage response and repair proteins



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07/03/2021

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. ↗

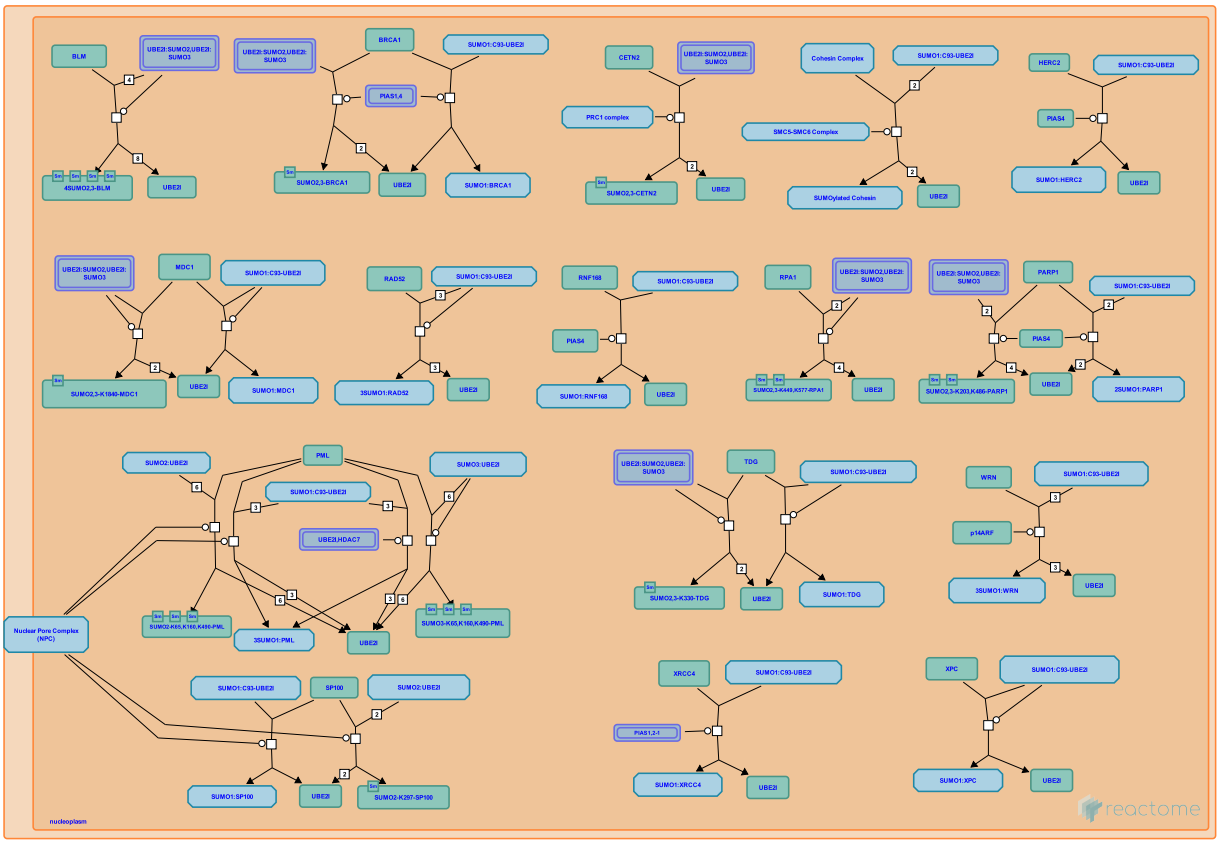
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 DNA damage response and repair proteins ↗

Stable identifier: R-HSA-3108214

Compartments: nucleoplasm



Several factors that participate in DNA damage response and repair are SUMOylated (reviewed in Dou et al. 2011, Bekker-Jensen and Mailand 2011, Ulrich 2012, Psakhye and Jentsch 2012, Bologna and Ferrari 2013, Flotho and Melchior 2013, Jackson and Durocher 2013). SUMOylation can alter enzymatic activity and protein stability or it can serve to recruit additional factors. For example, SUMOylation of Thymine DNA glycosylase (TDG) causes TDG to lose affinity for its product, an abasic site opposite a G residue, and thus increases turnover of the enzyme. During repair of double-strand breaks SUMO1, SUMO2, SUMO3, and the SUMO E3 ligases PIAS1 and PIAS4 accumulate at double-strand breaks where BRCA1, HERC1, RNF168, MDC1, and TP53BP1 are SUMOylated. SUMOylation of BRCA1 may increase its ubiquitin ligase activity while SUMOylation of MDC1 and HERC2 appears to play a role in recruitment of proteins such as RNF4 and RNF8 to double strand breaks. Similarly SUMOylation of RPA1 (RPA70) recruits RAD51 in the homologous recombination pathway.

Literature references

Dou, H., Huang, C., Van Nguyen, T., Lu, LS., Yeh, ET. (2011). SUMOylation and de-SUMOylation in response to DNA damage. *FEBS Lett., 585*, 2891-6. ↗

Flotho, A., Melchior, F. (2013). Sumoylation: a regulatory protein modification in health and disease. *Annu. Rev. Biochem., 82*, 357-85. ↗

Cremona, CA., Sarangi, P., Zhao, X. (2012). Sumoylation and the DNA damage response. *Biomolecules, 2*, 376-88. ↗

Bekker-Jensen, S., Mailand, N. (2011). The ubiquitin- and SUMO-dependent signaling response to DNA double-strand breaks. *FEBS Lett., 585*, 2914-9. ↗

Ulrich, HD. (2012). Ubiquitin and SUMO in DNA repair at a glance. *J. Cell. Sci., 125*, 249-54. ↗

Editions

2013-02-06	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

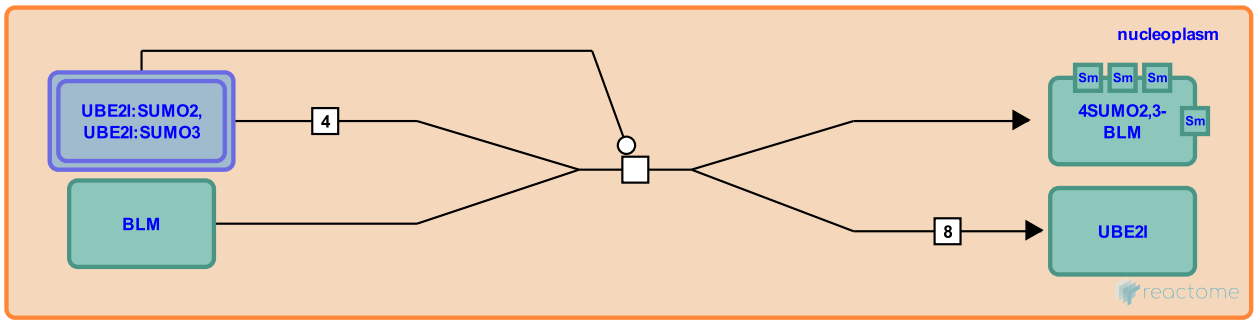
SUMOylation of BLM with SUMO2,3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4568914

Type: transition

Compartments: nucleoplasm



BLM is SUMOylated at lysine-317, lysine-331, lysine-344, and lysine-347 with SUMO2,3 (Eladad et al. 2005, Zhu et al. 2008, Ouyang et al. 2009, Ouyang et al. 2013, Hendriks et al. 2014). SUMOylation causes BLM to localize to PML bodies (Eladad et al. 2005). SUMOylated BLM recruits RAD51, which directly binds SUMO, and facilitates the substitution of RAD51 for RPA at stalled replication forks (Ouyang et al. 2009, 2013).

Literature references

Eladad, S., Ye, TZ., Hu, P., Leversha, M., Beresten, S., Matunis, MJ. et al. (2005). Intra-nuclear trafficking of the BLM helicase to DNA damage-induced foci is regulated by SUMO modification. *Hum. Mol. Genet., 14*, 1351-65. ↗

Zhu, J., Zhu, S., Guzzo, CM., Ellis, NA., Sung, KS., Choi, CY. et al. (2008). Small ubiquitin-related modifier (SUMO) binding determines substrate recognition and paralog-selective SUMO modification. *J. Biol. Chem., 283*, 29405-15. ↗

Ouyang, KJ., Woo, LL., Zhu, J., Huo, D., Matunis, MJ., Ellis, NA. (2009). SUMO modification regulates BLM and RAD51 interaction at damaged replication forks. *PLoS Biol., 7*, e1000252. ↗

Ouyang, KJ., Yagle, MK., Matunis, MJ., Ellis, NA. (2013). BLM SUMOylation regulates ssDNA accumulation at stalled replication forks. *Front Genet, 4*, 167. ↗

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36. ↗

Editions

2013-09-14	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

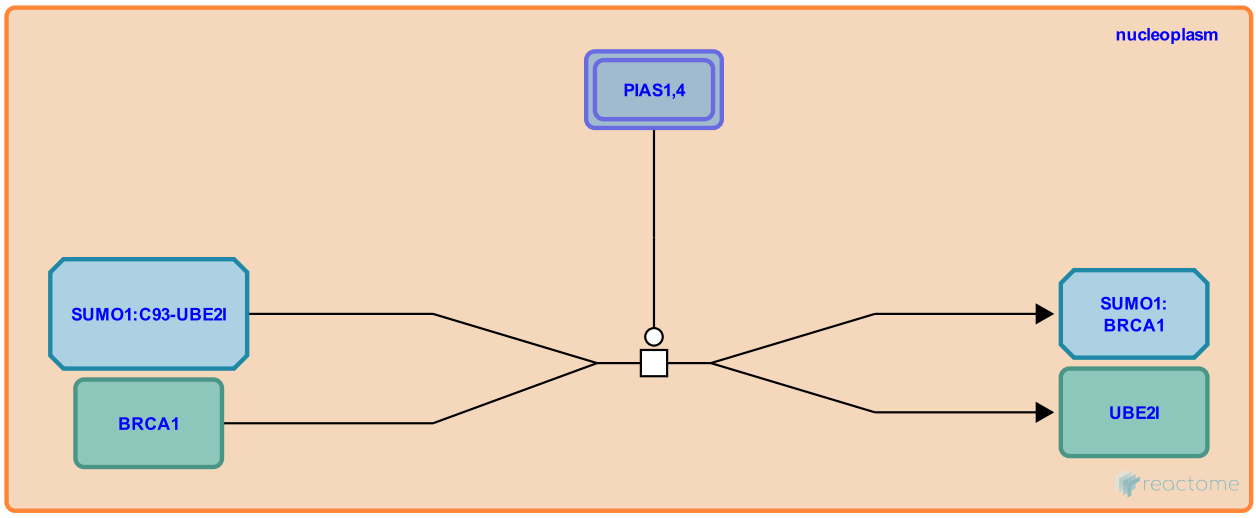
PIAS1,4 SUMOylates BRCA1 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-2997709

Type: transition

Compartments: nucleoplasm



PIAS1,4 SUMOylate BRCA1 with SUMO1 at lysine-109 (Morris et al. 2009, Xu et al. 2009). SUMOylation occurs in response to genotoxic stress and double-strand breaks to which PIAS1 and PIAS4 are recruited (Galanty et al. 2009). SUMOylation enhances the ability of BRCA1 to bind and modulate ESR1 (ERalpha) transcriptional activity (Xu et al. 2009). More SUMO2:BRCA1 than SUMO1:BRCA1 is observed in vivo (Morris et al. 2009, Galanty et al. 2009).

