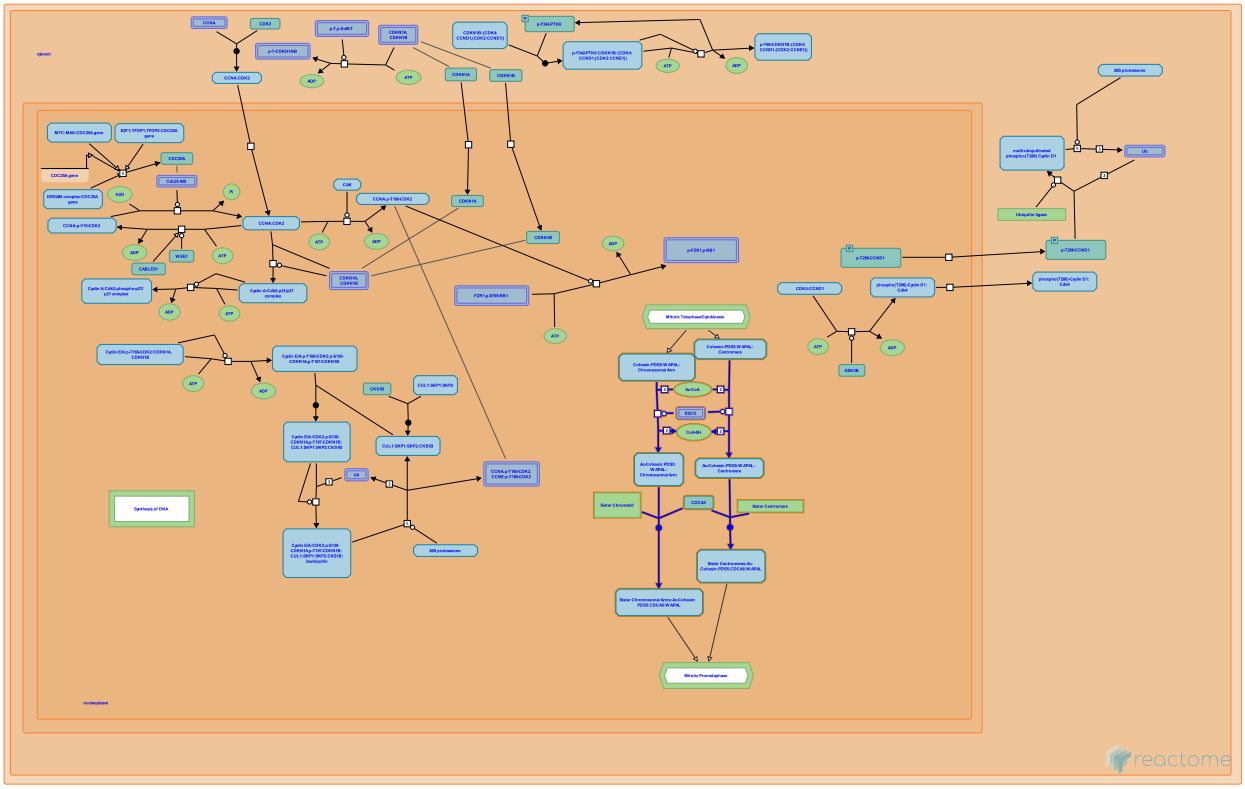
Establishment of Sister Chromatid Cohesion



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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

