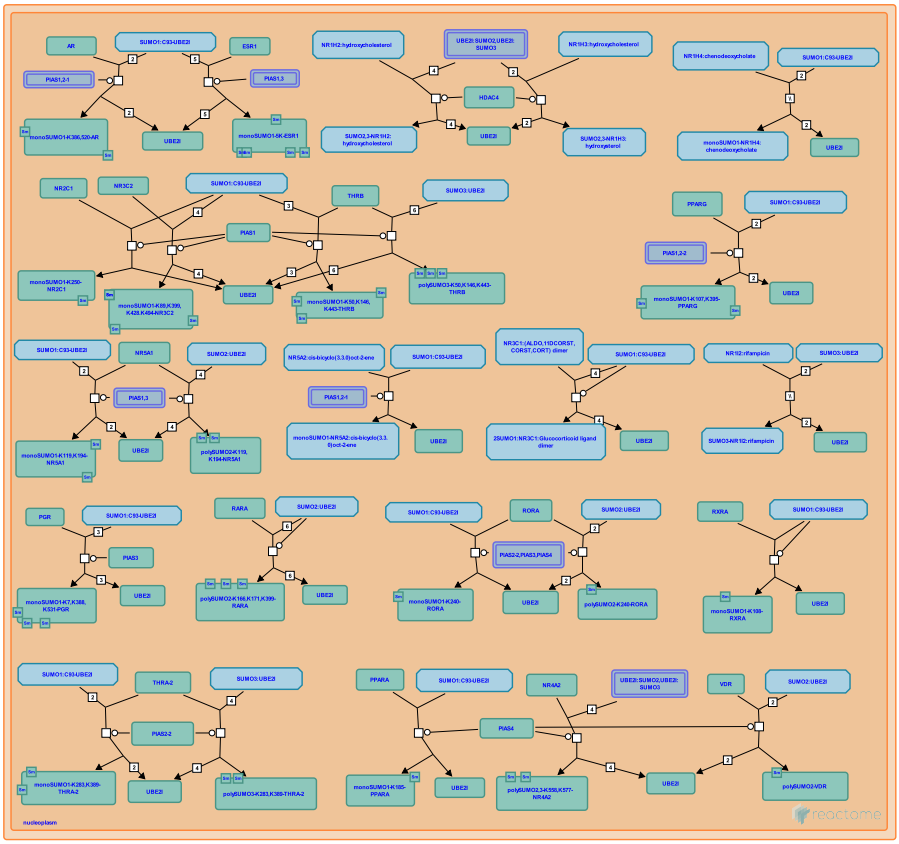
SUMOylation of intracellular receptors



May, B., Niskanen, E.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

27/04/2024

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

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. ↗

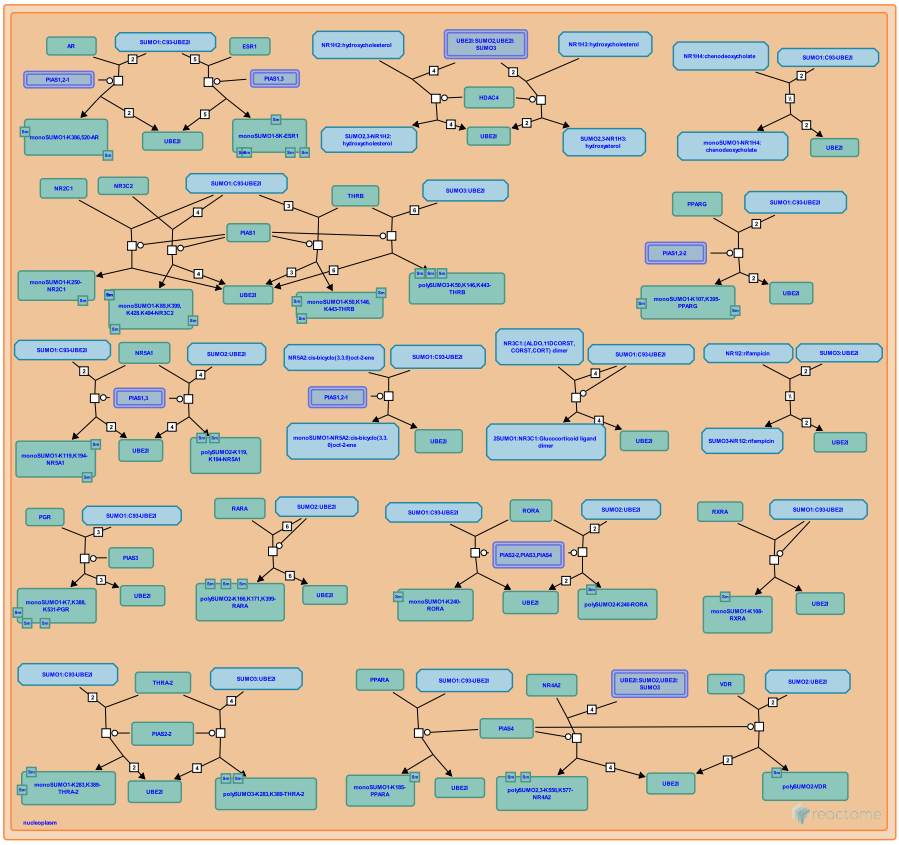
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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 intracellular receptors ↗

Stable identifier: R-HSA-4090294

Compartments: nucleoplasm



At least 17 nuclear receptors have been discovered to be SUMOylated (reviewed in Treuter and Venteclef 2011, Wadosky et al. 2012, Knutson and Lange 2013). In all but a few cases (notably AR and RORA) SUMOylation causes transcriptional repression. Repression by SUMOylation is believed to occur through several mechanisms: interference with DNA binding, recruitment of corepressors, retention of corepressors at non-target promoters (transrepression), re-localization of nuclear receptors within the nucleus, interference with dimerization of receptors, and interference (crosstalk) with other post-translational modifications. SUMOylation of receptors affects inflammation and disease processes (Anbalagan et al. 2012).

Literature references

Lange, CA., Knutson, TP. (2013). Dynamic regulation of steroid hormone receptor transcriptional activity by reversible SUMOylation. *Vitam. Horm., 93*, 227-61. ↗

Willis, MS., Wadosky, KM. (2012). The story so far: post-translational regulation of peroxisome proliferator-activated receptors by ubiquitination and SUMOylation. *Am. J. Physiol. Heart Circ. Physiol., 302*, H515-26. ↗

Venteclef, N., Treuter, E. (2011). Transcriptional control of metabolic and inflammatory pathways by nuclear receptor SUMOylation. *Biochim. Biophys. Acta, 1812*, 909-18. ↗

Rowan, BG., Murphy, L., Anbalagan, M., Huderson, B. (2012). Post-translational modifications of nuclear receptors and human disease. *Nucl Recept Signal, 10*, e001. ↗

Editions

2013-08-07	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

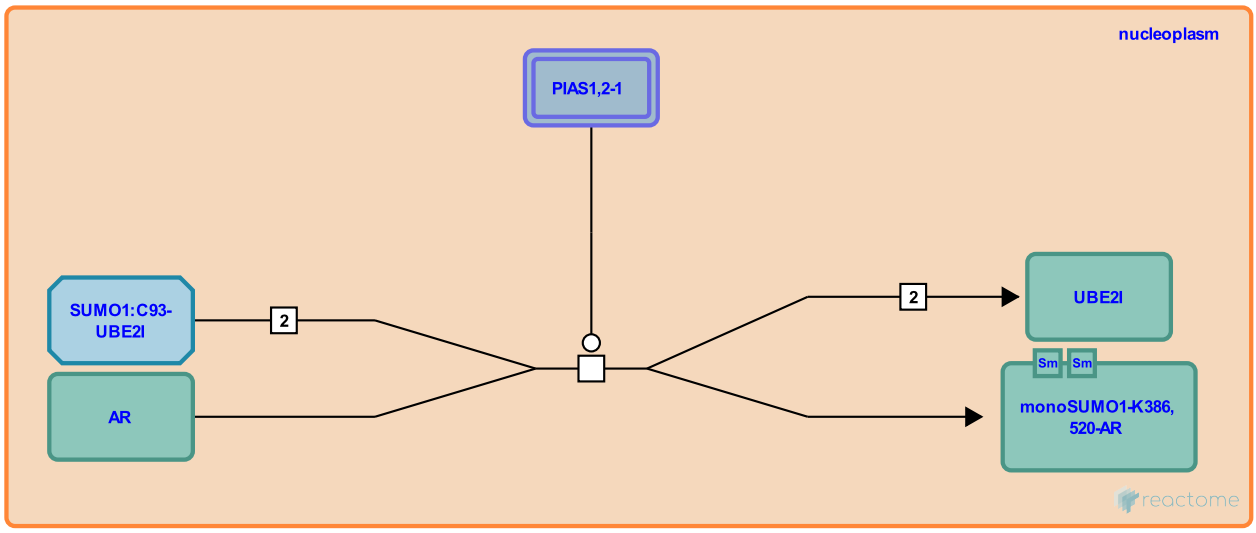
PIAS1,2-1 SUMOylates AR with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4090390

Type: transition

Compartments: nucleoplasm



PIAS1,2-1 SUMOylate AR at lysine-386 and lysine-520 with SUMO1 (Poukka et al. 2000, Kotaja et al. 2002, Nishida and Yasuda 2002). SUMOylation reduces transcription activation by AR.

Literature references

Nishida, T., Yasuda, H. (2002). PIAS1 and PIASxalpha function as SUMO-E3 ligases toward androgen receptor and repress androgen receptor-dependent transcription. *J. Biol. Chem., 277*, 41311-7. ↗

Karvonen, U., Palvimo, JJ., Janne, OA., Poukka, H. (2000). Covalent modification of the androgen receptor by small ubiquitin-like modifier 1 (SUMO-1). *Proc. Natl. Acad. Sci. U.S.A., 97*, 14145-50. ↗

Kotaja, N., Palvimo, JJ., Jänne, OA., Karvonen, U. (2002). PIAS proteins modulate transcription factors by functioning as SUMO-1 ligases. *Mol. Cell. Biol., 22*, 5222-34. ↗

Editions

2013-08-07	Authored, Edited	May, B.
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2018-08-08	Reviewed	Niskanen, E.