Literature references

Morris, JR., Boutell, C., Keppler, M., Densham, R., Weekes, D., Alamshah, A. et al. (2009). The SUMO modification pathway is involved in the BRCA1 response to genotoxic stress. *Nature, 462*, 886-90. ↗

Xu, J., Watkins, T., Reddy, A., Reddy, ES., Rao, VN. (2009). A novel mechanism whereby BRCA1/1a/1b fine tunes the dynamic complex interplay between SUMO-dependent/independent activities of Ubc9 on E2-induced ERalpha activation/repression and degradation in breast cancer cells. *Int. J. Oncol., 34*, 939-49. ↗

Galanty, Y., Belotserkovskaya, R., Coates, J., Polo, S., Miller, KM., Jackson, SP. (2009). Mammalian SUMO E3-ligases PIAS1 and PIAS4 promote responses to DNA double-strand breaks. *Nature, 462*, 935-9. ↗

Editions

2013-01-19	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

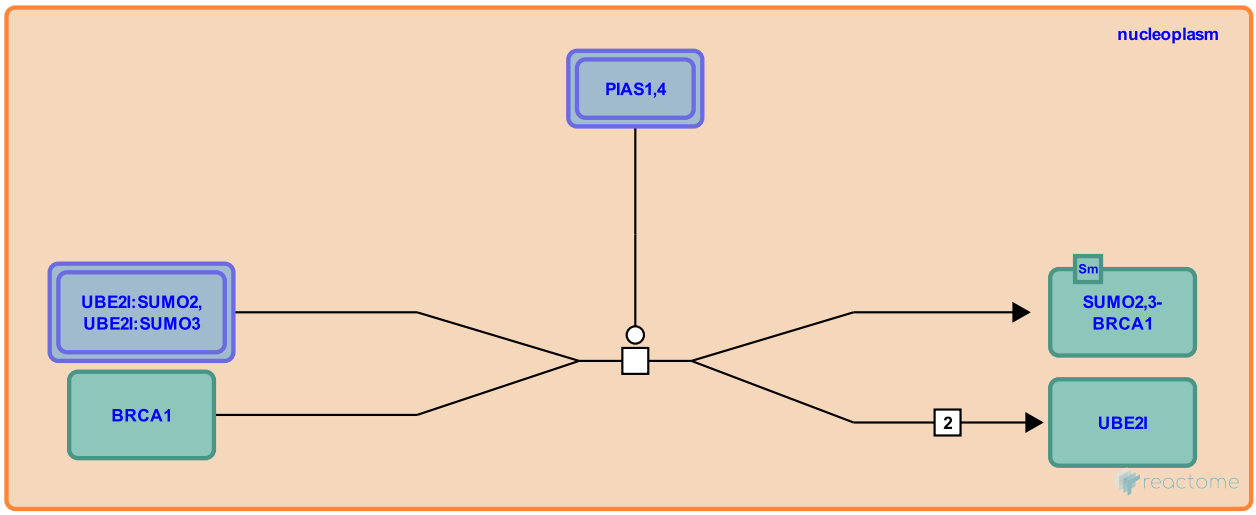
PIAS1,4 SUMOylates BRCA1 with SUMO2,3

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-2997616

Type: transition

Compartments: nucleoplasm



PIAS1,4 SUMOylate BRCA1 with SUMO2,3 (Galanty et al. 2009, Morris et al. 2009, Vialter et al. 2011, Hendriks et al. 2014). More SUMO2,3-BRCA1 than SUMO1-BRCA1 is observed in vivo (Morris et al. 2009, Galanty et al. 2009). SUMOylation with SUMO2,3 increases in response to oxidative stress (Vialter et al. 2011). SUMOylation of BRCA1 increases its ubiquitin ligase activity (Morris et al. 2009).

Literature references

Galanty, Y., Belotserkovskaya, R., Coates, J., Polo, S., Miller, KM., Jackson, SP. (2009). Mammalian SUMO E3-ligases PIAS1 and PIAS4 promote responses to DNA double-strand breaks. *Nature, 462*, 935-9.

Morris, JR., Boutell, C., Keppler, M., Densham, R., Weekes, D., Alamshah, A. et al. (2009). The SUMO modification pathway is involved in the BRCA1 response to genotoxic stress. *Nature, 462*, 886-90.

Vialter, A., Vincent, A., Demidem, A., Morvan, D., Stepien, G., Venezia, ND. et al. (2011). Cell cycle-dependent conjugation of endogenous BRCA1 protein with SUMO-2/3. *Biochim. Biophys. Acta, 1810*, 432-8.

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36.

Editions

2013-01-19	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

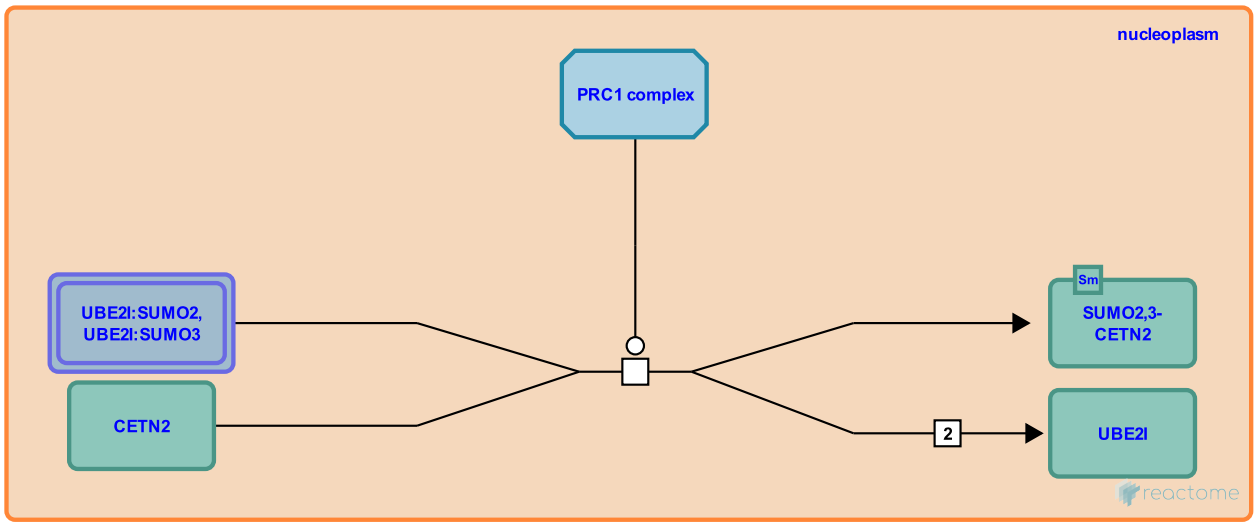
CBX4 (Pc2) SUMOylates CETN2 with SUMO2,3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4570463

Type: transition

Compartments: nucleoplasm



CBX4 (Pc2) in the PRC1 complex SUMOylates CETN2 at an unknown residue with SUMO2,3 (Klein and Nigg 2009). SUMOylation of CETN2 enhances its nuclear localization. Interaction with XPC is also required for nuclear localization of CETN2.

Literature references

Klein, UR., Nigg, EA. (2009). SUMO-dependent regulation of centrin-2. *J. Cell. Sci., 122*, 3312-21. ↗

Editions

2013-09-19	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

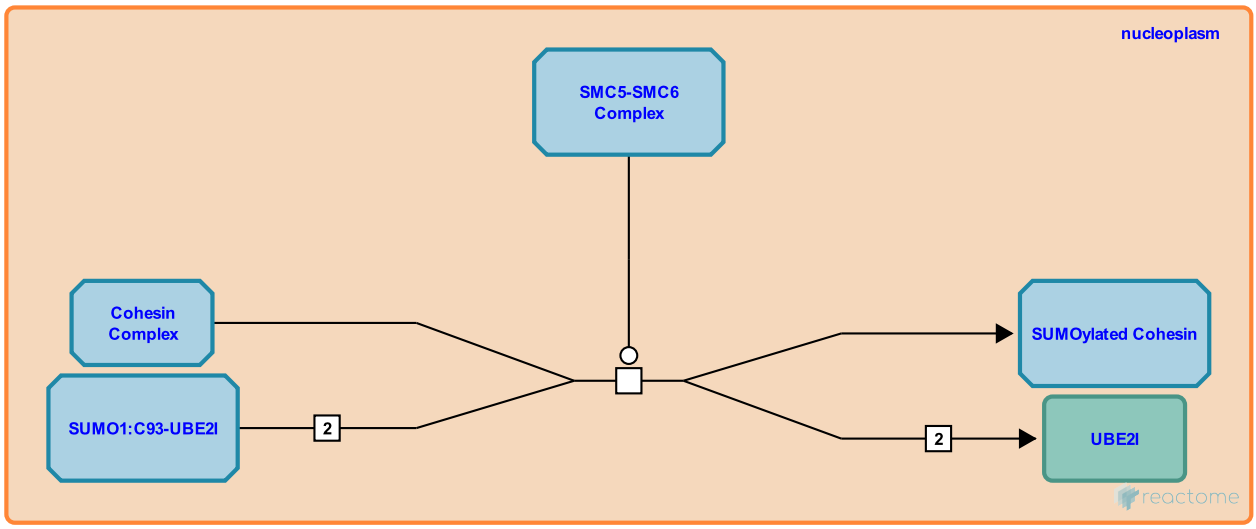
SMC5-SMC6 Complex SUMOylates Cohesin with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-3108212

Type: transition

Compartments: nucleoplasm



The NSMCE2 (NSE2, MMS21) subunit of the SMC5/6 complex SUMOylates the RAD21 and STAG2 subunits of cohesin with SUMO1 (Potts et al. 2006 supplementary data, reviewed in Stephan et al 2011). RAD21 (SCC1) is SUMOylated at several lysines (Wu et al. 2012). SUMOylation of RAD21 occurs during DNA damage repair and is necessary for sister chromatid recombination (Wu et al. 2012).