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. ↗

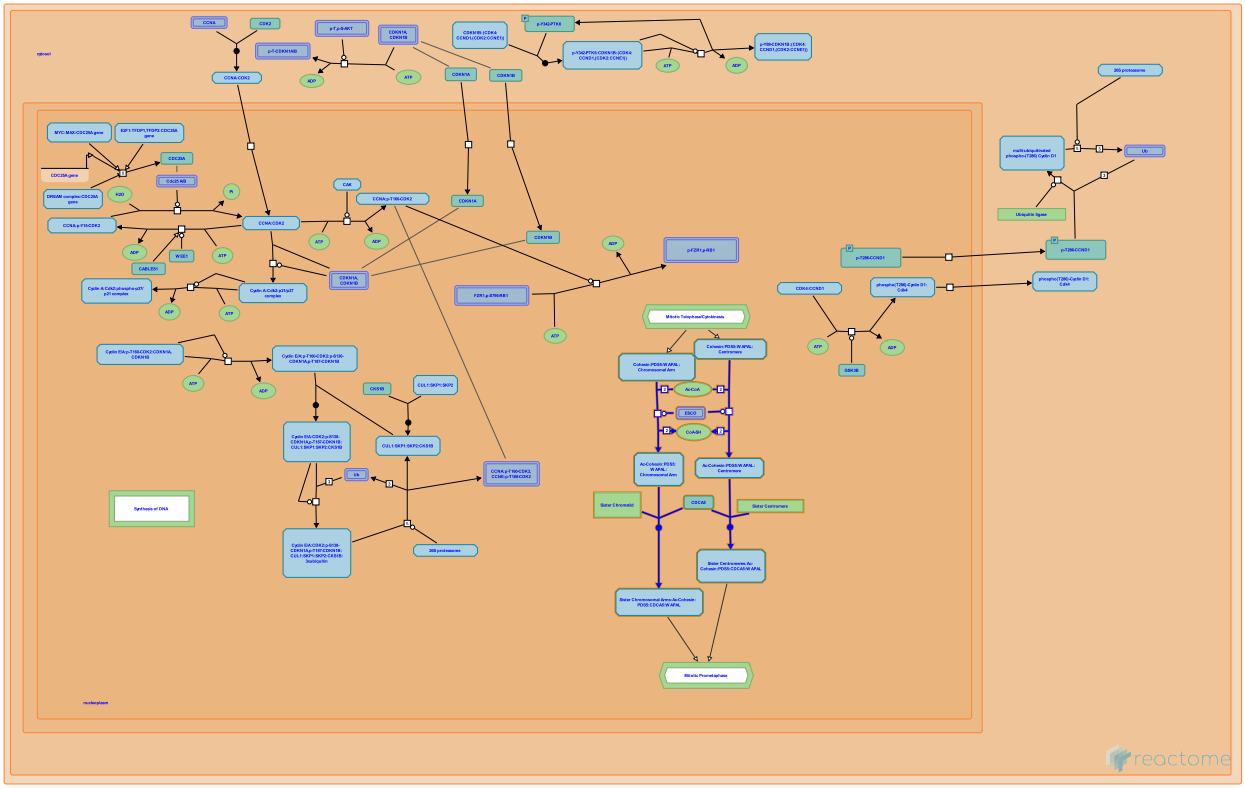
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Establishment of Sister Chromatid Cohesion ↗

Stable identifier: R-HSA-2468052

Compartments: chromosome, chromosome, centromeric region, nucleoplasm



The cohesin complex loads onto chromatin in telophase, but its association with chromatin remains transient, dynamic until the S-phase of the cell cycle, presumably because the cohesin-bound NIPBL:MAU2 (SCC2:SCC4) complex promotes chromatin loading, while cohesin-bound WAPAL promotes dissociation from chromatin. Stable binding of cohesin complexes to chromatin, measured by a mean residence time on chromatin, is triggered by DNA replication in S-phase (Gerlich et al. 2006), consistent with establishment of sister chromatid cohesion.

In S-phase, acetyltransferases ESCO1 and ESCO2 acetylate the SMC3 cohesin subunit (Hou and Zou 2005, Zhang et al. 2008, Nishiyama et al. 2010, Whelan et al. 2012). The acetylation of SMC3, in addition to DNA replication and the presence of PDS5 on cohesin, facilitates the recruitment of CDCA5 (Sororin) to cohesin complexes, an essential step in the establishment of sister chromatid cohesion in mammalian cells (Rankin et al. 2005, Nishiyama et al. 2010). CDCA5 (Sororin) displaces WAPAL from PDS5, thus preventing WAPAL to interfere with the establishment of sister chromatid cohesion (Nishiyama et al. 2010). The establishment and temporal regulation of sister chromatid cohesion is necessary for equal segregation of replicated chromosomes to daughter cells.