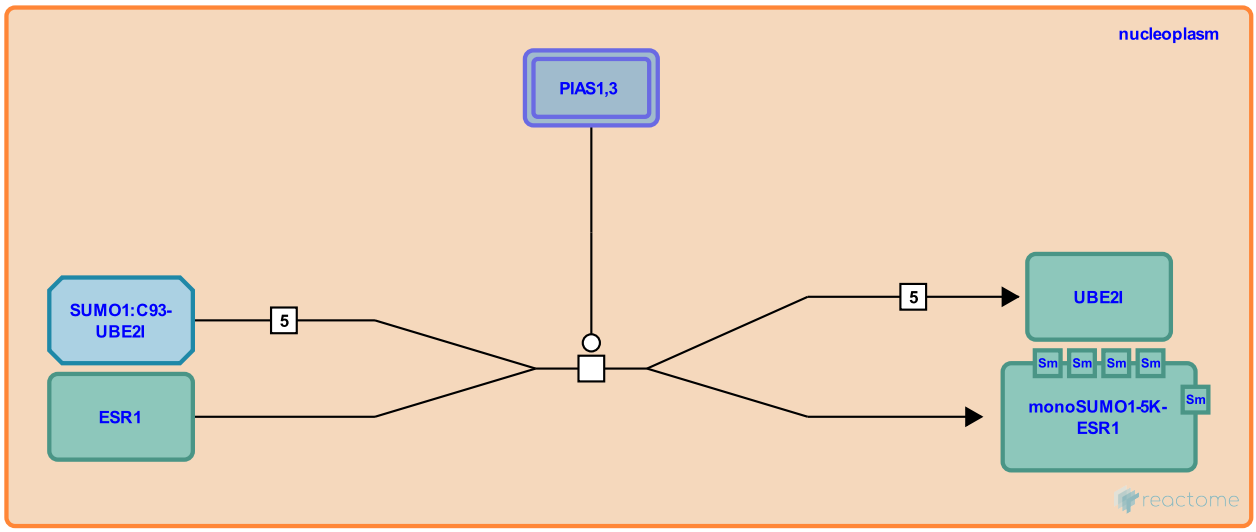
PIAS1,3 SUMOylate ESR1 with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4090408

Type: transition

Compartments: nucleoplasm



PIAS1,3 SUMOylate ESR1 (Estrogen Receptor alpha, ER-alpha, ER, NR3A1) at lysines-266,268,299,302,303 with SUMO1 (Sentis et al. 2005). SUMOylation reduces transcription activation by ESR1.

Literature references

Le Romancer, M., Rostan, MC., Corbo, L., Bianchin, C., Sentis, S. (2005). Sumoylation of the estrogen receptor alpha hinge region regulates its transcriptional activity. *Mol. Endocrinol., 19*, 2671-84. ↗

Editions

2013-08-07	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

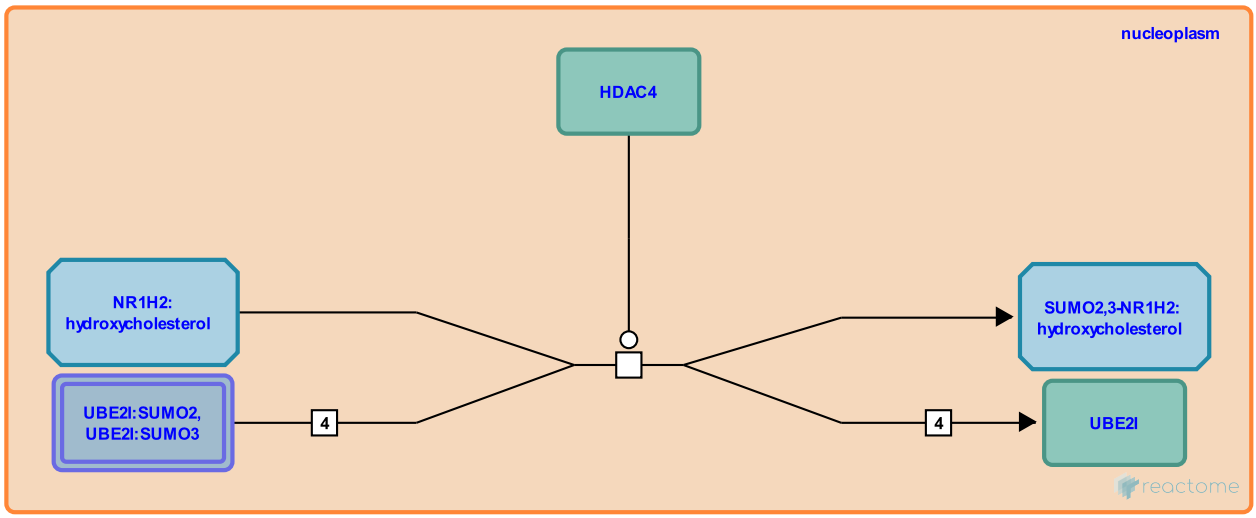
HDAC4 SUMOylates NR1H2 (LXRbeta) with SUMO2,3

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4720432

Type: transition

Compartments: nucleoplasm



HDAC4 SUMOylates NR1H2 (LXR-beta) with SUMO2,3 at lysine-409 and lysine-447 (lysine-410 and lysine-448 of the isoform used by Ghisletti et al. 2007) (Venteclef et al. 2010). SUMOylation is enhanced when NR1H2 binds specific oxysterols and causes NR1H2 to recruit the NCOR repressor and transrepress promoters such as iNOS.

Literature references

Jakobsson, T., Parini, P., Damdimopoulos, A., Jänne, OA., Gustafsson, JA., Nilsson, LM. et al. (2010). GPS2-dependent corepressor/SUMO pathways govern anti-inflammatory actions of LRH-1 and LXRbeta in the hepatic acute phase response. *Genes Dev., 24*, 381-95.

Ghisletti, S., Pascual, G., Huang, W., Lin, ME., Willson, TM., Ogawa, S. et al. (2007). Parallel SUMOylation-dependent pathways mediate gene- and signal-specific transrepression by LXRs and PPARgamma. *Mol. Cell, 25*, 57-70.

Editions

2013-10-19	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

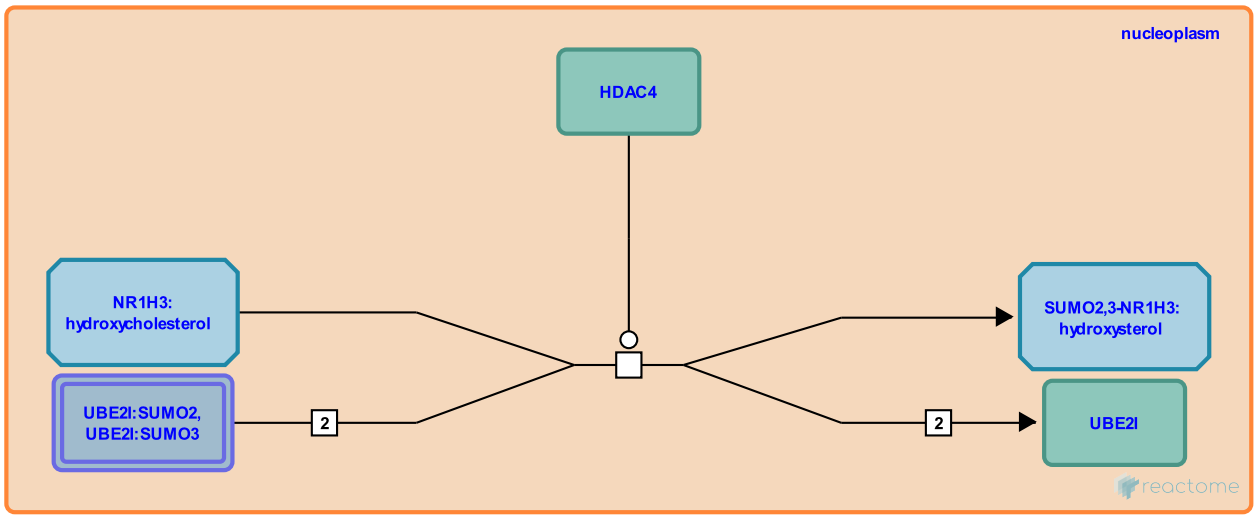
HDAC4 SUMOylates NR1H3 (LXRalpha) with SUMO2,3 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4720446

Type: transition

Compartments: nucleoplasm



HDAC4 SUMOylates NR1H3 with SUMO2,3 (Ghisletti et al. 2007). SUMOylation is enhanced when NR1H3 binds specific oxysterols. SUMOylation causes NR1H3 to recruit the NCOR repressor and act as a transrepressor at promoters such as iNOS.