Literature references

Wu, N., Kong, X., Ji, Z., Zeng, W., Potts, PR., Yokomori, K. et al. (2012). Scc1 sumoylation by Mms21 promotes sister chromatid recombination through counteracting Wapl. *Genes Dev., 26*, 1473-85. ↗

Potts, PR., Porteus, MH., Yu, H. (2006). Human SMC5/6 complex promotes sister chromatid homologous recombination by recruiting the SMC1/3 cohesin complex to double-strand breaks. *EMBO J., 25*, 3377-88. ↗

Stephan, AK., Kliszczak, M., Morrison, CG. (2011). The Nse2/Mms21 SUMO ligase of the Smc5/6 complex in the maintenance of genome stability. *FEBS Lett., 585*, 2907-13. ↗

Editions

2013-02-06	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

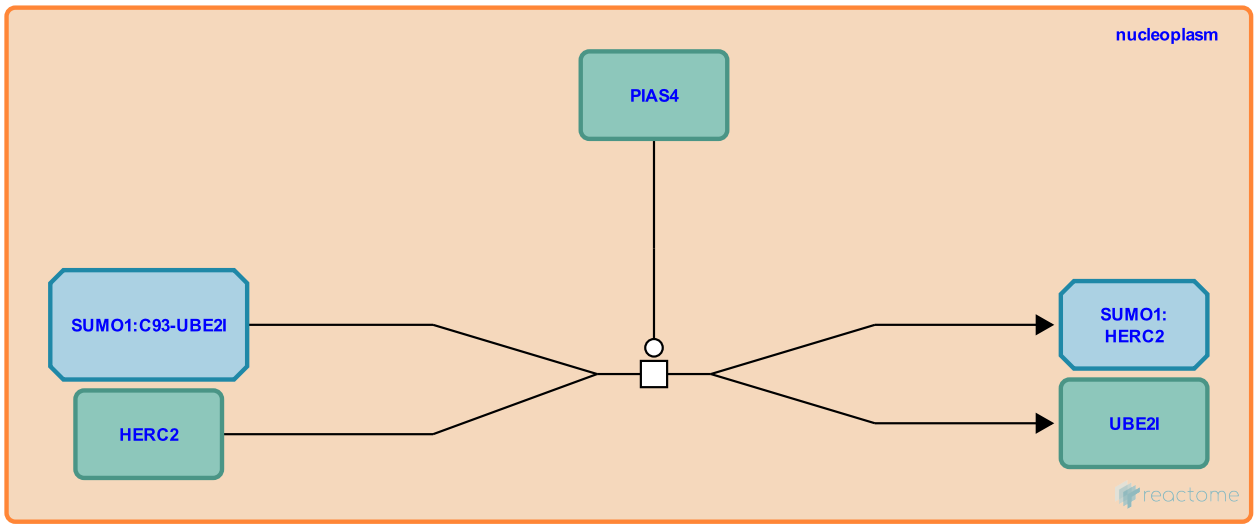
PIAS4 SUMOylates HERC2 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551724

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates HERC2 at an unknown lysine residue with SUMO1 (Danielsen et al. 2012). HERC2 binds SUMO1 and is then SUMOylated. SUMOylation of HERC2 promotes binding to RNF8 at double-strand breaks in DNA.

Literature references

Danielsen, JR., Povlsen, LK., Villumsen, BH., Streicher, W., Nilsson, J., Wikström, M. et al. (2012). DNA damage-inducible SUMOylation of HERC2 promotes RNF8 binding via a novel SUMO-binding Zinc finger. *J. Cell Biol., 197*, 179-87. ↗

Editions

2013-09-13	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

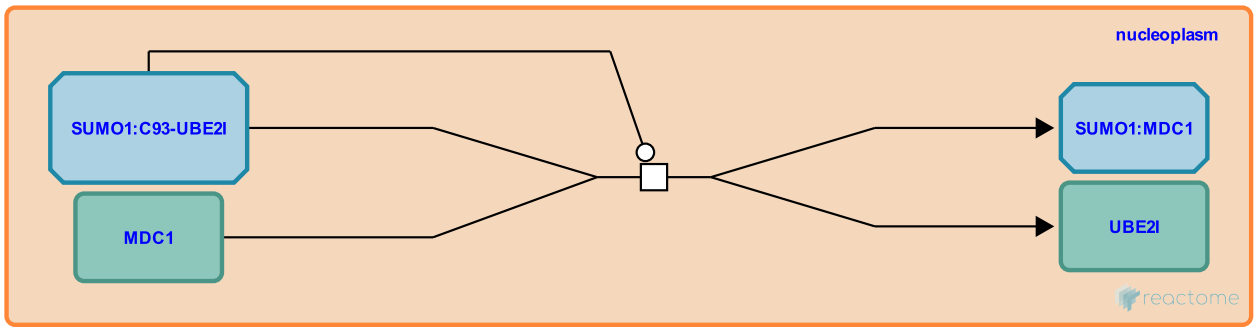
SUMOylation of MDC1 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4570554

Type: transition

Compartments: nucleoplasm



MDC1 is SUMOylated at lysine-1840 with SUMO1. SUMOyation of MDC1 is required for its degradation, which is thought to be directed by ubiquitinylation by RNF4 (Luo et al. 2012).

Literature references

Luo, K., Zhang, H., Wang, L., Yuan, J., Lou, Z. (2012). Sumoylation of MDC1 is important for proper DNA damage response. *EMBO J., 31*, 3008-19. ↗

Editions

2013-09-19	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

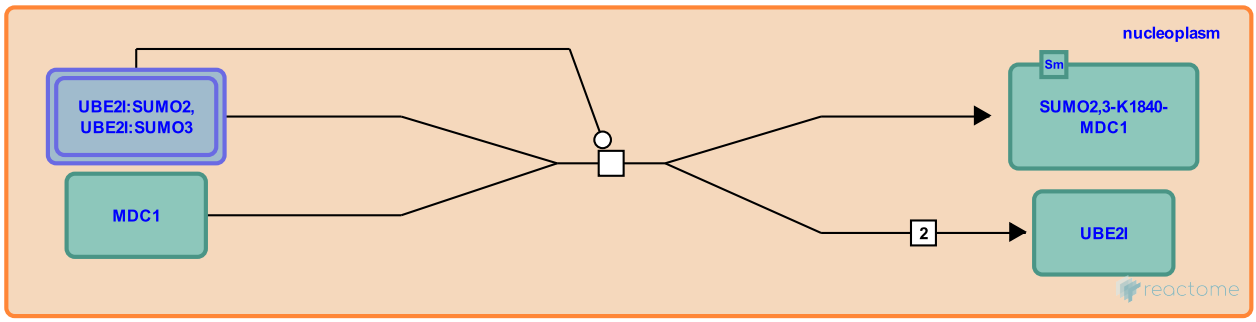
SUMOylation of MDC1 with SUMO2,3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4570553

Type: transition

Compartments: nucleoplasm



MDC1 is SUMOylated at lysine-1840 with SUMO2,3 (Luo et al. 2012, Hendriks et al. 2014, Tammsalu et al. 2014). SUMOylation is required for degradation of MDC1. SUMOylation of MDC1 is required for recruitment of RNF4 (Yin et al. 2012), which is believed to ubiquitinylate MDC1, resulting in degradation of MDC1.

