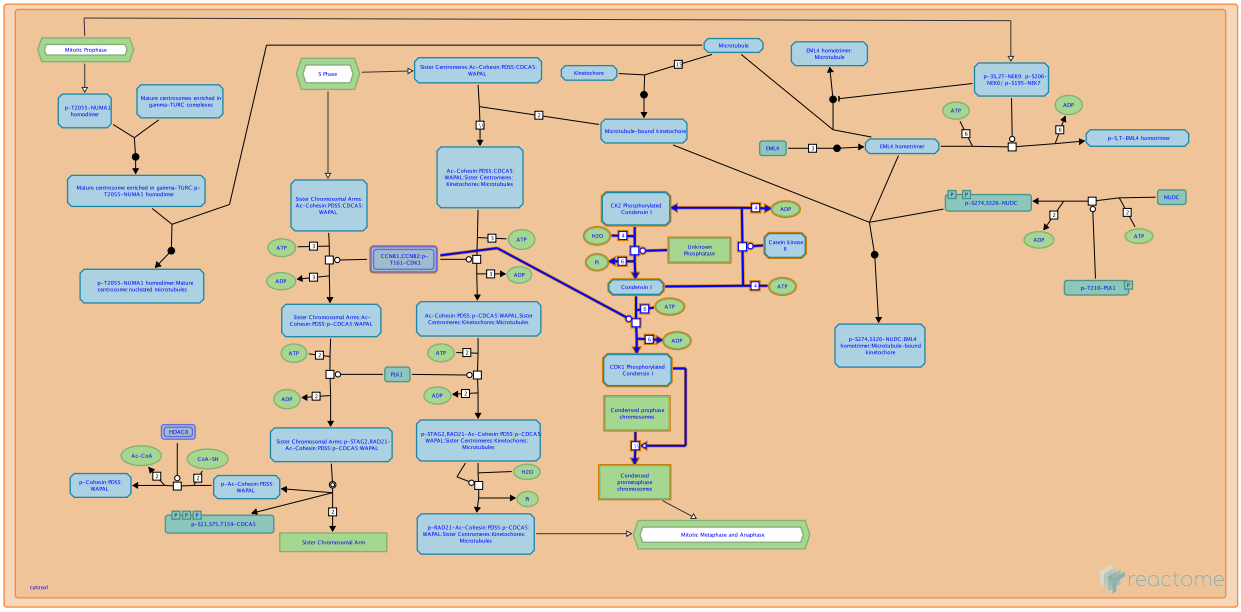
Condensation of Prometaphase Chromosomes



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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

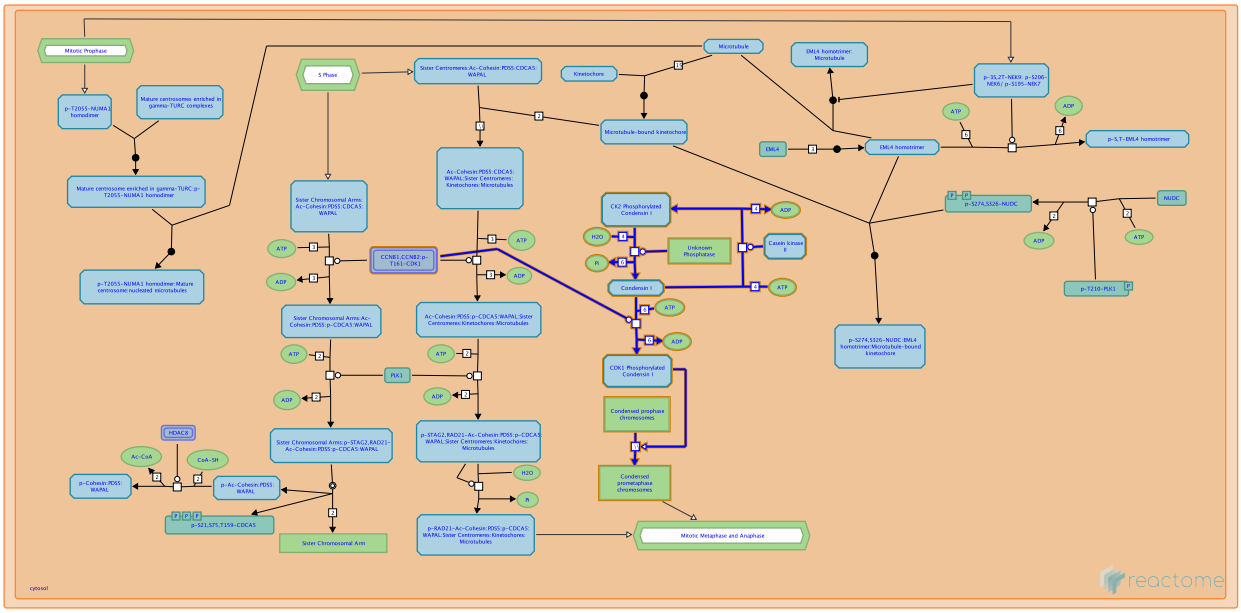
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Condensation of Prometaphase Chromosomes ↗