Literature references

Ghisletti, S., Pascual, G., Huang, W., Lin, ME., Willson, TM., Ogawa, S. et al. (2007). Parallel SUMOylation-dependent pathways mediate gene- and signal-specific transrepression by LXRs and PPARgamma. *Mol. Cell, 25*, 57-70. ↗

Editions

2013-10-19	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

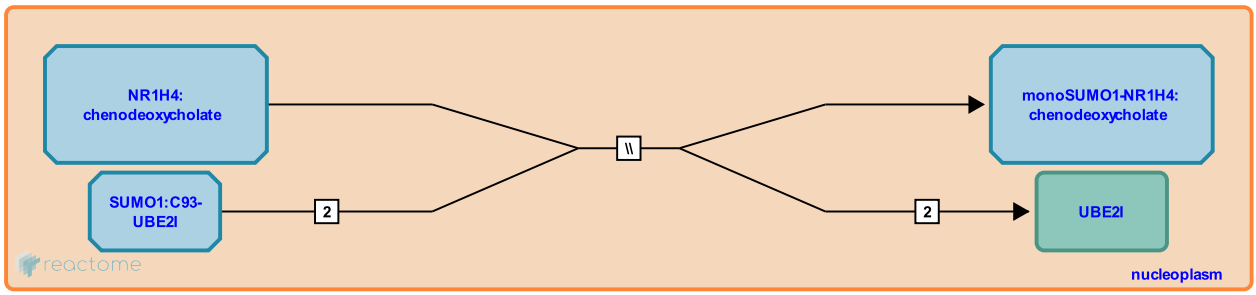
SUMOylation of NR1H4 with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4755419

Type: omitted

Compartments: nucleoplasm



NR1H4 (FXR, Bile Acid Receptor) is SUMOylated with SUMO1 at lysine-132 and lysine-289 (lysine-122 and lysine-275 of isoform 4, UniProt Q96RI1-2) (Vavassori et al. 2009, Balasubramaniyan et al. 2013). SUMOylation appears to be enhanced when NR1H4 binds ligands (Vavassori et al. 2009). SUMOylated NR1H4 transrepresses genes involved in inflammation (Vavassori et al. 2009) and inhibits ligand-induced activation of FXR targets: bile salt export pump (BSEP) and small heterodimer partner (SHP) (Balasubramaniya et al. 2013).

Literature references

Balasubramaniyan, N., Luo, Y., Suchy, FJ., Sun, AQ. (2013). SUMOylation of the farnesoid X receptor (FXR) regulates the expression of FXR target genes. *J. Biol. Chem., 288*, 13850-62. ↗

Vavassori, P., Fiorucci, S., Mencarelli, A., Renga, B., Distrutti, E. (2009). The bile acid receptor FXR is a modulator of intestinal innate immunity. *J. Immunol., 183*, 6251-61. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-06-11	Reviewed	Niskanen, E.

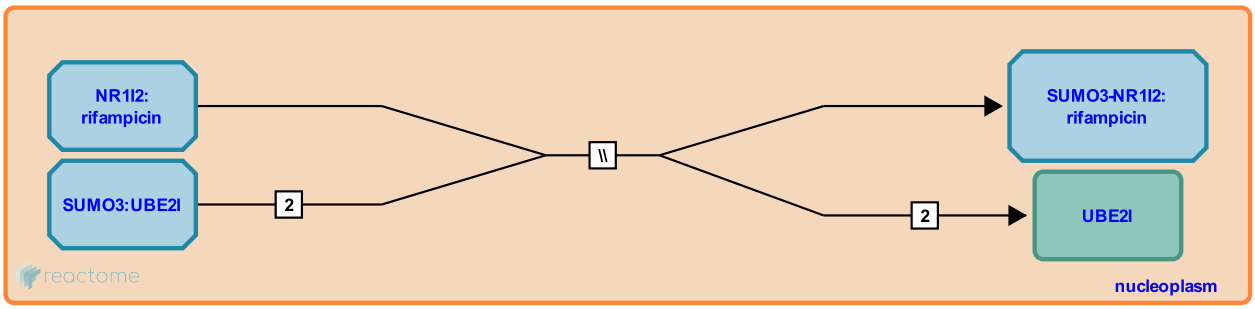
SUMOylation of NR1I2 with SUMO3 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4755524

Type: omitted

Compartments: nucleoplasm



NR1I2 (Pregnane X Receptor, PXR) is SUMOylated with SUMO3 (Hu et al. 2010). SUMOylation is stimulated when NR1I2 binds ligand (rifampicin) and causes NR1I2 to transrepress genes encoding inflammatory cytokines.

Literature references

Hu, G., Staudinger, JL., Xu, C. (2010). Pregnane X receptor is SUMOylated to repress the inflammatory response. *J. Pharmacol. Exp. Ther., 335*, 342-50. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

PIAS1 SUMOylates NR2C1 (TR2) ↗

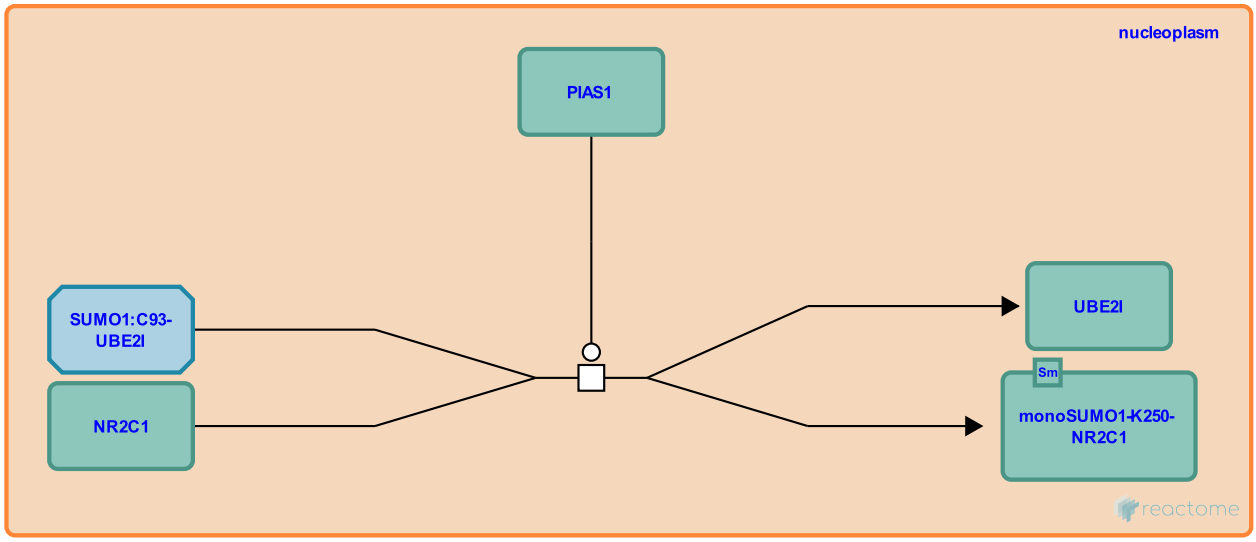
Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4717521

Type: transition

Compartments: nucleoplasm

Inferred from: Pias1 Sumoylates Nr2c1 (Tr2) (Mus musculus)



As inferred from mouse homologs, PIAS1 SUMOylates NR2C1 (TR2) with SUMO1 at lysine-250. UnSUMOylated NR2C1 is localized to PML bodies and activates expression of OCT4. SUMOylated NR2C1 delocalizes from PML bodies and acts as a repressor of transcription.

Editions

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2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

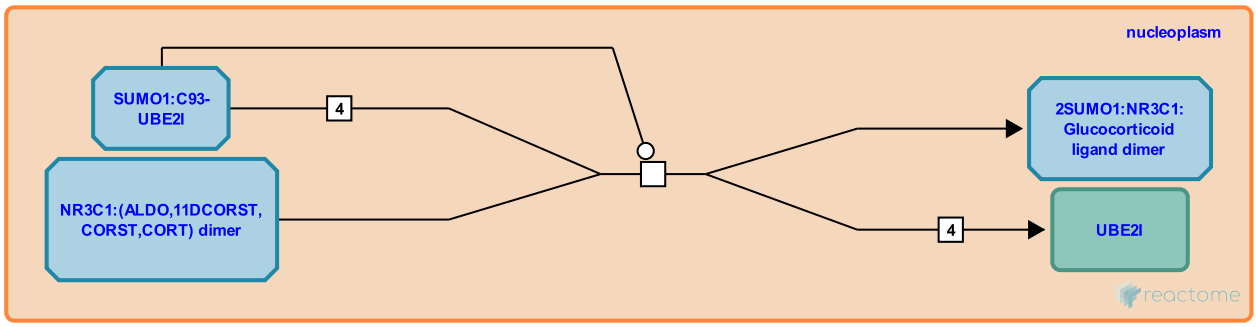
SUMOylation of NR3C1 (GR) with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4341025

Type: transition

Compartments: nucleoplasm



NR3C1 (Glucocorticoid receptor, GR) is SUMOylated at lysine-277 and lysine-293 with SUMO1 (Tian et al. 2002, Impens et al. 2014). SUMOylation is enhanced when NR3C1 binds ligand (dexamethasone). SUMOylation reduces transcription activation by NR3C1.

Literature references

Palvimo, JJ., Jänne, OA., Tian, S., Poukka, H. (2002). Small ubiquitin-related modifier-1 (SUMO-1) modification of the glucocorticoid receptor. *Biochem. J., 367*, 907-11. ↗

Impens, F., Cossart, P., Radoshevich, L., 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. ↗

Editions

2013-08-14	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

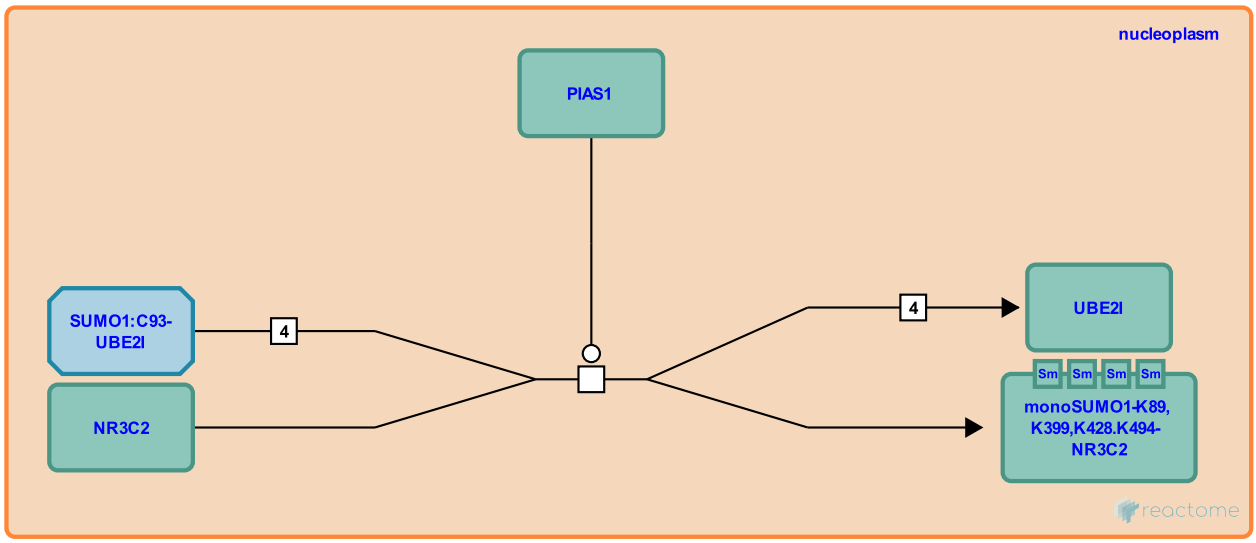
PIAS1 SUMOylates NR3C2 (Mineralcorticoid Receptor) with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4341016

Type: transition

Compartments: nucleoplasm



PIAS1 SUMOylates NR3C2 (Mineralcorticoid receptor, MR) at lysine-89, lysine-399, lysine-428, and lysine 494 with SUMO1 (Tallec et al. 2003, Tirard et al. 2007, Yokota et al. 2007). SUMOylation represses the transcription activation activity of NR3C2.