Literature references

Luo, K., Zhang, H., Wang, L., Yuan, J., Lou, Z. (2012). Sumoylation of MDC1 is important for proper DNA damage response. *EMBO J., 31*, 3008-19. ↗

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36. ↗

Tammsalu, T., Matic, I., Jaffray, EG., Ibrahim, AF., Tatham, MH., Hay, RT. (2014). Proteome-wide identification of SUMO2 modification sites. *Sci Signal, 7*, rs2. ↗

Yin, Y., Seifert, A., Chua, JS., Maure, JF., Golebiowski, F., Hay, RT. (2012). SUMO-targeted ubiquitin E3 ligase RNF4 is required for the response of human cells to DNA damage. *Genes Dev., 26*, 1196-208. ↗

Editions

2013-09-19	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

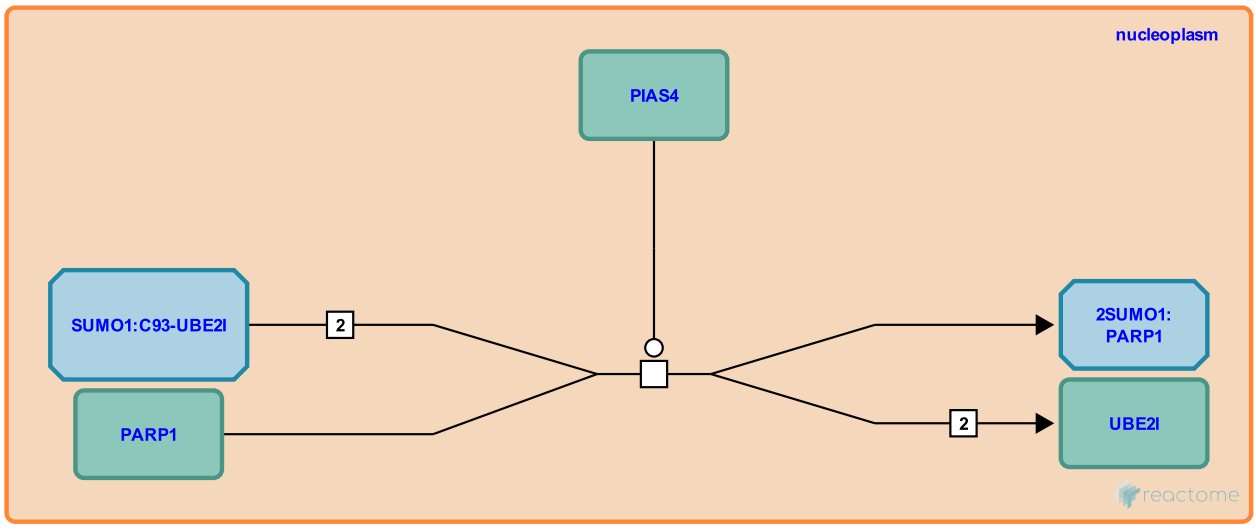
PIAS4 SUMOylates PARP1 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551604

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates PARP1 at lysine-203 and lysine-486 with SUMO1 (Martin et al. 2009, Matafora et al. 2009, Messner et al. 2009, Zilio et al. 2013, Impens et al. 2014). SUMOylation abrogates acetylation of PARP1 by p300 (Messner et al. 2009). PARP1 reciprocally poly(ADP-ribose)ylates PIAS4 (Martin et al. 2009). PARP1 is SUMOylated in response to heat shock and SUMOylation is required for full activation of the HSP70.1 promoter (Martin et al 2009).

Literature references

Messner, S., Schuermann, D., Altmeyer, M., Kassner, I., Schmidt, D., Schär, P. et al. (2009). Sumoylation of poly(ADP-ribose) polymerase 1 inhibits its acetylation and restrains transcriptional coactivator function. *FASEB J., 23*, 3978-89. ↗

Martin, N., Schwamborn, K., Schreiber, V., Werner, A., Guillier, C., Zhang, XD. et al. (2009). PARP-1 transcriptional activity is regulated by sumoylation upon heat shock. *EMBO J., 28*, 3534-48. ↗

Impens, F., Radoshevich, L., Cossart, P., Ribet, D. (2014). Mapping of SUMO sites and analysis of SUMOylation changes induced by external stimuli. *Proc. Natl. Acad. Sci. U.S.A., 111*, 12432-7. ↗

Zilio, N., Williamson, CT., Eustermann, S., Shah, R., West, SC., Neuhaus, D. et al. (2013). DNA-dependent SUMO modification of PARP-1. *DNA Repair (Amst.), 12*, 761-73. ↗

Matafora, V., D'Amato, A., Mori, S., Blasi, F., Bachi, A. (2009). Proteomics analysis of nucleolar SUMO-1 target proteins upon proteasome inhibition. *Mol. Cell Proteomics, 8*, 2243-55. ↗

Editions

2013-09-13	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

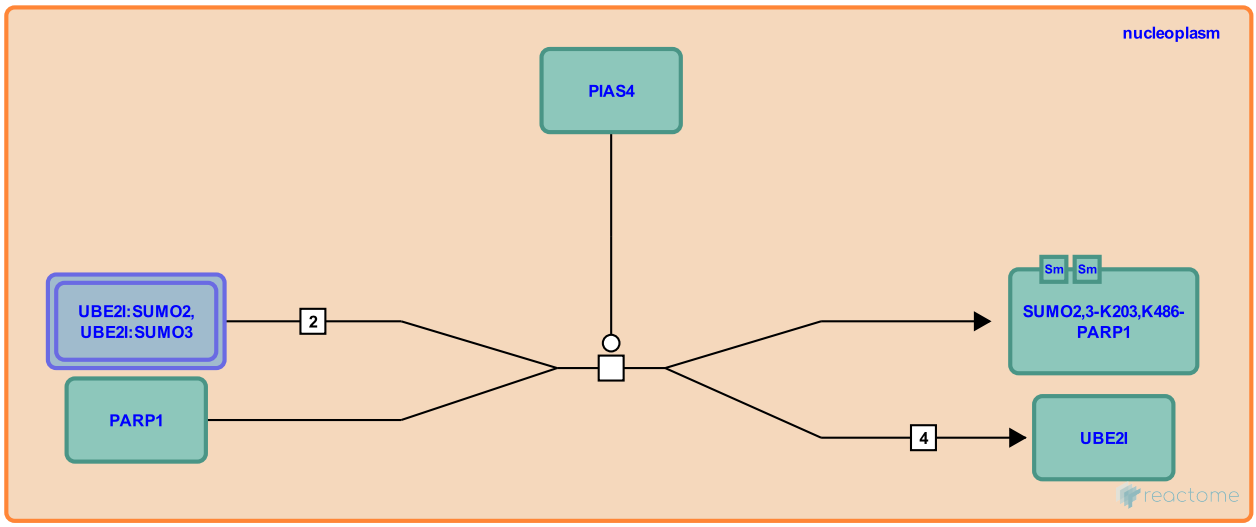
PIAS4 SUMOylates PARP1 with SUMO2,3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551768

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates PARP1 at lysine-203 and lysine-486 with SUMO2,3 in response to heat shock (Martin et al. 2009, Lamoliatte et al. 2013, Hendriks et al. 2014, Tammsalu et al. 2014). PARP1 reciprocally poly(ADP-ribose)ylates PIAS4 (Martin et al. 2009). SUMOylation of PARP1 is required for full activation of the HSP70.1 promoter (Martin et al. 2009).

Literature references

Martin, N., Schwamborn, K., Schreiber, V., Werner, A., Guillier, C., Zhang, XD. et al. (2009). PARP-1 transcriptional activity is regulated by sumoylation upon heat shock. *EMBO J., 28*, 3534-48. ↗

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36. ↗

Lamoliatte, F., Bonneil, E., Durette, C., Caron-Lizotte, O., Wildemann, D., Zerweck, J. et al. (2013). Targeted identification of SUMOylation sites in human proteins using affinity enrichment and paralog-specific reporter ions. *Mol. Cell Proteomics, 12*, 2536-50. ↗

Tammsalu, T., Matic, I., Jaffray, EG., Ibrahim, AF., Tatham, MH., Hay, RT. (2014). Proteome-wide identification of SUMO2 modification sites. *Sci Signal, 7*, rs2. ↗

Editions

2013-09-13	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

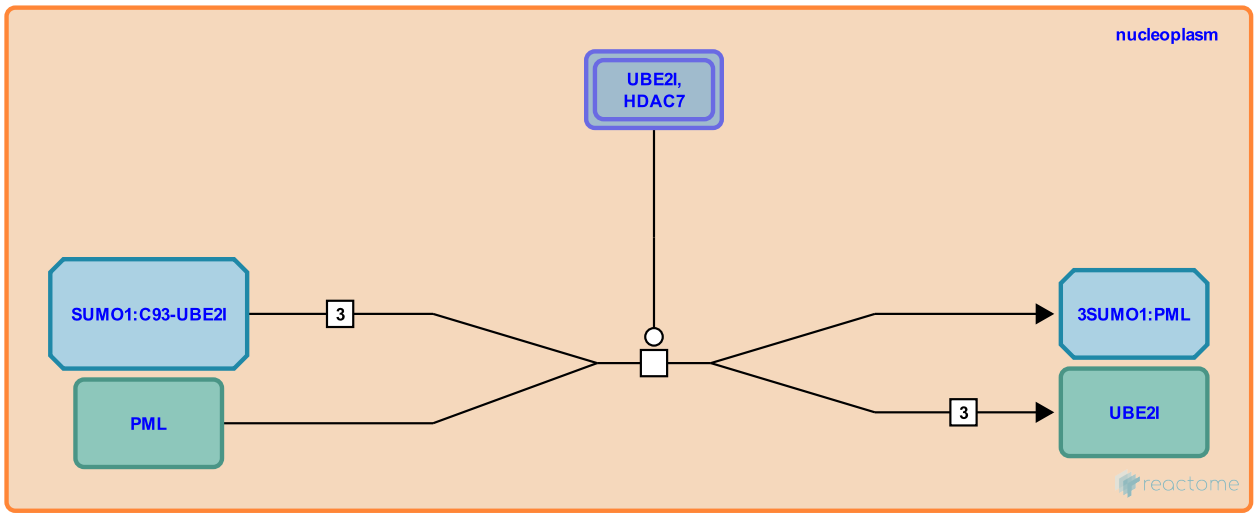
UBE2I, HDAC7 SUMOylate PML with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-3000383

Type: transition

Compartments: nucleoplasm



UBE2I (UBC9) alone and in association with HDAC7 can SUMOylate PML with SUMO1 at lysine-65, lysine-160, and lysine-490 (Sternsdorf et al. 1997, Kamitani et al. 1998, Duprez et al. 1999, Knipscheer et al. 2008). SUMOylated PML is observed during interphase but not during mitosis (Everett et al. 1999). Knockdown of HDAC7 reduces the number of PML bodies (Gao et al. 2008).