Stable identifier: R-HSA-2514853

Compartments: cytosol



The condensin I complex is evolutionarily conserved and consists of five subunits: two SMC (structural maintenance of chromosomes) family subunits, SMC2 and SMC4, and three non-SMC subunits, NCAPD2, NCAPH and NCAPG. The stoichiometry of the complex is 1:1:1:1:1 (Hirano and Mitchinson 1994, Hirano et al. 1997, Kimura et al. 2001). SMC2 and SMC4 subunits, shared between condensin I and condensin II, are DNA-dependent ATPases, and condensins are able to introduce positive supercoils into DNA in an ATP-dependent manner (Kimura and Hirano 1997).

Protein levels of condensin subunits are constant during the cell cycle, however condensins are enriched on mitotic chromosomes. Four of the five subunits, SMC4, NCAPD2, NCAPG and NCAPH, are phosphorylated in both mitotic and interphase HeLa cells, but on different sites (Takemoto et al. 2004). CDK1 (CDC2) in complex with CCNB (cyclin B) phosphorylates NCAPD2, NCAPG and NCAPH in mitosis (Kimura et al. 1998, Kimura et al. 2001, Takemoto et al. 2006, Murphy et al. 2008), but other mitotic kinases, such as PLK1 (St-Pierre et al. 2009), and other post-translational modifications, such as acetylation, may also be involved (reviewed by Bazile et al. 2010). Global proteomic analysis of human cell lines has identified N6-acetylation of lysine residues in condensin subunits SMC2, SMC4 and NCAPH (Choudhary et al. 2009). Another high throughput proteomic study showed that condensin I subunits NCAPD2 and NCAPH are phosphorylated upon DNA damage, probably by ATM or ATR kinase (Matsuoka et al. 2007).

As condensin I is cytosolic, it gains access to chromosomes only after the nuclear envelope breakdown at the start of prometaphase (Ono et al. 2004). Condensin I, activated by CDK1-mediated phosphorylation, promotes hypercondensation of chromosomes that were condensed in prophase through the action of condensin II (Hirota et al. 2004). AURKB may also regulate association of condensin I complex with chromatin (Lipp et al. 2007). Protein phosphatase PP2A acts independently of its catalytic activity to target condensin II complex to chromatin, but does not interact with condensin I (Takemoto et al. 2009). Full activation of condensin I requires dephosphorylation of sites modified by CK2 during interphase (Takemoto et al. 2006). Besides being essential for chromosome condensation in mitosis, condensin I may also contribute to cohesin removal from chromosome arms in prometaphase, but the exact mechanism is not known (Hirota et al. 2004).