Literature references

Kobayashi, S., Shibata, H., Itoh, H., Suda, N., Murai-Takeda, A., Kurihara, I. et al. (2007). Coactivation of the N-terminal transactivation of mineralocorticoid receptor by Ubc9. *J. Biol. Chem., 282*, 1998-2010. ↗

Tirard, M., Hutzler, P., Melchior, F., Michaelidis, TM., Almeida, OF. (2007). Sumoylation and proteasomal activity determine the transactivation properties of the mineralocorticoid receptor. *Mol. Cell. Endocrinol., 268*, 20-9. ↗

Dejean, A., Zennaro, MC., Lecomte, MC., Viengchareun, S., Kirsh, O., Lombès, M. et al. (2003). Protein inhibitor of activated signal transducer and activator of transcription 1 interacts with the N-terminal domain of mineralocorticoid receptor and represses its transcriptional activity: implication of small ubiquitin-related modifier 1 modification. *Mol. Endocrinol., 17*, 2529-42. ↗

Editions

2013-08-14	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

PIAS4 SUMOylates NR4A2 with SUMO2,3 ↗

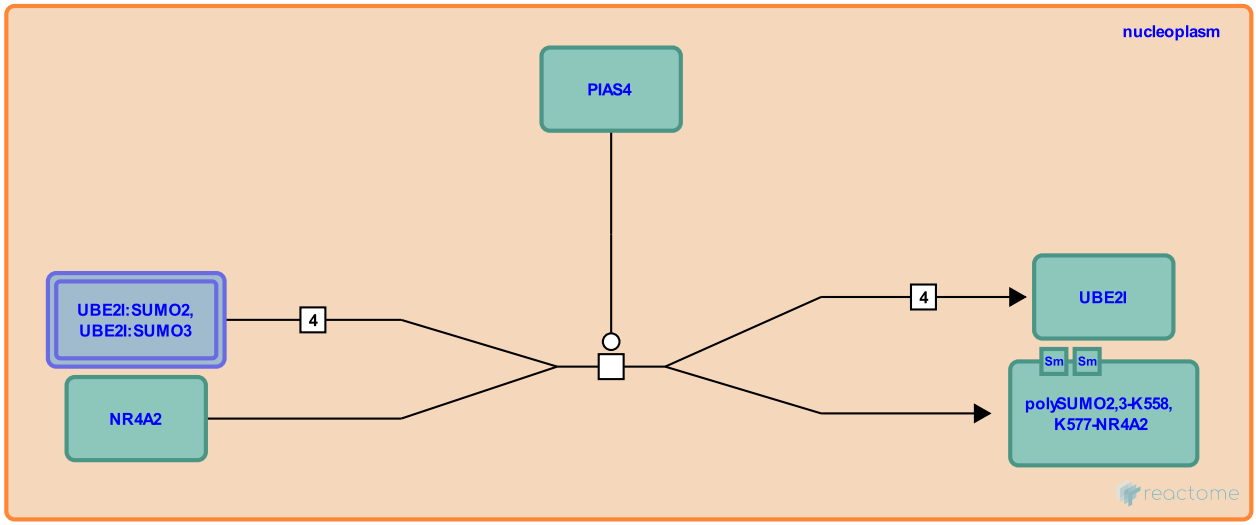
Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4755526

Type: transition

Compartments: nucleoplasm

Inferred from: Pias4 Sumoylates Nr4a2 with Sumo2,3 (Mus musculus)



As inferred from mouse homologs, PIAS4 SUMOylates NR4A2 (NUR1) with SUMO2,3 at lysine-558 and lysine-577. SUMOylation causes NR4A2 to interact as a monomer with the Co-REST complex and transrepress promoters of genes involved in inflammation.

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

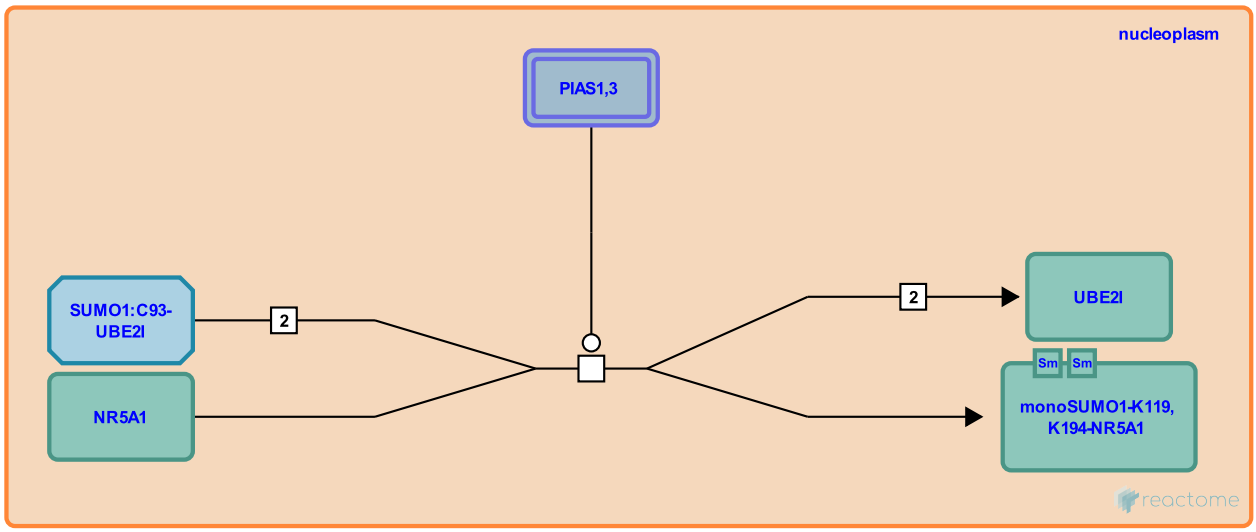
PIAS1,3 SUMOylates NR5A1 with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4546386

Type: transition

Compartments: nucleoplasm



PIAS1,3 SUMOylate NR5A1 (Steroidogenic factor 1, SF1, SF-1) at lysine-119 and lysine-194 with SUMO1 (Chen et al. 2004, Komatsu et al. 2004, Suda et al. 2011). SUMOylation reduces the synergistic activation of SOX9 by NR5A1.

Literature references

Nakagawa, K., Shibata, H., Murai-Takeda, A., Kurihara, I., Yokota, K., Ikeda, Y. et al. (2011). Coactivation of SF-1-mediated transcription of steroidogenic enzymes by Ubc9 and PIAS1. *Endocrinology, 152*, 2266-77. ↗

Shirakawa, M., Baba, D., Kikuchi, A., Mukai, T., Komatsu, T., Mizusaki, H. et al. (2004). Small ubiquitin-like modifier 1 (SUMO-1) modification of the synergy control motif of Ad4 binding protein/steroidogenic factor 1 (Ad4BP/SF-1) regulates synergistic transcription between Ad4BP/SF-1 and Sox9. *Mol. Endocrinol., 18*, 2451-62. ↗

Hsu, NC., Lee, WC., Chung, BC., Huang, F., Chen, WY. (2004). SUMO modification of repression domains modulates function of nuclear receptor 5A1 (steroidogenic factor-1). *J. Biol. Chem., 279*, 38730-5. ↗

Editions

2013-08-19	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

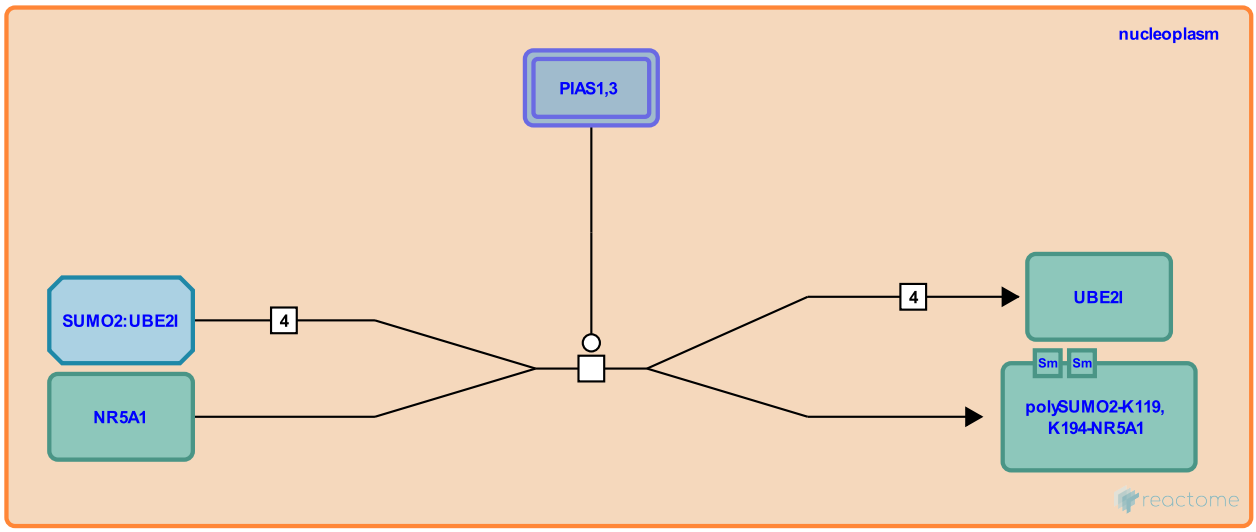
PIAS1,3 SUMOylates NR5A1 with SUMO2 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4546385

Type: transition

Compartments: nucleoplasm



PIAS1,3 SUMOylate NR5A1 (Steroidogenic factor 1, SF1, SF-1) at lysine-119 and lysine-194 with SUMO2 (Chen et al. 2004, Komatsu et al. 2004, Suda et al. 2011). SUMOylation reduces synergistic activation of SOX9 by NR5A1.