Literature references

Kamitani, T., Kito, K., Nguyen, HP., Wada, H., Fukuda-Kamitani, T., Yeh, ET. (1998). Identification of three major sentrinization sites in PML. *J. Biol. Chem., 273*, 26675-82. ↗

Kamitani, T., Nguyen, HP., Kito, K., Fukuda-Kamitani, T., Yeh, ET. (1998). Covalent modification of PML by the sentrin family of ubiquitin-like proteins. *J. Biol. Chem., 273*, 3117-20. ↗

Duprez, E., Saurin, AJ., Desterro, JM., Lallemand-Breitenbach, V., Howe, K., Boddy, MN. et al. (1999). SUMO-1 modification of the acute promyelocytic leukaemia protein PML: implications for nuclear localisation. *J. Cell. Sci., 112*, 381-93. ↗

Sternsdorf, T., Jensen, K., Will, H. (1997). Evidence for covalent modification of the nuclear dot-associated proteins PML and Sp100 by PIC1/SUMO-1. *J. Cell Biol., 139*, 1621-34. ↗

Everett, RD., Lomonte, P., Sternsdorf, T., van Driel, R., Orr, A. (1999). Cell cycle regulation of PML modification and ND10 composition. *J. Cell. Sci., 112*, 4581-8. ↗

Editions

2013-01-24	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

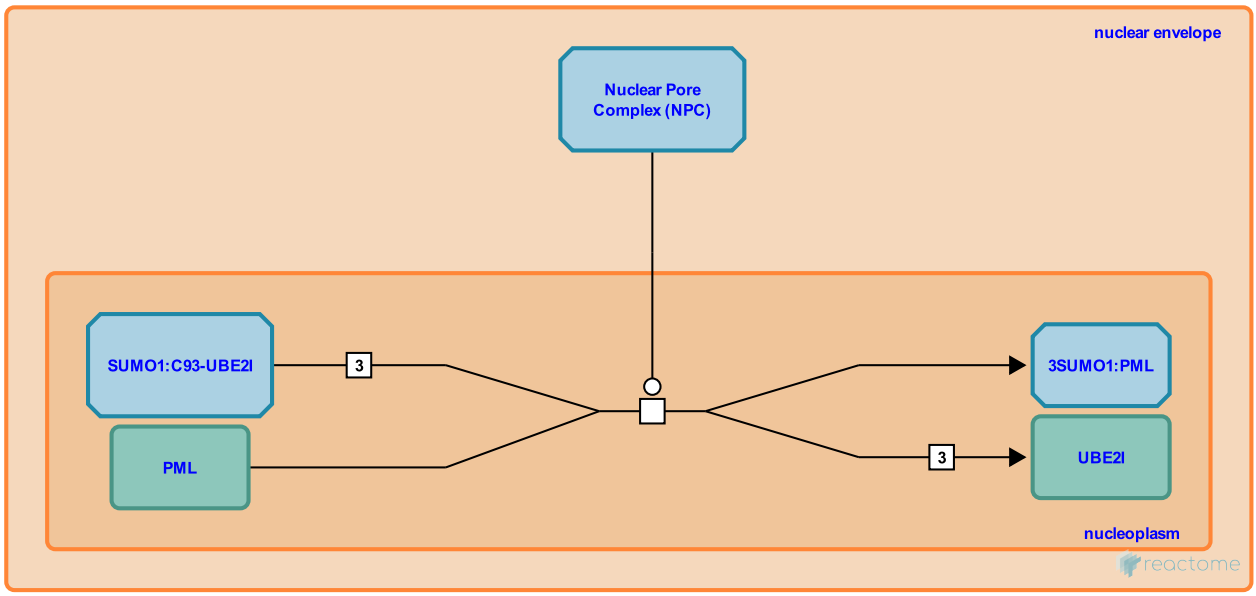
RANBP2 SUMOylates PML with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-5228508

Type: transition

Compartments: nucleoplasm, nuclear envelope



RANBP2 of the nuclear pore complex SUMOylates PML with SUMO1 at lysine-65, lysine-160, and lysine-490 (Sternsdorf et al. 1997, Kamitani et al. 1998, Duprez et al. 1999). SUMOylated PML is observed during interphase but not during mitosis (Everett et al. 1999). RANBP2 contains both a binding site for SUMO1 and a binding site for UBE2I (Tatham et al. 2005). The binding site for SUMO1 may play a role in SUMOylation of PML with SUMO1. Knockdown of RANBP2 reduces the number of PML bodies (Saitoh et al. 2006).

Literature references

Kamitani, T., Kito, K., Nguyen, HP., Wada, H., Fukuda-Kamitani, T., Yeh, ET. (1998). Identification of three major sentrinization sites in PML. *J. Biol. Chem., 273*, 26675-82. ↗

Kamitani, T., Nguyen, HP., Kito, K., Fukuda-Kamitani, T., Yeh, ET. (1998). Covalent modification of PML by the sentrin family of ubiquitin-like proteins. *J. Biol. Chem., 273*, 3117-20. ↗

Duprez, E., Saurin, AJ., Desterro, JM., Lallemand-Breitenbach, V., Howe, K., Boddy, MN. et al. (1999). SUMO-1 modification of the acute promyelocytic leukaemia protein PML: implications for nuclear localisation. *J. Cell. Sci., 112*, 381-93. ↗

Sternsdorf, T., Jensen, K., Will, H. (1997). Evidence for covalent modification of the nuclear dot-associated proteins PML and Sp100 by PIC1/SUMO-1. *J. Cell Biol., 139*, 1621-34. ↗

Everett, RD., Lomonte, P., Sternsdorf, T., van Driel, R., Orr, A. (1999). Cell cycle regulation of PML modification and ND10 composition. *J. Cell. Sci., 112*, 4581-8. ↗

Editions

2013-01-24	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

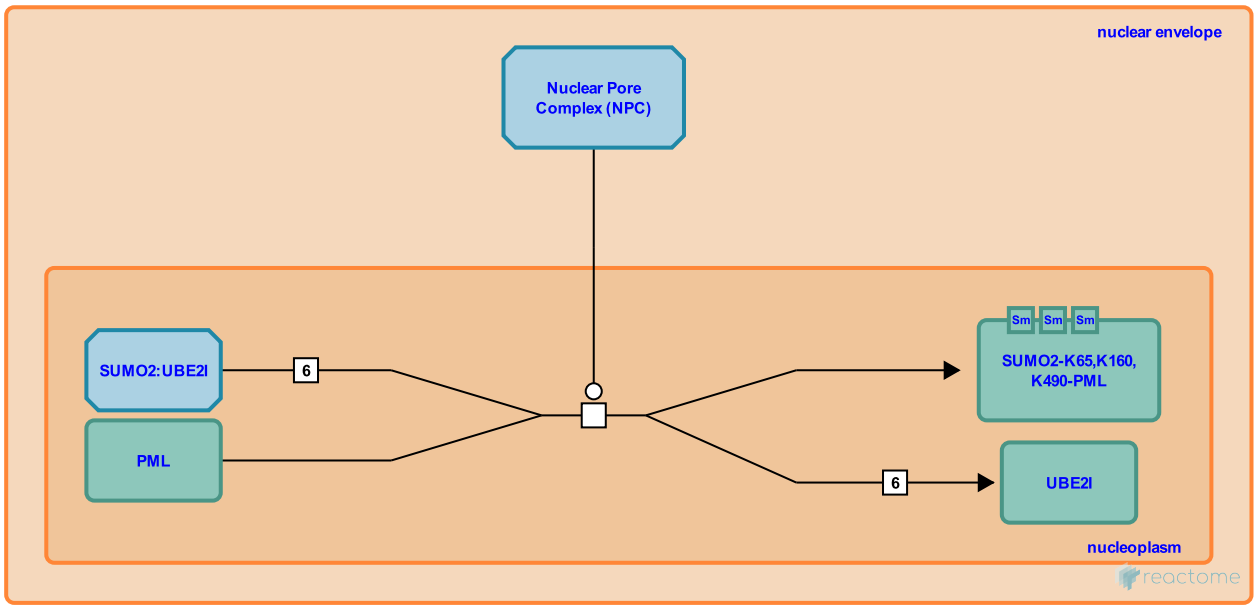
RANBP2 SUMOylates PML with SUMO2 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-3000411

Type: transition

Compartments: nucleoplasm, nuclear envelope



RANBP2 of the nuclear pore complex SUMOylates PML with SUMO2 at lysine-65, lysine-160, and lysine-490 (Kamitani et al. 1998, Tatham et al. 2005). RANBP2 contains both a binding site for SUMO1 and a binding site for UBE2I (Tatham et al. 2005). The binding site for UBE2I participates in SUMOylation of PML with SUMO2. SUMO2 colocalizes significantly with PML bodies (Vertegaal et al. 2004).

Literature references

Kamitani, T., Nguyen, HP., Kito, K., Fukuda-Kamitani, T., Yeh, ET. (1998). Covalent modification of PML by the sentrin family of ubiquitin-like proteins. *J. Biol. Chem., 273*, 3117-20. ↗

Tatham, MH., Kim, S., Jaffray, E., Song, J., Chen, Y., Hay, RT. (2005). Unique binding interactions among Ubc9, SUMO and RanBP2 reveal a mechanism for SUMO paralog selection. *Nat. Struct. Mol. Biol., 12*, 67-74. ↗

Vertegaal, AC., Ogg, SC., Jaffray, E., Rodriguez, MS., Hay, RT., Andersen, JS. et al. (2004). A proteomic study of SUMO-2 target proteins. *J. Biol. Chem., 279*, 33791-8. ↗

Tammsalu, T., Matic, I., Jaffray, EG., Ibrahim, AF., Tatham, MH., Hay, RT. (2014). Proteome-wide identification of SUMO2 modification sites. *Sci Signal, 7*, rs2. ↗

Editions

2013-01-24	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

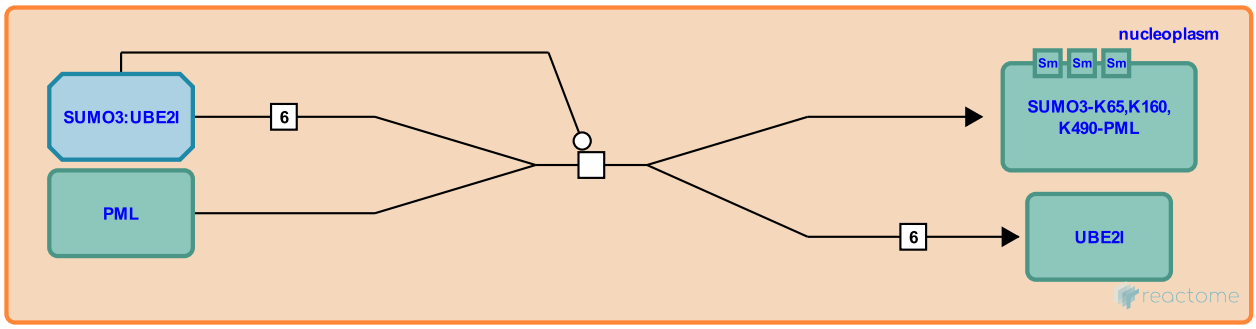
SUMOylation of PML with SUMO3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-3000433

Type: transition

Compartments: nucleoplasm



PML is observed to be SUMOylated with SUMO3 at lysine-65, lysine-160, and lysine-490 (Kamitani et al. 1998). SUMO3 is almost identical with SUMO2 therefore the same E3 ligase (RANBP2) that SUMOylate PML with SUMO2 may also be active with SUMO3, but this has not been proven. PML colocalizes with SUMO3 in nuclear bodies and disruption of SUMO3 expression reduces the number of nuclear bodies (Fu et al. 2005).