Literature references

Zou, H., Hou, F. (2005). Two human orthologues of Eco1/Ctf7 acetyltransferases are both required for proper sister-chromatid cohesion. *Mol. Biol. Cell, 16*, 3908-18. ↗

Kreidl, E., Wutz, G., Peters, JM., Egner, A., Whelan, G., Eichele, G. (2012). Cohesin acetyltransferase Esco2 is a cell viability factor and is required for cohesion in pericentric heterochromatin. *EMBO J., 31*, 71-82. ↗

Ayad, NG., Rankin, S., Kirschner, MW. (2005). Sororin, a substrate of the anaphase-promoting complex, is required for sister chromatid cohesion in vertebrates. *Mol. Cell, 18*, 185-200. ↗

Wang, Y., Zhang, J., Shi, X., Fu, X., Qin, J., Kim, ST. et al. (2008). Acetylation of Smc3 by Eco1 is required for S phase sister chromatid cohesion in both human and yeast. *Mol. Cell, 31*, 143-51. ↗

Peters, JM., Koch, B., Ellenberg, J., Gerlich, D., Dupeux, F. (2006). Live-cell imaging reveals a stable cohesin-chromatin interaction after but not before DNA replication. *Curr. Biol., 16*, 1571-8. ↗

Editions

2012-10-02	Authored	Orlic-Milacic, M.
2012-10-05	Edited	Gillespie, ME., Matthews, L.
2012-10-22	Reviewed	Zhang, N.
2012-11-20	Reviewed	Watanabe, Y., Tanno, Y.

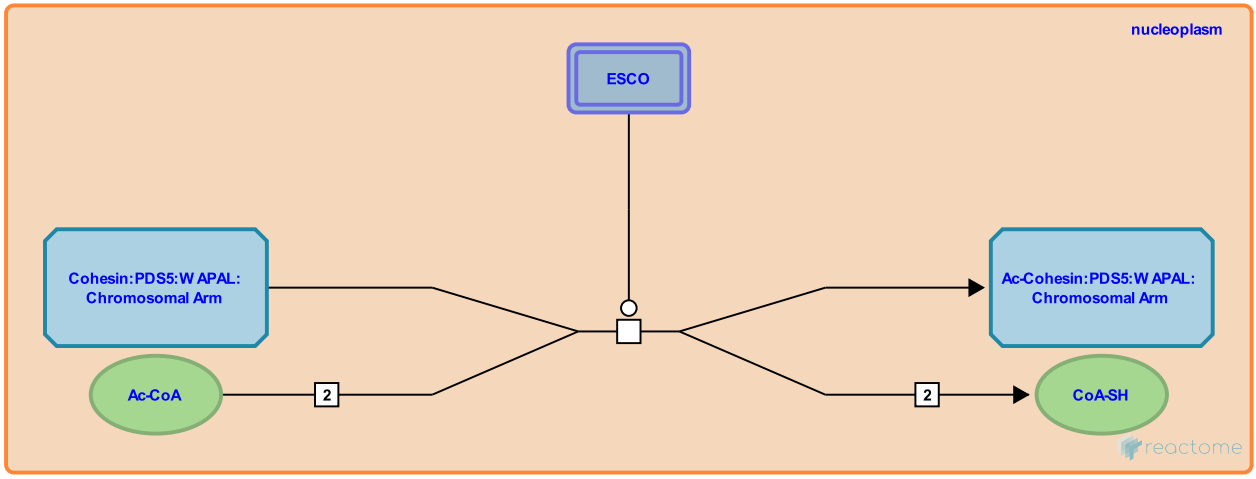
Acetylation of SMC3 subunit of chromosomal arm associated cohesin by ESCO1 or ESCO2 ↗