Literature references

Nakagawa, K., Shibata, H., Murai-Takeda, A., Kurihara, I., Yokota, K., Ikeda, Y. et al. (2011). Coactivation of SF-1-mediated transcription of steroidogenic enzymes by Ubc9 and PIAS1. *Endocrinology, 152*, 2266-77. ↗

Shirakawa, M., Baba, D., Kikuchi, A., Mukai, T., Komatsu, T., Mizusaki, H. et al. (2004). Small ubiquitin-like modifier 1 (SUMO-1) modification of the synergy control motif of Ad4 binding protein/steroidogenic factor 1 (Ad4BP/SF-1) regulates synergistic transcription between Ad4BP/SF-1 and Sox9. *Mol. Endocrinol., 18*, 2451-62. ↗

Hsu, NC., Lee, WC., Chung, BC., Huang, F., Chen, WY. (2004). SUMO modification of repression domains modulates function of nuclear receptor 5A1 (steroidogenic factor-1). *J. Biol. Chem., 279*, 38730-5. ↗

Editions

2013-08-19	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

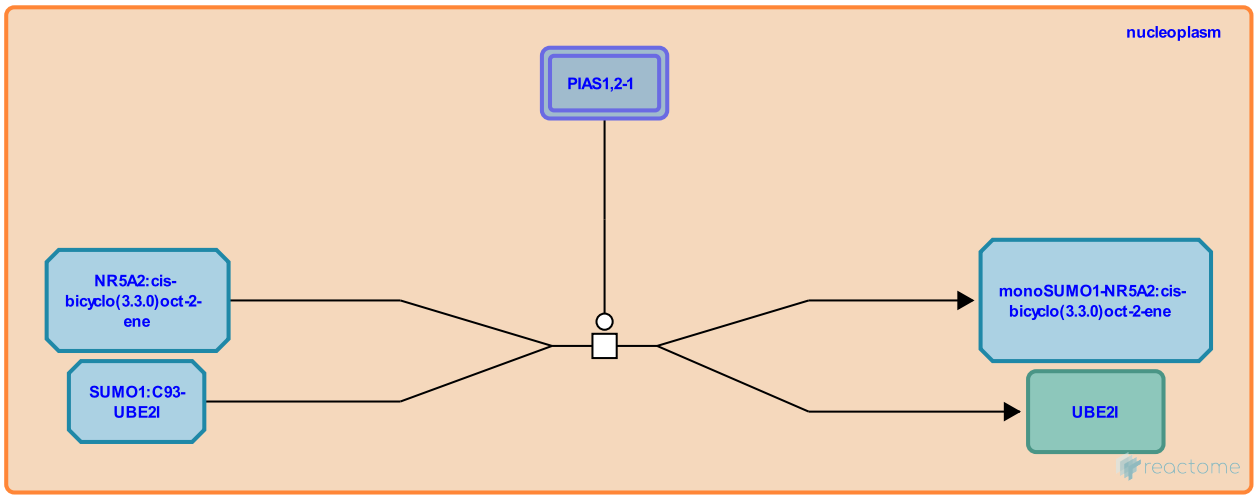
PIAS1,2-1 SUMOylate NR5A2 with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4755494

Type: transition

Compartments: nucleoplasm



PIAS1,2-1 SUMOylate NR5A2 (LRH-1) with SUMO1 at lysine-270 (lysine-224 in the shorter isoform) (Chalkiadaki and Talianidis 2005, Ogawa et al. 2009, Venteclef et al. 2010). SUMOylation is enhanced when NR5A2 is bound to ligand. SUMOylated NR5A2 acts as a transrepressor of genes involved in inflammation such as haptoglobin, SAA, and CRP.

Literature references

Hiraoka, Y., Komatsu, T., Ogawa, H., Morohashi, K. (2009). Transcriptional Suppression by Transient Recruitment of ARIP4 to Sumoylated nuclear receptor Ad4BP/SF-1. *Mol. Biol. Cell, 20*, 4235-45. ↗

Jakobsson, T., Parini, P., Damdimopoulos, A., Jänne, OA., Gustafsson, JA., Nilsson, LM. et al. (2010). GPS2-dependent corepressor/SUMO pathways govern anti-inflammatory actions of LRH-1 and LXRbeta in the hepatic acute phase response. *Genes Dev., 24*, 381-95. ↗

Talianidis, I., Chalkiadaki, A. (2005). SUMO-dependent compartmentalization in promyelocytic leukemia protein nuclear bodies prevents the access of LRH-1 to chromatin. *Mol. Cell. Biol., 25*, 5095-105. ↗

Editions

2013-10-20	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

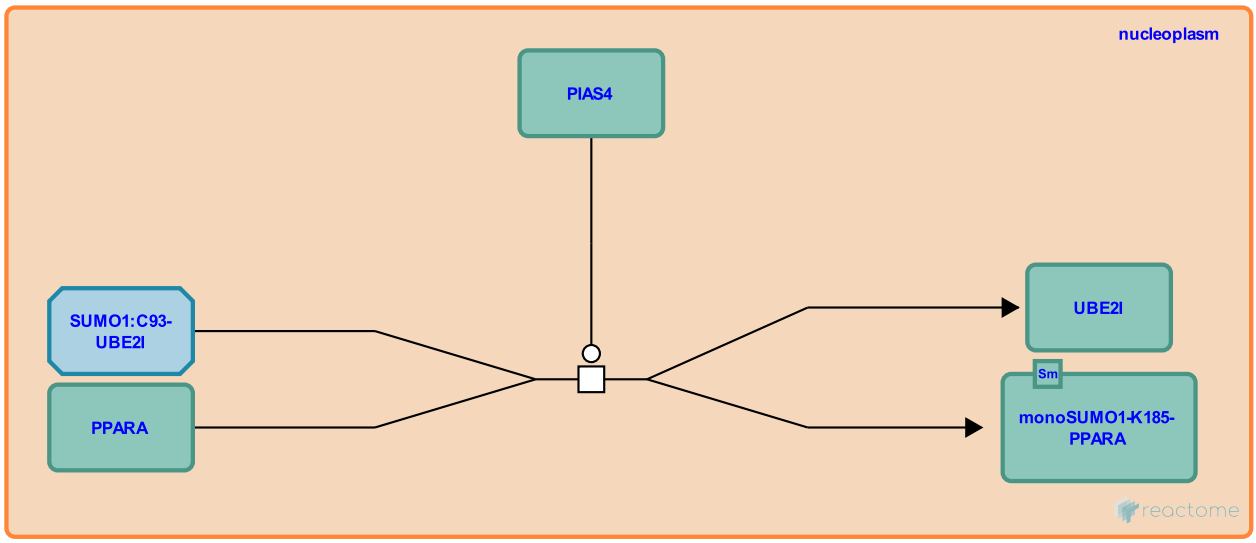
PIAS4 SUMOylates PPARA with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4341070

Type: transition

Compartments: nucleoplasm



PIAS4 SUMOylates PPARA at lysine-185 with SUMO1 (Pourcet et al. 2010). SUMOylation decreases the transactivation activity of PPARA. SUMOylation is decreased in the presence of ligand of PPARA.

Literature references

Derudas, B., Glineur, C., Staels, B., Pineda-Torra, I., Pourcet, B. (2010). SUMOylation of human peroxisome proliferator-activated receptor alpha inhibits its trans-activity through the recruitment of the nuclear corepressor NCoR. *J. Biol. Chem., 285*, 5983-92. ↗

Editions

2013-08-14	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

PIAS1,2-2 SUMOylate PPARG with SUMO1 ↗

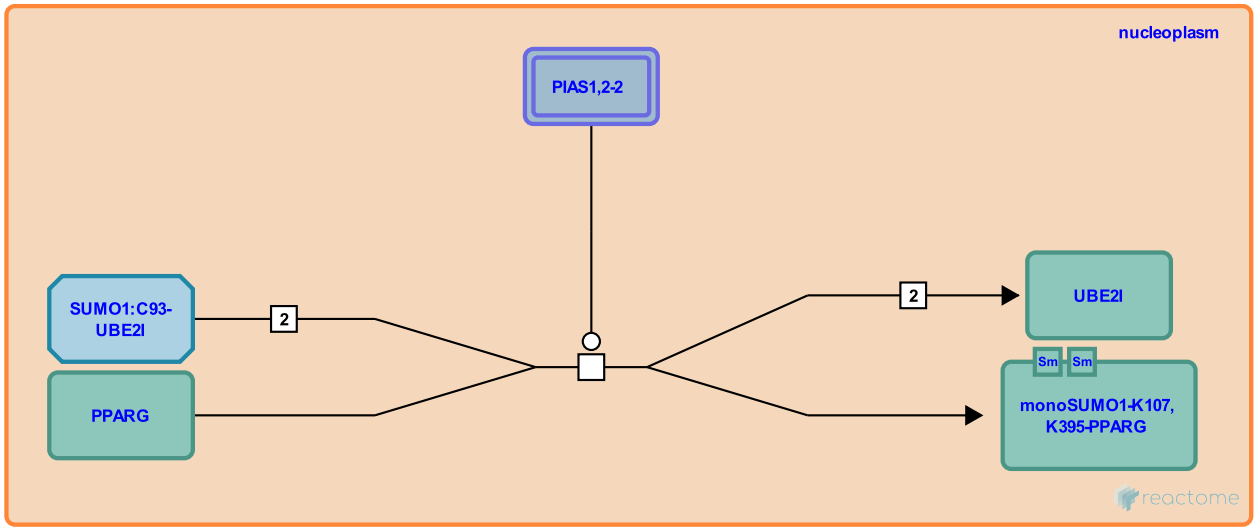
Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4717461

Type: transition

Compartments: nucleoplasm

Inferred from: Pias1,2-2 Sumoylate Pparg with Sumo1 (Mus musculus)



As inferred from mouse homologs, PIAS1,2-2 SUMOylate PPARG with SUMO1 at lysine-107 and lysine-395 (lysine-77 and lysine-365 of the shorter variant 1). SUMOylation decreases the transcriptional activation activity of PPARG. SUMOylation at lysine-395 is ligand-dependent and causes PPARG to recruit corepressors such as NCOR and HDAC3.