Literature references

Fu, C., Ahmed, K., Ding, H., Ding, X., Lan, J., Yang, Z. et al. (2005). Stabilization of PML nuclear localization by conjugation and oligomerization of SUMO-3. *Oncogene, 24*, 5401-13. ↗

Kamitani, T., Nguyen, HP., Kito, K., Fukuda-Kamitani, T., Yeh, ET. (1998). Covalent modification of PML by the sentrin family of ubiquitin-like proteins. *J. Biol. Chem., 273*, 3117-20. ↗

Gong, L., Yeh, ET. (2006). Characterization of a family of nucleolar SUMO-specific proteases with preference for SUMO-2 or SUMO-3. *J. Biol. Chem., 281*, 15869-77. ↗

Editions

2013-01-24	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

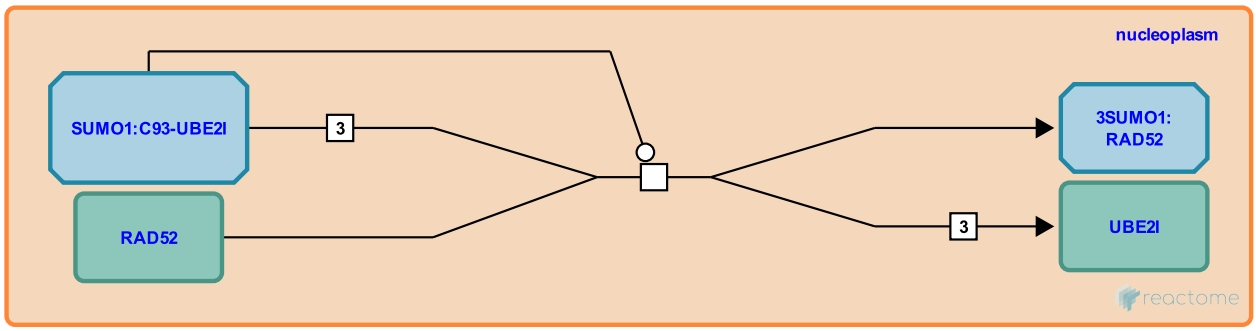
SUMOylation of RAD52 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4568863

Type: transition

Compartments: nucleoplasm



RAD52 is SUMOylated at lysine-411, lysine-412, and lysine-414 with SUMO1. SUMOylation is important for localization of RAD52 to the nucleus.

Literature references

Saito, K., Kagawa, W., Suzuki, T., Suzuki, H., Yokoyama, S., Saitoh, H. et al. (2010). The putative nuclear localization signal of the human RAD52 protein is a potential sumoylation site. *J. Biochem., 147*, 833-42. ↗

Editions

2013-09-14	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

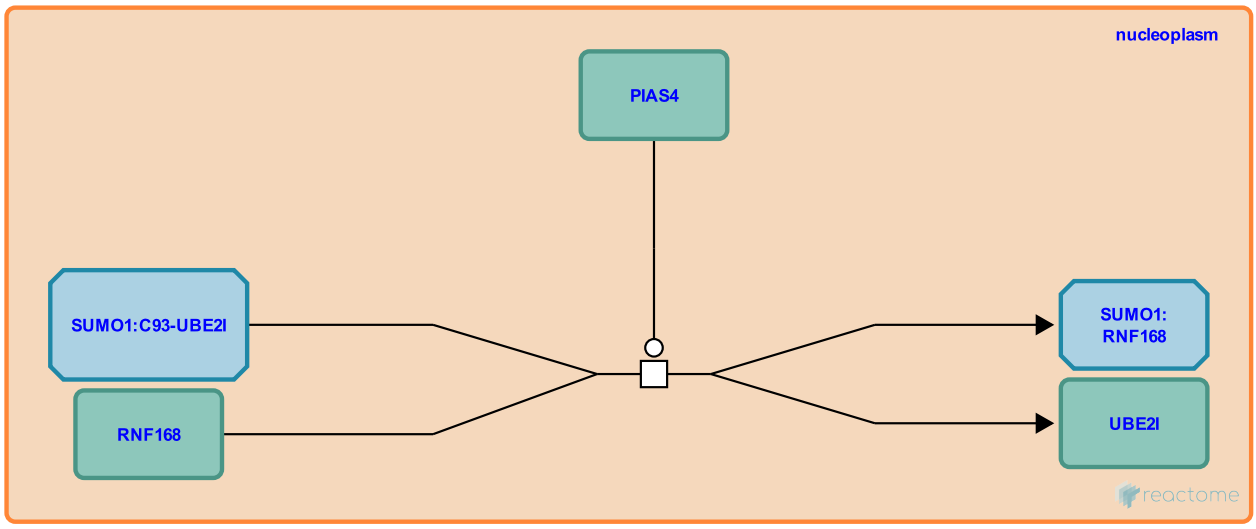
PIAS4 SUMOylates RNF168 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551661

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates RNF168 at an unknown lysine residue (Danielsen et al. 2012). Both RNF168 and HERC2 are SUMOylated at double-strand breaks in DNA. SUMOylation of RNF168 is required for its retention at double-strand breaks.

Literature references

Danielsen, JR., Povlsen, LK., Villumsen, BH., Streicher, W., Nilsson, J., Wikström, M. et al. (2012). DNA damage-inducible SUMOylation of HERC2 promotes RNF8 binding via a novel SUMO-binding Zinc finger. *J. Cell Biol., 197*, 179-87. ↗

Editions

2013-09-13	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

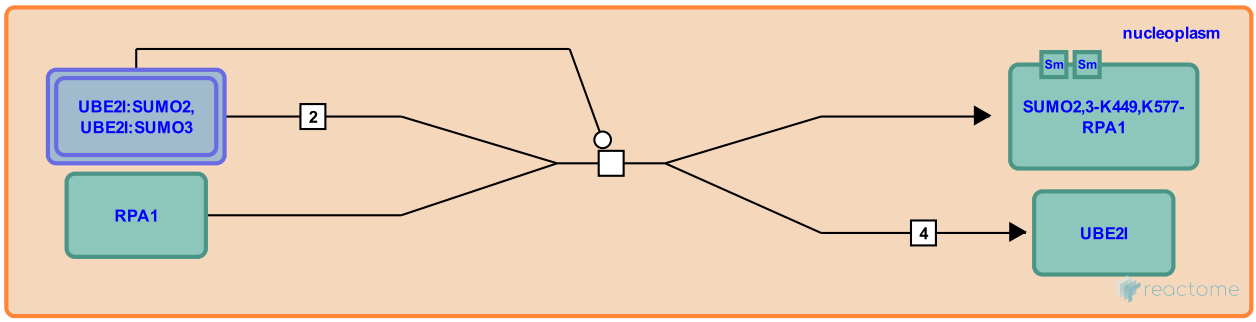
SUMOylation of RPA1 (RPA70) with SUMO2,3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551616

Type: transition

Compartments: nucleoplasm



RPA1 (RPA70) is SUMOylated at lysine-449 and lysine-577 with SUMO2,3 (Dou et al. 2010, Tammsalu et al. 2014). SUMOylation of RPA1 recruits RAD51 to sites of DNA damage to initiate repair through homologous recombination.

Literature references

Dou, H., Huang, C., Singh, M., Carpenter, PB., Yeh, ET. (2010). Regulation of DNA repair through deSUMOylation and SUMOylation of replication protein A complex. *Mol. Cell, 39*, 333-45. ↗

Tammsalu, T., Matic, I., Jaffray, EG., Ibrahim, AF., Tatham, MH., Hay, RT. (2014). Proteome-wide identification of SUMO2 modification sites. *Sci Signal, 7*, rs2. ↗