Location: Establishment of Sister Chromatid Cohesion

Stable identifier: R-HSA-2468039

Type: transition

Compartments: nucleoplasm, chromosome



Acetyltransferases ESCO1 and ESCO2 are homologs of the S. cerevisiae acetyltransferase Eco1, essential for viability in yeast. ESCO1 and ESCO2 share sequence homology in the C-terminal region, consisting of a H2C2 zinc finger motif and an acetyltransferase domain (Hou and Zou 2005). Both ESCO1 and ESCO2 acetylate the cohesin subunit SMC3 on two lysine residues, K105 and K106 (Zhang et al. 2008), an important step in the establishment of sister-chromatid cohesion during the S-phase of the cell cycle. These dual acetylations on SMC3 are deacetylated by HDAC8 after the cohesin removal from chromatin for the dissociation and recycling of cohesin subunits (Deardorff et al. 2012). ESCO1 and ESCO2 differ in their N-termini, which are necessary for chromatin binding, and may perform distinct functions in sister chromatid cohesion (Hou and Zou 2005), as suggested by the study of Esco2 knockout mice (Whelan et al. 2012).

Followed by: CDCA5 (Sororin) enables cohesion of sister chromosomal arms

Literature references

Zou, H., Hou, F. (2005). Two human orthologues of Eco1/Ctf7 acetyltransferases are both required for proper sister-chromatid cohesion. *Mol. Biol. Cell, 16*, 3908-18. ↗

Shirahige, K., Kiyono, T., Magnaghi-Jaulin, L., Clark, D., Katou, Y., Krantz, ID. et al. (2012). HDAC8 mutations in Cornelia de Lange syndrome affect the cohesin acetylation cycle. *Nature, 489*, 313-7. ↗

Kreidl, E., Wutz, G., Peters, JM., Egner, A., Whelan, G., Eichele, G. (2012). Cohesin acetyltransferase Esco2 is a cell viability factor and is required for cohesion in pericentric heterochromatin. *EMBO J., 31*, 71-82. ↗

Wang, Y., Zhang, J., Shi, X., Fu, X., Qin, J., Kim, ST. et al. (2008). Acetylation of Smc3 by Eco1 is required for S phase sister chromatid cohesion in both human and yeast. *Mol. Cell, 31*, 143-51. ↗

Kreidl, E., Ladurner, R., Hyman, AA., Peters, JM., Bando, M., Mechtler, K. et al. (2010). Sororin mediates sister chromatid cohesion by antagonizing Wapl. *Cell, 143*, 737-49. ↗

Editions

2012-10-02	Authored	Orlic-Milacic, M.
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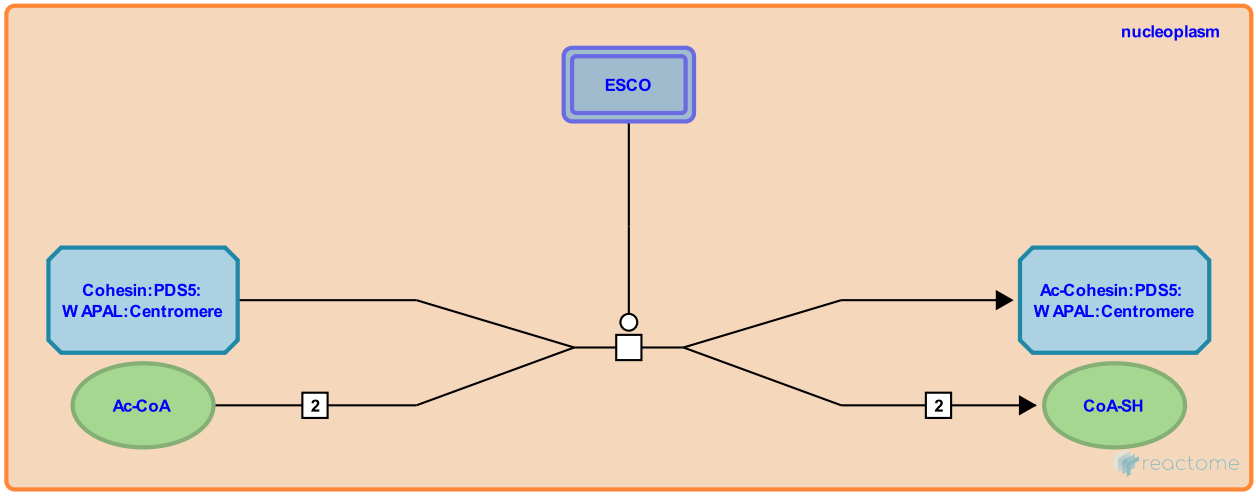
Acetylation of SMC3 subunit of centromeric chromatin associated cohesin by ESCO1 or ESCO2 ↗