Literature references

Takemoto, A., Kimura, K., Yokoyama, S., Hanaoka, F. (2004). Cell cycle-dependent phosphorylation, nuclear localization, and activation of human condensin. *J. Biol. Chem., 279*, 4551-9. ↗

Hirano, T., Mitchison, TJ. (1994). A heterodimeric coiled-coil protein required for mitotic chromosome condensation in vitro. *Cell, 79*, 449-58. ↗

Takemoto, A., Maeshima, K., Ikehara, T., Yamaguchi, K., Murayama, A., Imamura, S. et al. (2009). The chromosomal association of condensin II is regulated by a noncatalytic function of PP2A. *Nat. Struct. Mol. Biol., 16*, 1302-8. ↗

St-Pierre, J., Douziech, M., Bazile, F., Pascariu, M., Bonneil, E., Sauvé, V. et al. (2009). Polo kinase regulates mitotic chromosome condensation by hyperactivation of condensin DNA supercoiling activity. *Mol. Cell, 34*, 416-26. ↗

Takemoto, A., Kimura, K., Yanagisawa, J., Yokoyama, S., Hanaoka, F. (2006). Negative regulation of condensin I by CK2-mediated phosphorylation. *EMBO J., 25*, 5339-48. ↗

Editions

2012-10-12	Authored	Orlic-Milacic, M.
2012-10-18	Edited	Matthews, L.
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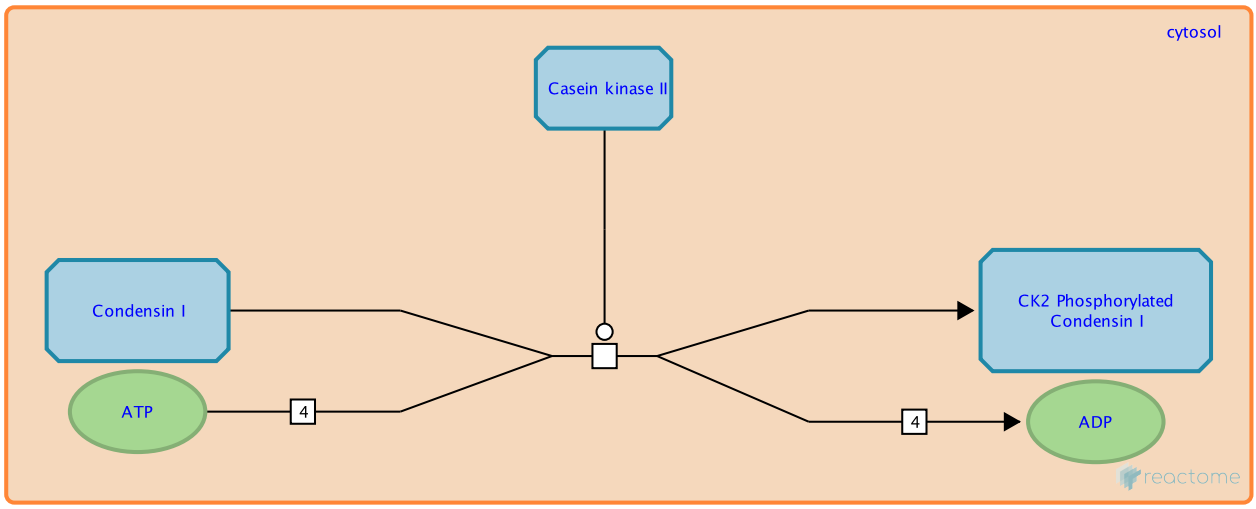
CK2 phosphorylates condensin I subunits ↗

Location: Condensation of Prometaphase Chromosomes

Stable identifier: R-HSA-2529020

Type: transition

Compartments: cytosol



Protein levels of condensin subunits are constant during the cell cycle. Four subunits, SMC4, NCAPD2, NCAPG and NCAPH, are phosphorylated in interphase cells (Takemoto et al. 2004) by CK2 i.e. casein kinase II (Takemoto et al. 2006). Except for the phosphorylation of NCAPH subunit on serine residue S570, CK2 phosphorylation sites in condensin I subunits have not been identified. Phosphorylation by CK2 inhibits condensin I-mediated introduction of positive supercoils into DNA and chromatin condensation. Mitotic activation of condensin I involves removal of phosphate groups added by CK2 (Takemoto et al. 2006), but the responsible phosphatase has not been identified.