Editions

2013-09-13	Authored, Edited	May, B.
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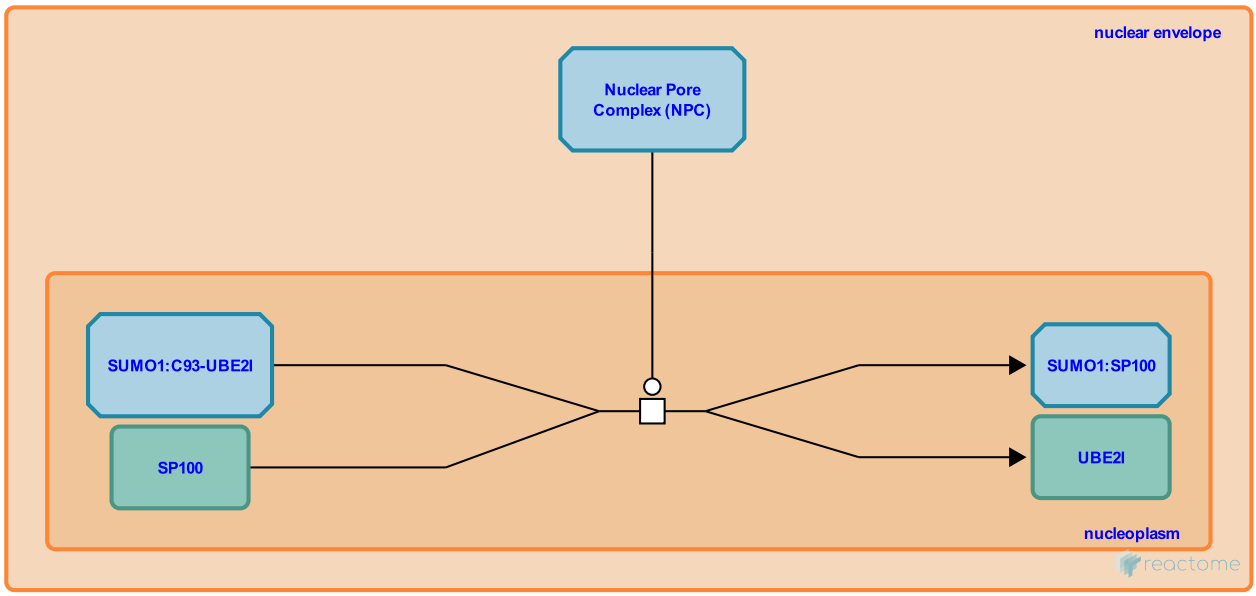
RANBP2 SUMOylates SP100 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-3000399

Type: transition

Compartments: nucleoplasm, nuclear envelope



RANBP2 SUMOylates SP100 with SUMO1 at lysine-297 (Pichler et al. 2002, Tatham et al. 2005). RANBP2 has a binding site for SUMO1 and a binding site for UBE2I (UBC9) which may recruit the SUMO1:UBE2I (SUMO1:UBC9) complex (Tatham et al. 2005). RANBP2 is located on the cytoplasmic filaments of the nuclear pore so that SUMOylation may occur during nuclear import of SP100 (Pichler et al. 2002)

Literature references

Tatham, MH., Kim, S., Jaffray, E., Song, J., Chen, Y., Hay, RT. (2005). Unique binding interactions among Ubc9, SUMO and RanBP2 reveal a mechanism for SUMO paralog selection. *Nat. Struct. Mol. Biol., 12*, 67-74. ↗

Pichler, A., Gast, A., Seeler, JS., Dejean, A., Melchior, F. (2002). The nucleoporin RanBP2 has SUMO1 E3 ligase activity. *Cell, 108*, 109-20. ↗

Knipscheer, P., Flotho, A., Klug, H., Olsen, JV., van Dijk, WJ., Fish, A. et al. (2008). Ubc9 sumoylation regulates SUMO target discrimination. *Mol. Cell, 31*, 371-82. ↗

Editions

2013-01-24	Authored, Edited	May, B.
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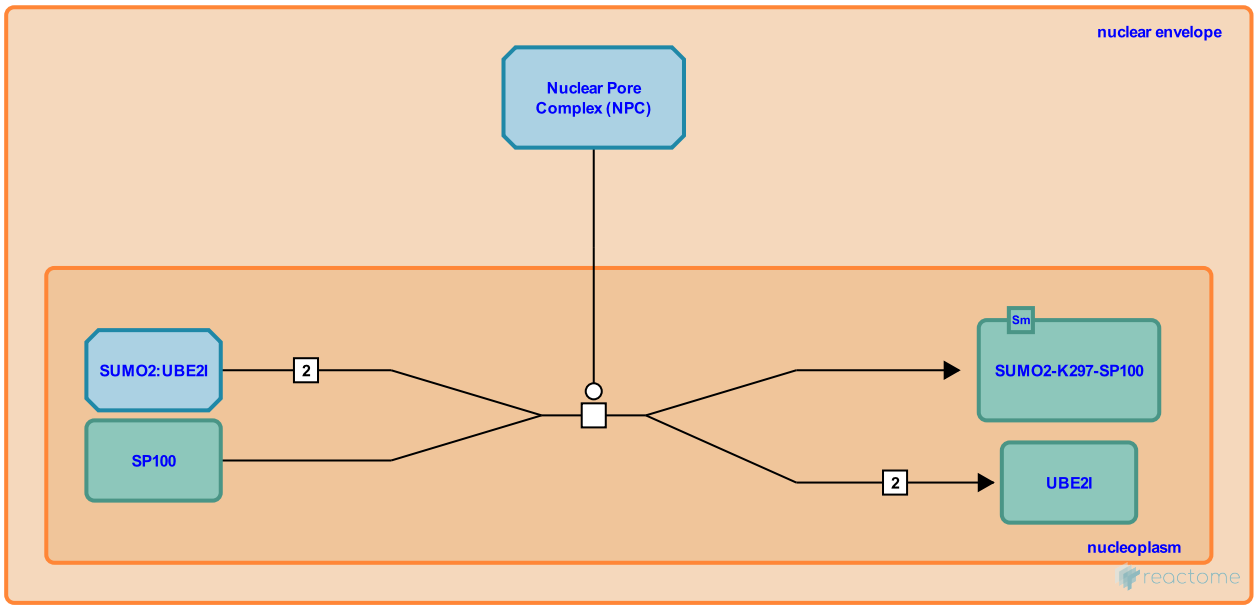
RANBP2 SUMOylates SP100 with SUMO2 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-3000348

Type: transition

Compartments: nucleoplasm, nuclear envelope



RANBP2 of the nuclear pore complex SUMOylates SP100 with SUMO2 at lysine-297 (Tatham et al. 2005, Hendriks et al. 2014). RANBP2 binds UBE2I (UBC9) to facilitate the transfer of SUMO2 from SUMO2:UBE2I to SP100 (Tatham et al. 2005).

Literature references

Tatham, MH., Kim, S., Jaffray, E., Song, J., Chen, Y., Hay, RT. (2005). Unique binding interactions among Ubc9, SUMO and RanBP2 reveal a mechanism for SUMO paralog selection. *Nat. Struct. Mol. Biol., 12*, 67-74. ↗

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36. ↗

Editions

2013-01-24	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

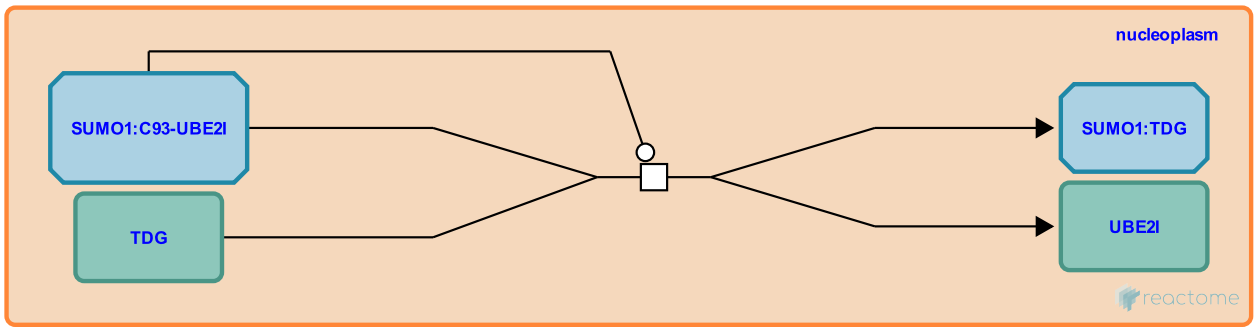
SUMOylation of TDG with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551648

Type: transition

Compartments: nucleoplasm



TDG is SUMOylated at lysine-330 with SUMO1 by UBE2I (Hardeland et al. 2002, Baba et al. 2005, Steinacher et al. 2005, Knipscheer et al. 2008, Smet-Nocca et al. 2011). Conjugation of SUMO1 to TDG induces dissociation of TDG from its product, an abasic site, and increases turnover of TDG with G:U substrate but abolishes activity with G:T substrate (Hardeland et al. 2002).

Literature references

Hardeland, U., Steinacher, R., Jiricny, J., Schär, P. (2002). Modification of the human thymine-DNA glycosylase by ubiquitin-like proteins facilitates enzymatic turnover. *EMBO J., 21*, 1456-64. ↗

Steinacher, R., Schär, P. (2005). Functionality of human thymine DNA glycosylase requires SUMO-regulated changes in protein conformation. *Curr. Biol., 15*, 616-23. ↗

Knipscheer, P., Flotho, A., Klug, H., Olsen, JV., van Dijk, WJ., Fish, A. et al. (2008). Ubc9 sumoylation regulates SUMO target discrimination. *Mol. Cell, 31*, 371-82. ↗

Baba, D., Maita, N., Jee, JG., Uchimura, Y., Saitoh, H., Sugasawa, K. et al. (2005). Crystal structure of thymine DNA glycosylase conjugated to SUMO-1. *Nature, 435*, 979-82. ↗

Smet-Nocca, C., Wieruszeski, JM., Léger, H., Eilebrecht, S., Benecke, A. (2011). SUMO-1 regulates the conformational dynamics of thymine-DNA Glycosylase regulatory domain and competes with its DNA binding activity. *BMC Biochem., 12*, 4. ↗

Editions

2013-09-13	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

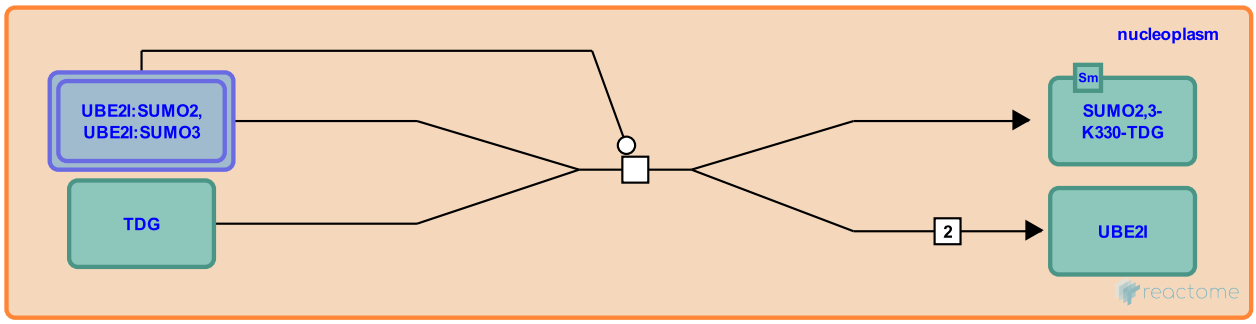
SUMOylation of TDG with SUMO2,3 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4551738

Type: transition

Compartments: nucleoplasm



TDG is SUMOylated at lysine-330 with SUMO2,3 by UBE2I and perhaps another E3 ligase (Hardeland et al. 2002, Baba et al. 2006, Hendriks et al. 2014, Tammsalu et al. 2014). SUMOylation increases turnover of TDG with G:U substrate and abolishes activity with G:T substrate (Hardeland et al. 2002).