Location: Establishment of Sister Chromatid Cohesion

Stable identifier: R-HSA-2473152

Type: transition

Compartments: nucleoplasm, chromosome, centromeric region



Acetyltransferases ESCO1 and ESCO2 are homologs of the S. cerevisiae acetyltransferase Eco1, essential for viability in yeast. ESCO1 and ESCO2 share sequence homology in the C-terminal region, consisting of a H2C2 zinc finger motif and an acetyltransferase domain (Hou and Zou 2005). Both ESCO1 and ESCO2 acetylate the cohesin subunit SMC3 on two lysine residues, K105 and K106 (Zhang et al. 2008), an important step in the establishment of sister-chromatid cohesion during the S-phase of the cell cycle. Divergent N-termini of ESCO1 and ESCO2, necessary for chromatin binding, suggest that ESCO1 and ESCO2 may perform distinct functions in sister chromatid cohesion (Hou and Zou 2005). Several studies suggest that ESCO2 may be predominantly involved in acetylation of the SMC3 subunit of centromeric cohesin. A conditional targeting of Esco2 locus in mice leads to pre-implantational loss of homozygous Esco2 -/- embryos at the eight-cell stage. Prometaphase chromosomes isolated from two-cell stage Esco2 knockout embryos show marked cohesion defect at centromeres (Whelan et al. 2012). ESCO2 protein appears in the S-phase (Hou and Zou 2005, Whelan et al. 2012) and in mouse embryonic fibroblasts Esco2 predominantly localizes to pericentric heterochromatin (Whelan et al. 2012). Mutations in the ESCO2 gene (Vega et al. 2005) that impair ESCO2 acetyltransferase activity (Gordillo et al. 2008) are the cause of the Roberts syndrome, an autosomal recessive disorder characterized by craniofacial and limb abnormalities, and intellectual disability. Metaphase chromosomes of Roberts syndrome patients exhibit loss of cohesion at heterochromatic regions of centromeres and the Y chromosome, with a characteristic 'railroad track appearance' (Van den Berg and Francke 1993, Vega et al. 2005).

Followed by: CDCA5 (Sororin) enables cohesion of sister centromeres

Literature references

Zou, H., Hou, F. (2005). Two human orthologues of Eco1/Ctf7 acetyltransferases are both required for proper sister-chromatid cohesion. *Mol. Biol. Cell, 16*, 3908-18. ↗

Van Den Berg, DJ., Francke, U. (1993). Roberts syndrome: a review of 100 cases and a new rating system for severity. *Am. J. Med. Genet., 47*, 1104-23. ↗

Ozono, K., Joenje, H., Yanagihara, I., Waisfisz, Q., van Gosliga, D., Vega, H. et al. (2005). Roberts syndrome is caused by mutations in ESCO2, a human homolog of yeast ECO1 that is essential for the establishment of sister chromatid cohesion. *Nat. Genet., 37*, 468-70. ↗

Kreidl, E., Wutz, G., Peters, JM., Egner, A., Whelan, G., Eichele, G. (2012). Cohesin acetyltransferase Esco2 is a cell viability factor and is required for cohesion in pericentric heterochromatin. *EMBO J., 31*, 71-82. ↗

Ozono, K., Zou, H., Hennekam, RC., Vega, H., Sakai, N., Simola, KO. et al. (2008). The molecular mechanism underlying Roberts syndrome involves loss of ESCO2 acetyltransferase activity. *Hum. Mol. Genet., 17*, 2172-80. ↗

Editions

2012-10-02	Authored	Orlic-Milacic, M.
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2012-11-20	Reviewed	Watanabe, Y., Tanno, Y.