Followed by: Dephosphorylation of CK2-modified condensin I

Literature references

Takemoto, A., Kimura, K., Yanagisawa, J., Yokoyama, S., Hanaoka, F. (2006). Negative regulation of condensin I by CK2-mediated phosphorylation. *EMBO J., 25*, 5339-48. ↗

Takemoto, A., Kimura, K., Yokoyama, S., Hanaoka, F. (2004). Cell cycle-dependent phosphorylation, nuclear localization, and activation of human condensin. *J. Biol. Chem., 279*, 4551-9. ↗

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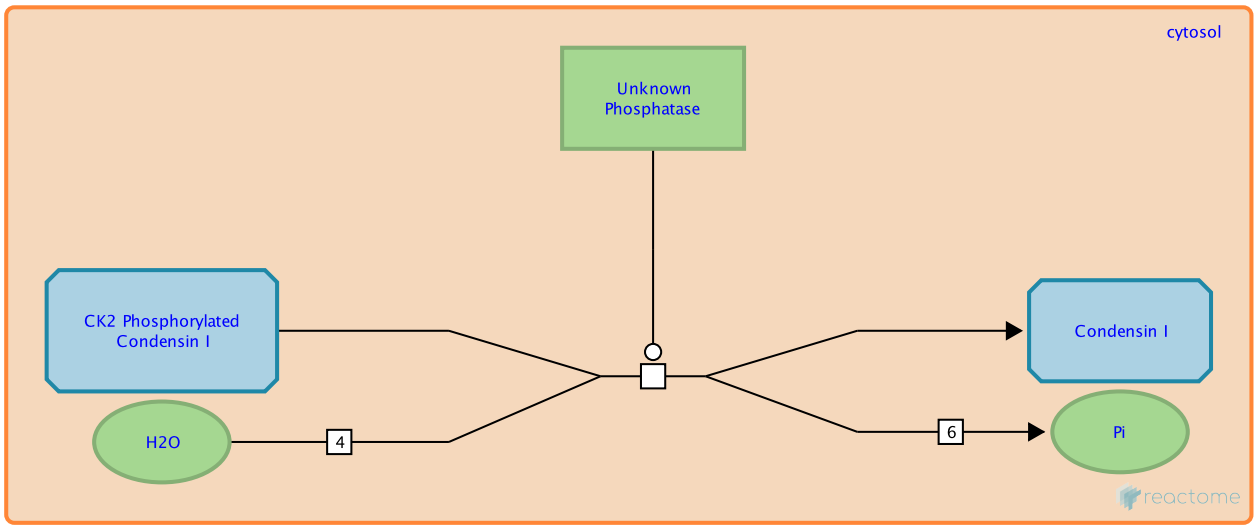
Dephosphorylation of CK2-modified condensin I ↗

Location: Condensation of Prometaphase Chromosomes

Stable identifier: R-HSA-2529015

Type: transition

Compartments: cytosol



Inhibitory phosphate groups that were added to condensin I subunits by CK2 during interphase have to be removed for full mitotic activation of condensin I (Takemoto et al. 2006). The responsible phosphatase has not been identified.

Preceded by: CK2 phosphorylates condensin I subunits

Followed by: CDK1 phosphorylates condensin I

Literature references

Takemoto, A., Kimura, K., Yanagisawa, J., Yokoyama, S., Hanaoka, F. (2006). Negative regulation of condensin I by CK2-mediated phosphorylation. *EMBO J., 25*, 5339-48. ↗

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CDK1 phosphorylates condensin I ↗