Literature references

Hardeland, U., Steinacher, R., Jiricny, J., Schär, P. (2002). Modification of the human thymine-DNA glycosylase by ubiquitin-like proteins facilitates enzymatic turnover. *EMBO J., 21*, 1456-64. ↗

Hendriks, IA., D'Souza, RC., Yang, B., Verlaan-de Vries, M., Mann, M., Vertegaal, AC. (2014). Uncovering global SUMOylation signaling networks in a site-specific manner. *Nat. Struct. Mol. Biol., 21*, 927-36. ↗

Tammsalu, T., Matic, I., Jaffray, EG., Ibrahim, AF., Tatham, MH., Hay, RT. (2014). Proteome-wide identification of SUMO2 modification sites. *Sci Signal, 7*, rs2. ↗

Baba, D., Maita, N., Jee, JG., Uchimura, Y., Saitoh, H., Sugasawa, K. et al. (2006). Crystal structure of SUMO-3-modified thymine-DNA glycosylase. *J. Mol. Biol., 359*, 137-47. ↗

Editions

2013-09-13	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

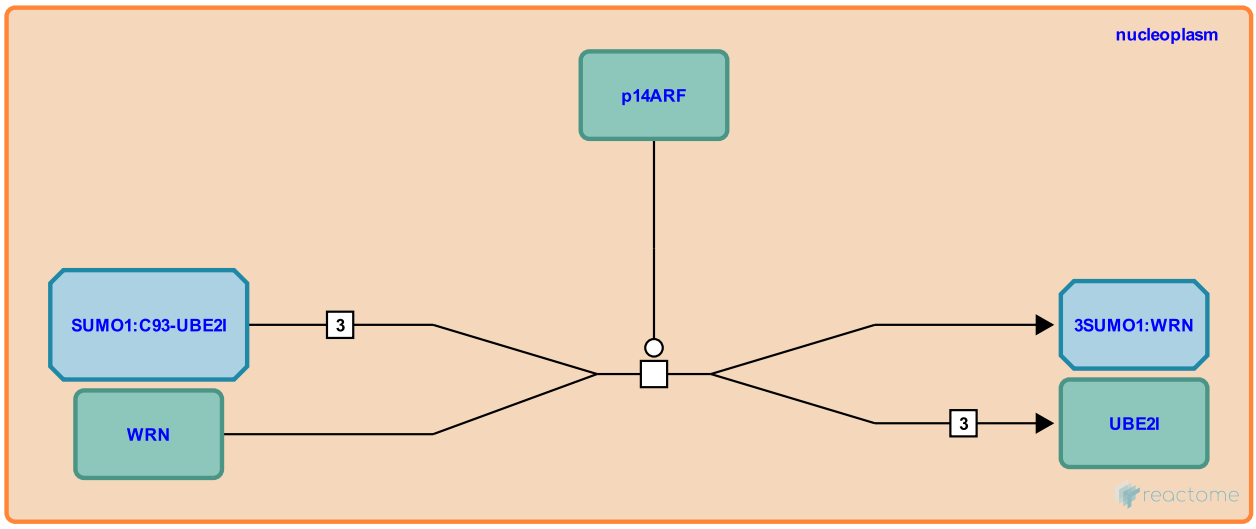
CDKN2A (p14-ARF) SUMOylates WRN with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4568846

Type: transition

Compartments: nucleoplasm



CDKN2A (p14-ARF) SUMOylates WRN at lysine-356, lysine-496, and lysine-898 with SUMO1 (Woods et al. 2004). SUMOylation of WRN causes it to be released from the nucleolus.

Literature references

Woods, YL., Xirodimas, DP., Prescott, AR., Sparks, A., Lane, DP., Saville, MK. (2004). p14 Arf promotes small ubiquitin-like modifier conjugation of Werners helicase. *J. Biol. Chem., 279*, 50157-66. ↗

Editions

2013-09-14	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

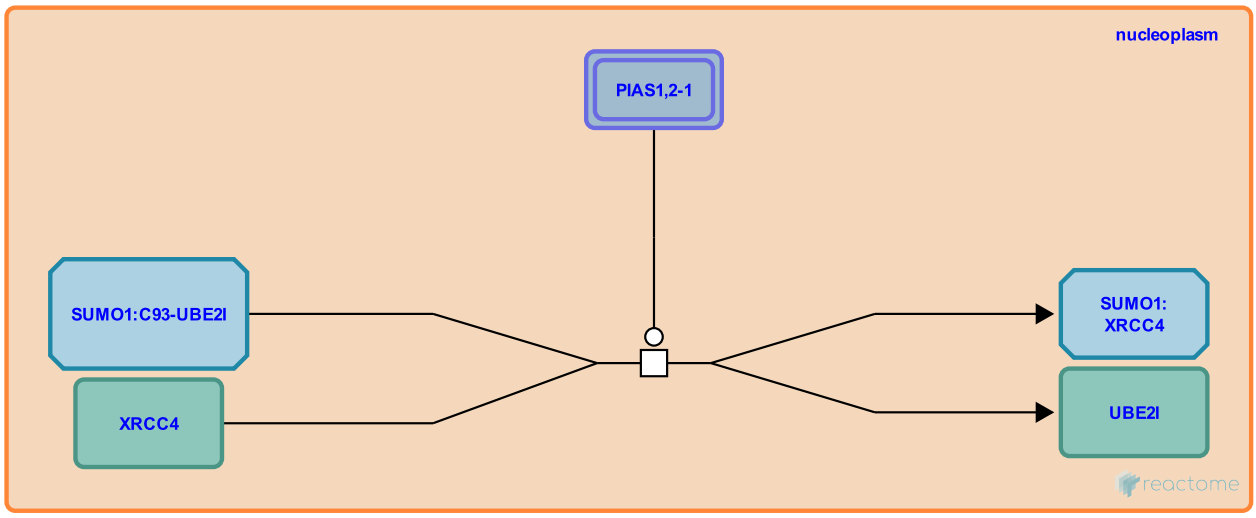
PIAS1,2-1 SUMOylates XRCC4 with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4568848

Type: transition

Compartments: nucleoplasm



PIAS1,2-1 SUMOylate XRCC4 at lysine-210 with SUMO1 (Yurchenko et al. 2006). SUMOylation causes localization of XRCC4 to the nucleus. (An unSUMOylatable mutant of XRCC4 is localized to the cytosol.)

Literature references

Yurchenko, V., Xue, Z., Sadofsky, MJ. (2006). SUMO modification of human XRCC4 regulates its localization and function in DNA double-strand break repair. *Mol. Cell. Biol., 26*, 1786-94. ↗

Editions

2013-09-14	Authored, Edited	May, B.
2015-02-21	Reviewed	Ferrari, S.

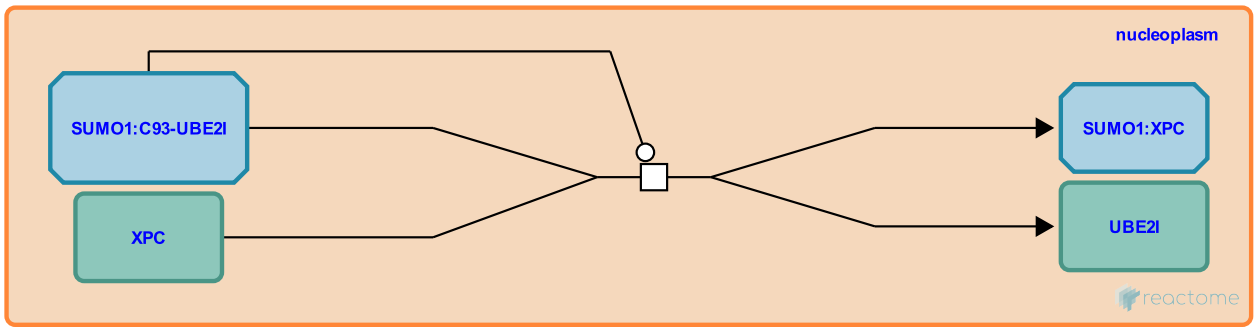
SUMOylation of XPC with SUMO1 ↗

Location: SUMOylation of DNA damage response and repair proteins

Stable identifier: R-HSA-4570528

Type: transition

Compartments: nucleoplasm



XPC is SUMOylated at lysine-655 with SUMO1 (Wang et al. 2005, 2007). SUMOylation occurs after UV irradiation and may target XPC for destruction (Wang et al. 2007).

Literature references

Wang, QE., Zhu, Q., Wani, G., El-Mahdy, MA., Li, J., Wani, AA. (2005). DNA repair factor XPC is modified by SUMO-1 and ubiquitin following UV irradiation. *Nucleic Acids Res., 33*, 4023-34. ↗

Wang, QE., Praetorius-Ibba, M., Zhu, Q., El-Mahdy, MA., Wani, G., Zhao, Q. et al. (2007). Ubiquitylation-independent degradation of Xeroderma pigmentosum group C protein is required for efficient nucleotide excision repair. *Nucleic Acids Res., 35*, 5338-50. ↗

Editions

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