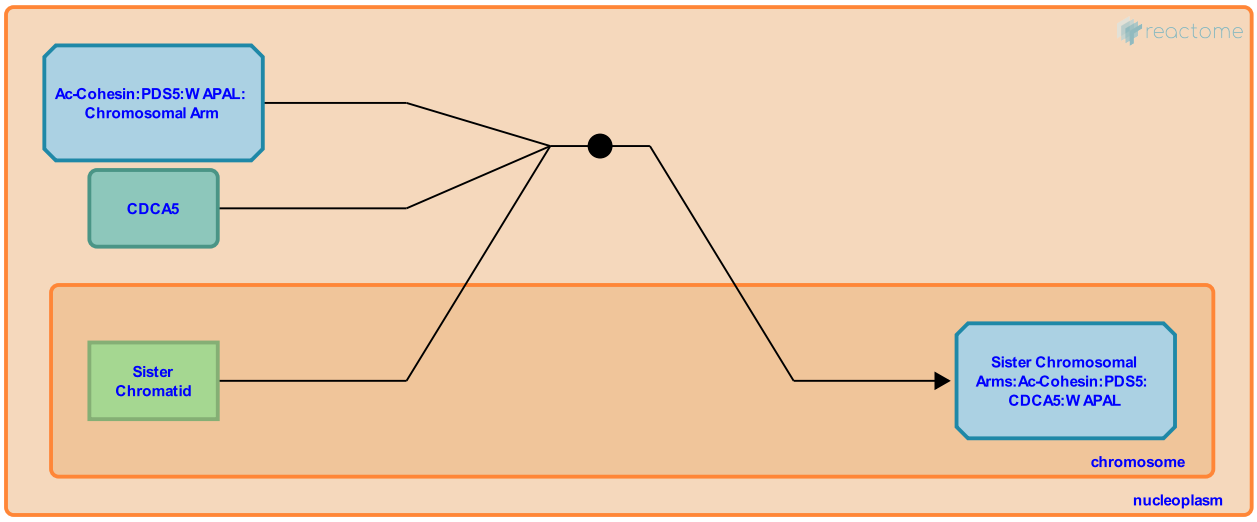
CDCA5 (Sororin) enables cohesion of sister chromosomal arms ↗

Location: Establishment of Sister Chromatid Cohesion

Stable identifier: R-HSA-2468041

Type: binding

Compartments: nucleoplasm, chromosome



CDCA5 (Sororin) is essential for the establishment of sister chromatid cohesion in mammalian cells (Rankin et al. 2005) in the S-phase of the cell cycle (Nishiyama et al. 2010). Several factors contribute to the recruitment of CDCA5 to chromatin-associated cohesin: DNA replication (i.e. presence of two sister chromatids), association of cohesin complex with PDS5, and acetylation of the SMC3 cohesin subunit by ESCO1/ESCO2 acetyltransferases. Experiments in which a recombinant tagged mouse CDCA5 was expressed in human HeLa cell line showed that CDCA5 starts to accumulate on chromatin in S-phase and dissociates from chromosomal arms in prophase (Nishiyama et al. 2010).

CDCA5 is essential for the establishment of chromosomal cohesion only in the presence of WAPAL, suggesting that the key role of CDCA5 (Sororin) is to antagonize WAPAL. Both CDCA5 and WAPAL contain an FGF (phenylalanine-glycine-phenylalanine) motif that is essential for PDS5 binding and is also essential for CDCA5 function in cohesion establishment. Indeed, CDCA5 is able to displace WAPAL from PDS5:WAPAL heterodimers in vitro. In vivo experiments in Xenopus egg extracts suggest that CDCA5 rearranges the topology of cohesin associated proteins so that WAPAL is no longer able to inhibit sister chromatid cohesion but remains associated with cohesin (Nishiyama et al. 2010).