Editions

2013-10-11	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

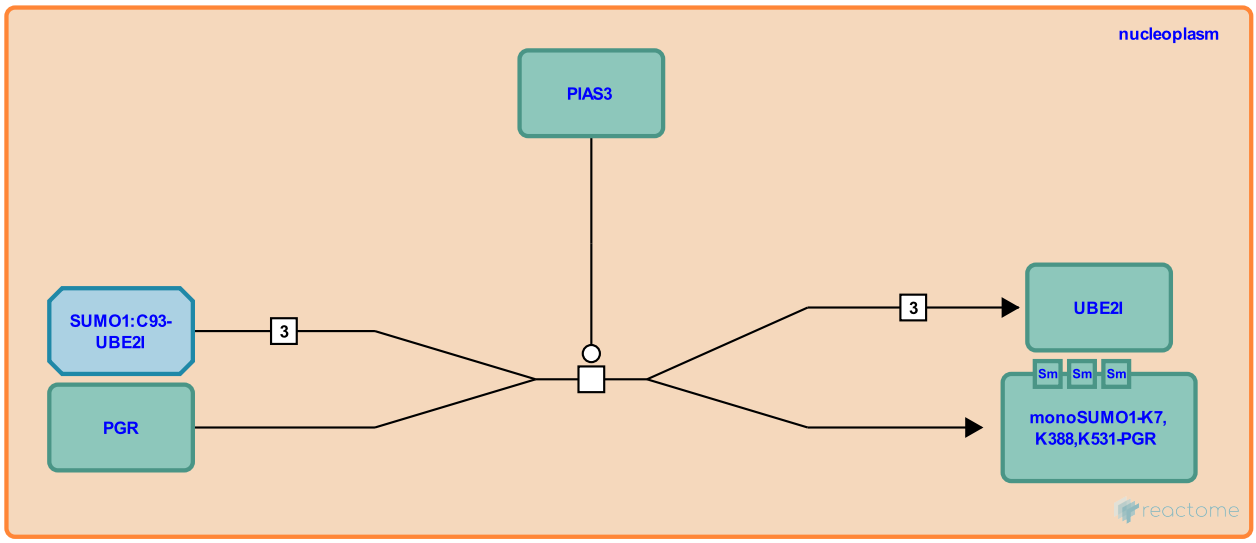
PIAS3 SUMOylates PGR with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4341073

Type: transition

Compartments: nucleoplasm



PIAS3 SUMOylates PGR (Progesterone receptor, PR) at lysine-7, lysine-388, and lysine-531 with SUMO1 (Man et al. 2006, Daniel et al. 2007, Abdel-Hafiz et al. 2009). SUMOylation inhibits hormone-dependent transcription activation by PGR.

Literature references

Shen, BF., Li, HY., Zhang, PJ., He, K., Pan, X., Zhou, T. et al. (2006). PIAS3 induction of PRB sumoylation represses PRB transactivation by destabilizing its retention in the nucleus. *Nucleic Acids Res., 34*, 5552-66. ↗

Dudevoir, ML., Abdel-Hafiz, H., Horwitz, KB. (2009). Mechanisms underlying the control of progesterone receptor transcriptional activity by SUMOylation. *J. Biol. Chem., 284*, 9099-108. ↗

Lange, CA., Faivre, EJ., Daniel, AR. (2007). Phosphorylation-dependent antagonism of sumoylation derepresses progesterone receptor action in breast cancer cells. *Mol. Endocrinol., 21*, 2890-906. ↗

Editions

2013-08-14	Authored, Edited	May, B.
2018-05-09	Reviewed	Niskanen, E.
2018-08-08	Reviewed	Niskanen, E.

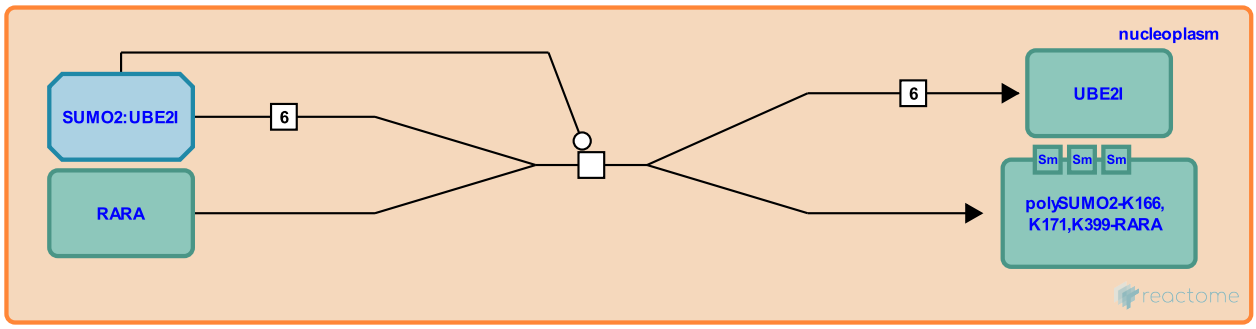
SUMOylation of RARA with SUMO2 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4341072

Type: transition

Compartments: nucleoplasm



RARA (Retinoic acid receptor alpha) is SUMOylated at lysine-166, lysine-171, and lysine-399 with SUMO2 (Zhu et al. 2009). SUMOylation at lysine-166 and lysine-171 is induced by all-trans retinoic acid and inhibits nuclear localization of RARA. SUMOylation at lysine-399 is observed in the absence of all-trans retinoic acid and enhances nuclear localization of RARA. SUMOylation of all 3 sites inhibits transcriptional activation by RARA.

Literature references

Santos, NC., Zhu, L., Kim, KH. (2009). Small ubiquitin-like modifier-2 modification of retinoic acid receptor-alpha regulates its subcellular localization and transcriptional activity. *Endocrinology, 150*, 5586-95. ↗

Editions

2013-08-14	Authored, Edited	May, B.
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2018-08-08	Reviewed	Niskanen, E.

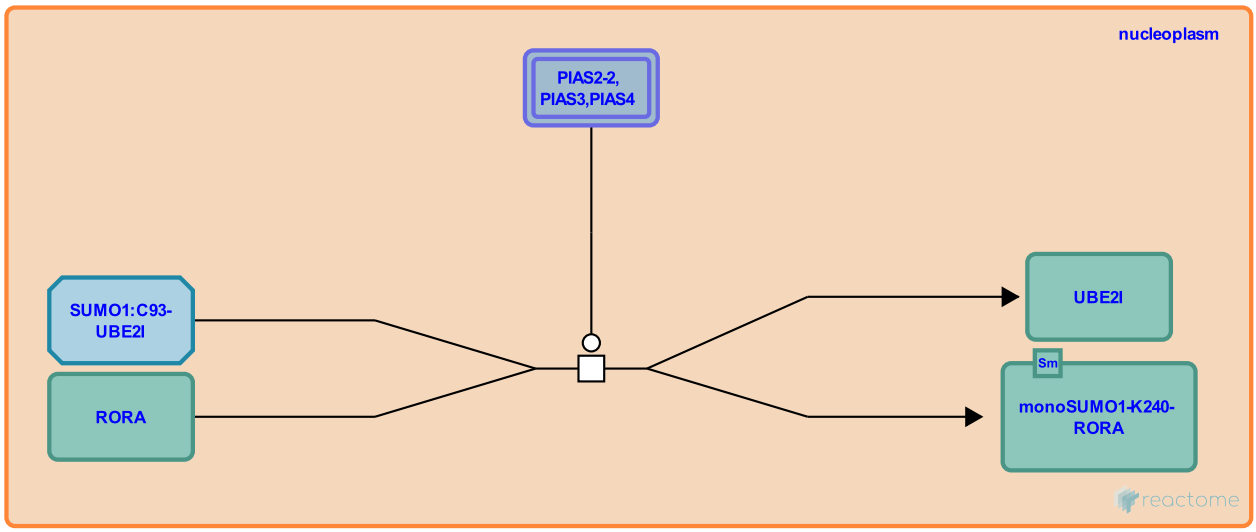
PIAS2,3,4 SUMOylate RORA with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4719436

Type: transition

Compartments: nucleoplasm



PIAS2-2 (PIASx-alpha), PIAS3, and PIAS4 SUMOylate RORA with SUMO1 at lysine-240 (Hwang et al. 2009). SUMOylation increases transcriptional activation by RORA.

Literature references

Kim, KI., Park, JH., Yang, Y., Hwang, EJ., Baek, SH., Lee, JM. et al. (2009). SUMOylation of RORalpha potentiates transcriptional activation function. *Biochem. Biophys. Res. Commun., 378*, 513-7. ↗

Editions

2013-10-18	Authored, Edited	May, B.
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2018-08-08	Reviewed	Niskanen, E.

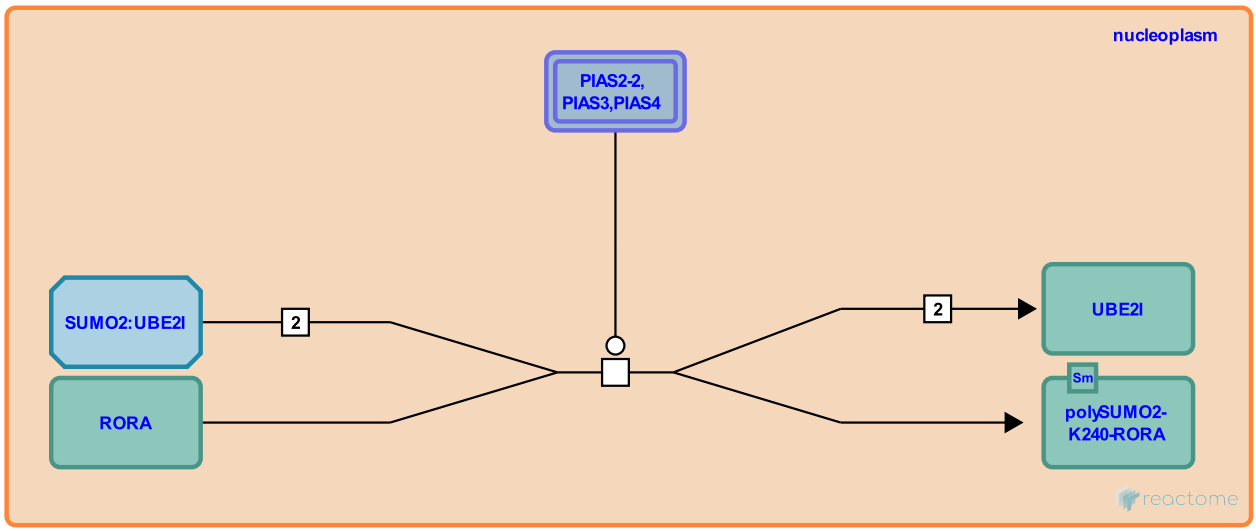
PIAS2,3,4 SUMOylate RORA with SUMO2 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4719413

Type: transition

Compartments: nucleoplasm



PIAS2-2 (PIASx-alpha, PIAS3, and PIAS4 SUMOylate RORA with SUMO2 at lysine-240 (Hwang et al. 2009). SUMOylation increases the transcriptional activity of RORA.

Literature references

Kim, KI., Park, JH., Yang, Y., Hwang, EJ., Baek, SH., Lee, JM. et al. (2009). SUMOylation of RORalpha potentiates transcriptional activation function. *Biochem. Biophys. Res. Commun., 378*, 513-7. ↗

Editions

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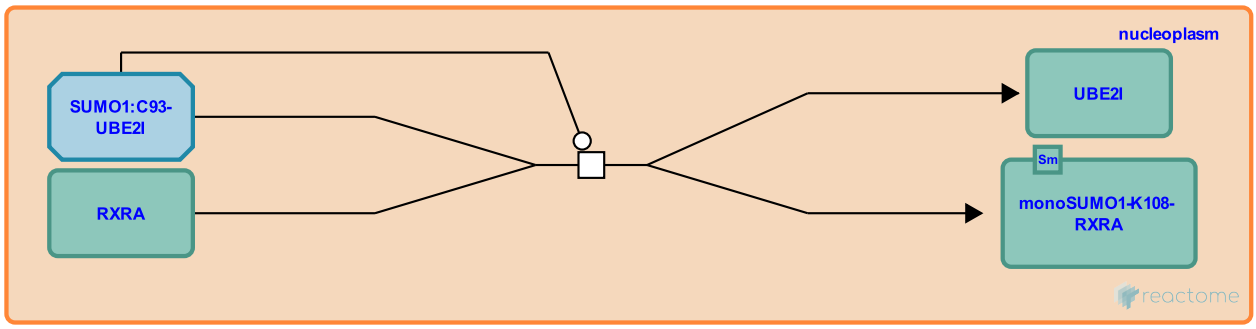
SUMOylation of RXRA with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4341048

Type: transition

Compartments: nucleoplasm



RXRA (Retinoid X receptor alpha) is SUMOylated at lysine-108 with SUMO1 (Choi et al. 2006). SUMOylation represses transcription activation by RXRA.

Literature references

Lee, MH., Chung, SS., Seol, JH., Lee, HW., Baek, SH., Choi, SJ. et al. (2006). Negative modulation of RXRalpha transcriptional activity by small ubiquitin-related modifier (SUMO) modification and its reversal by SUMO-specific protease SUSP1. *J. Biol. Chem., 281*, 30669-77. ↗

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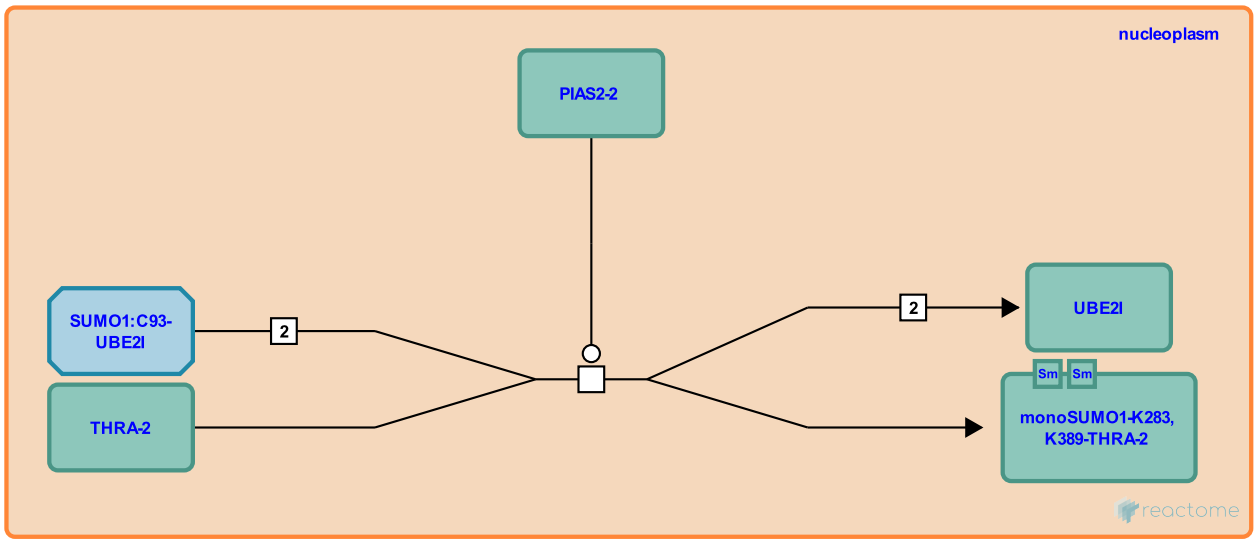
PIAS2-2 SUMOylates THRA with SUMO1 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4719447

Type: transition

Compartments: nucleoplasm



PIAS2-2 (PIASx-alpha) SUMOylates THRA (alpha-1 isoform) with SUMO1 at lysine-283 and lysine-389 (Liu et al. 2012). (A lysine residue corresponding to lysine-389 does not exist in the alpha-2 isoform.) SUMOylation by SUMO3 but not SUMO1 enhances induction of gene expression in response to the ligand triiodothyroxine.

Literature references

Schultz, JJ., Liu, YY., Kogai, T., Mody, K., Brent, GA. (2012). Thyroid hormone receptor isoform-specific modification by small ubiquitin-like modifier (SUMO) modulates thyroid hormone-dependent gene regulation. *J. Biol. Chem., 287*, 36499-508. ↗

Editions

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2018-08-08	Reviewed	Niskanen, E.

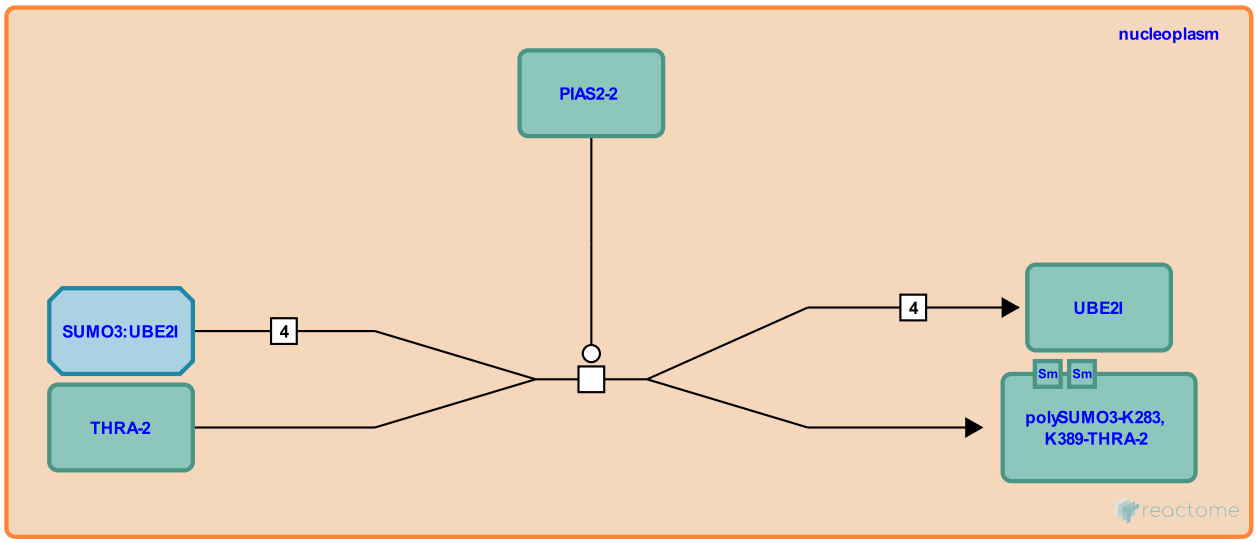
PIAS2-2 SUMOylates THRA with SUMO3 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4719423

Type: transition

Compartments: nucleoplasm



PIAS2-2 (PIasx-alpha) SUMOylates THRA (isoform alpha-1) with SUMO3 at lysine-283 and lysine-389 (Liu et al. 2012). (A lysine residue corresponding to lysine-389 does not exist in the alpha-2 isoform of THRA.) SUMOylation by SUMO3 enhances transcription in response to ligand binding.