Preceded by: Acetylation of SMC3 subunit of chromosomal arm associated cohesin by ESCO1 or ESCO2

Literature references

Ayad, NG., Rankin, S., Kirschner, MW. (2005). Sororin, a substrate of the anaphase-promoting complex, is required for sister chromatid cohesion in vertebrates. *Mol. Cell, 18*, 185-200. ↗

Kreidl, E., Ladurner, R., Hyman, AA., Peters, JM., Bando, M., Mechtler, K. et al. (2010). Sororin mediates sister chromatid cohesion by antagonizing Wapl. *Cell, 143*, 737-49. ↗

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2012-11-20	Reviewed	Watanabe, Y., Tanno, Y.

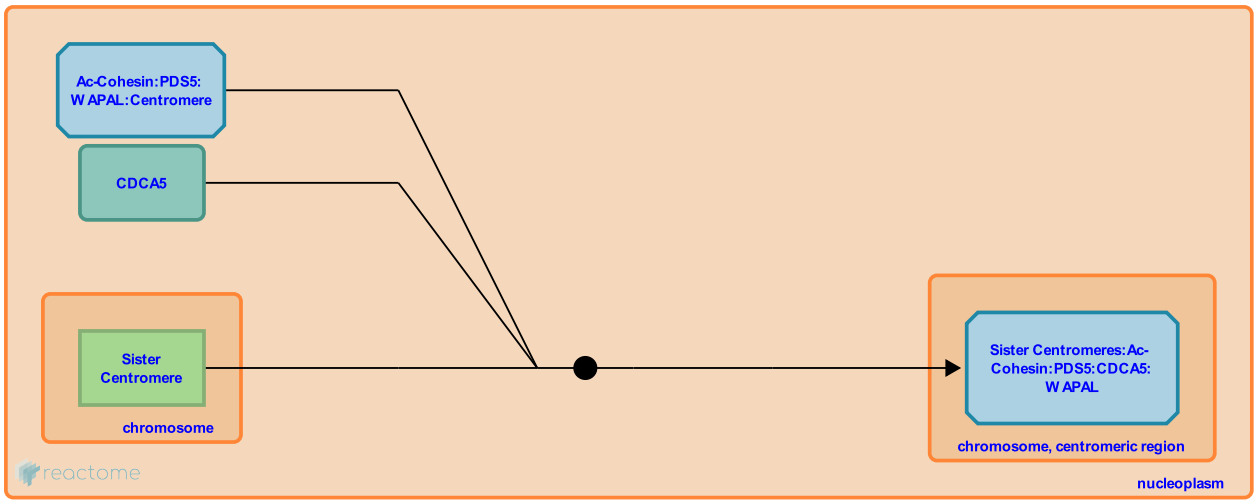
CDCA5 (Sororin) enables cohesion of sister centromeres ↗

Location: Establishment of Sister Chromatid Cohesion

Stable identifier: R-HSA-2473151

Type: binding

Compartments: nucleoplasm, chromosome, centromeric region



CDCA5 (Sororin) is essential for the establishment of sister chromatid cohesion at centromeres. Experiments in which a recombinant tagged mouse CDCA5 was expressed in human HeLa cell line showed that CDCA5 starts to accumulate on chromatin in S-phase and dissociates from centromeres in anaphase (Nishiyama et al. 2010).

Preceded by: Acetylation of SMC3 subunit of centromeric chromatin associated cohesin by ESCO1 or ESCO2

Literature references

Kreidl, E., Ladurner, R., Hyman, AA., Peters, JM., Bando, M., Mechtler, K. et al. (2010). Sororin mediates sister chromatid cohesion by antagonizing Wapl. *Cell, 143*, 737-49. ↗

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