Literature references

Schultz, JJ., Liu, YY., Kogai, T., Mody, K., Brent, GA. (2012). Thyroid hormone receptor isoform-specific modification by small ubiquitin-like modifier (SUMO) modulates thyroid hormone-dependent gene regulation. *J. Biol. Chem., 287*, 36499-508. ↗

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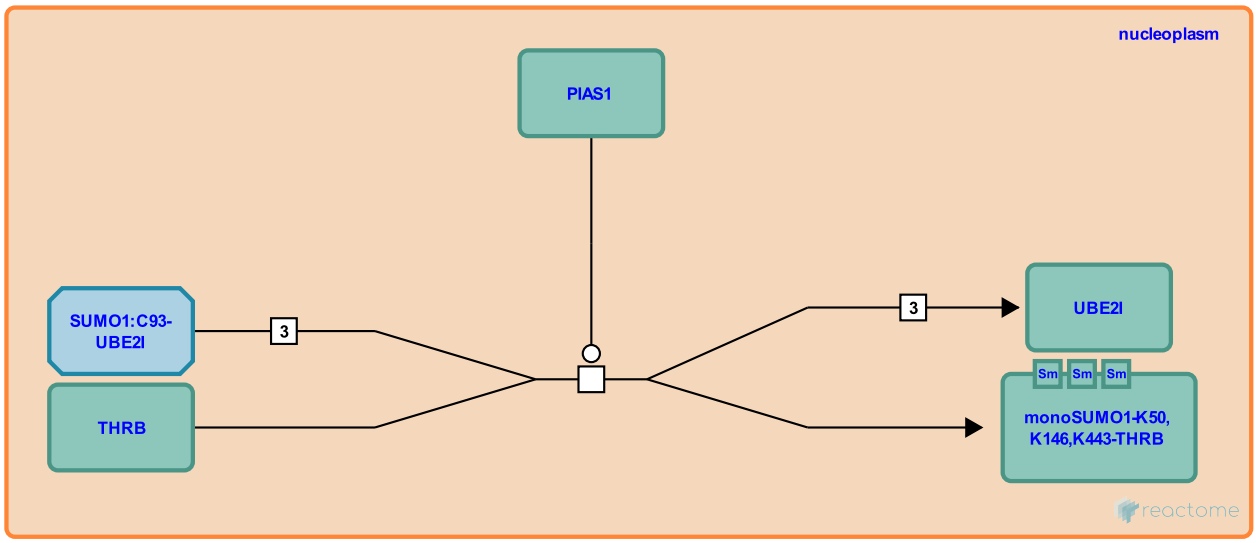
PIAS1 SUMOylates THRB with SUMO1. ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4719424

Type: transition

Compartments: nucleoplasm



PIAS1 SUMOylates THRB with SUMO1 at lysine-50, lysine-146, and lysine-443 (Liu et al. 2012). SUMOylation is required for induction of gene expression in response to ligand (triiodothyroxine). In the absence of SUMOylation the repressor NCOR is not dismissed in response to ligand binding.

Literature references

Schultz, JJ., Liu, YY., Kogai, T., Mody, K., Brent, GA. (2012). Thyroid hormone receptor isoform-specific modification by small ubiquitin-like modifier (SUMO) modulates thyroid hormone-dependent gene regulation. *J. Biol. Chem., 287*, 36499-508. ↗

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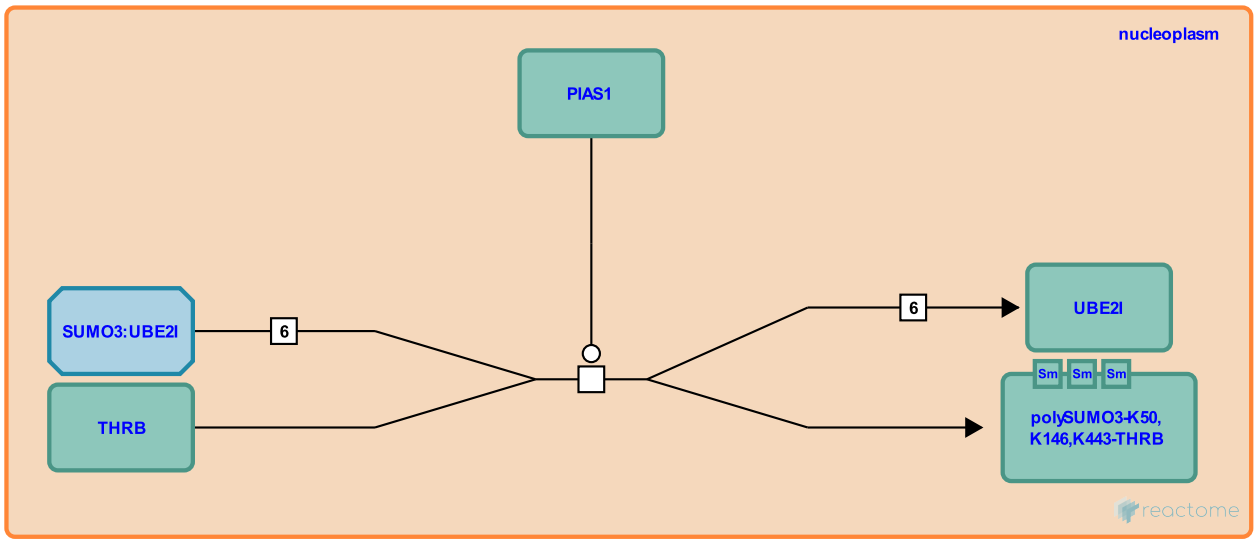
PIAS1 SUMOylates THRB with SUMO3 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4719448

Type: transition

Compartments: nucleoplasm



PIAS1 SUMOylates THRB with SUMO3 at lysine-50, lysine-146, and lysine-443 (Liu et al. 2012). SUMOylation is required for induction of transcription in response to ligand binding.

Literature references

Schultz, JJ., Liu, YY., Kogai, T., Mody, K., Brent, GA. (2012). Thyroid hormone receptor isoform-specific modification by small ubiquitin-like modifier (SUMO) modulates thyroid hormone-dependent gene regulation. *J. Biol. Chem., 287*, 36499-508. ↗

Editions

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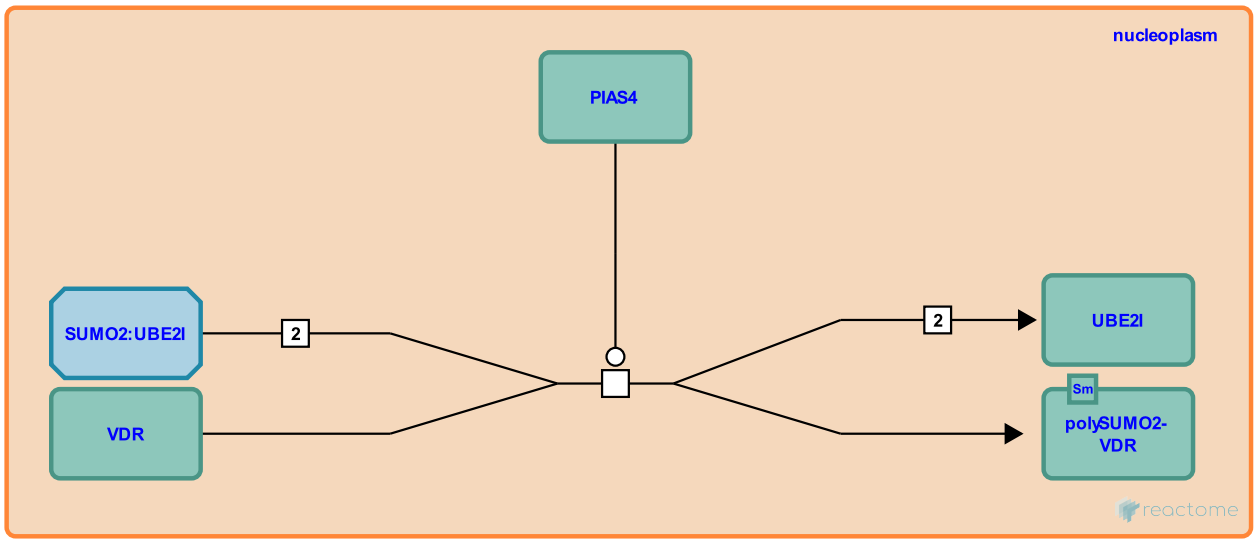
PIAS4 SUMOylates VDR with SUMO2 ↗

Location: SUMOylation of intracellular receptors

Stable identifier: R-HSA-4546387

Type: transition

Compartments: nucleoplasm



E3 SUMO-protein ligase (PIAS4) SUMOylates Vitamin D3 receptor (VDR) with SUMO2 (Jena et al. 2012). SUMOylation inhibits transcriptional activation by VDR in response to vitamin D.

Literature references

Lee, WP., Thompson, PD., Doherty, D., Jena, S. (2012). PIAS4 represses vitamin D receptor-mediated signaling and acts as an E3-SUMO ligase towards vitamin D receptor. *J. Steroid Biochem. Mol. Biol., 132*, 24-31. ↗

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2018-05-09	Reviewed	Niskanen, E.
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