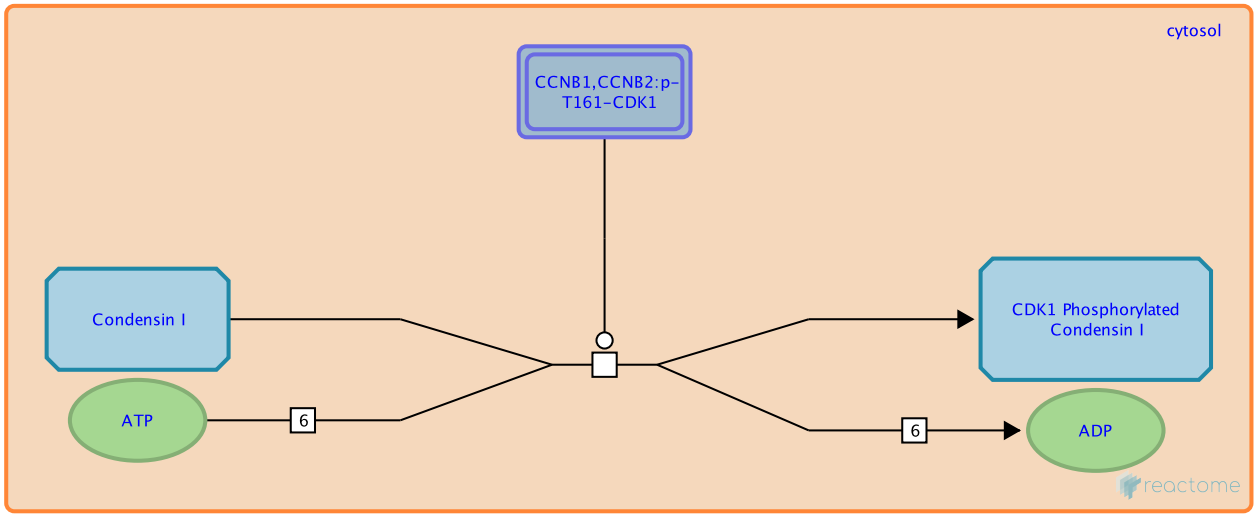
Location: Condensation of Prometaphase Chromosomes

Stable identifier: R-HSA-2514854

Type: transition

Compartments: cytosol

Inferred from: Cdk1 phosphorylates condensin I (Xenopus laevis)



CDK1 (CDC2) in complex with CCNB (cyclin B) phosphorylates condensin I subunits NCAPD2, NCAPG and NCAPH in mitosis (Kimura et al. 2001, Takemoto et al. 2006), but other mitotic kinases may also be involved. CDK1 phosphorylation sites in NCAPH have not been established. NCAPD2 threonine residues T1339, T1384 and T1389 are inferred to be phosphorylated by CDK1 based on homologues sites in Xenopus laevis Ncapd2 (Kimura et al. 1998). NCAPG threonine residues T308 and T332 are phosphorylated by CDK1 in vitro and functionally important. The functional importance of threonine T931, also phosphorylated by CDK1 in vitro, has not been demonstrated (Murphy et al. 2008). Phosphorylation by CDK1 is required for mitotic activation of condensin I and promotes chromosomal binding, introduction of positive supercoils into DNA, and chromatin condensation (Kimura et al. 1998, Kimura et al. 2001, Takemoto et al. 2006).

Preceded by: Dephosphorylation of CK2-modified condensin I

Followed by: Phosphorylated condensin I promotes condensation of prometaphase chromosomes

Literature references

Kimura, K., Cuvier, O., Hirano, T. (2001). Chromosome condensation by a human condensin complex in Xenopus egg extracts. *J. Biol. Chem., 276*, 5417-20. ↗

Takemoto, A., Kimura, K., Yanagisawa, J., Yokoyama, S., Hanaoka, F. (2006). Negative regulation of condensin I by CK2-mediated phosphorylation. *EMBO J., 25*, 5339-48. ↗

Kimura, K., Hirano, M., Kobayashi, R., Hirano, T. (1998). Phosphorylation and activation of 13S condensin by Cdc2 in vitro. *Science, 282*, 487-90. ↗

Murphy, LA., Sarge, KD. (2008). Phosphorylation of CAP-G is required for its chromosomal DNA localization during mitosis. *Biochem. Biophys. Res. Commun., 377*, 1007-11. ↗

Editions

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2012-10-18	Edited	Matthews, L.
2012-10-19	Edited	D'Eustachio, P.

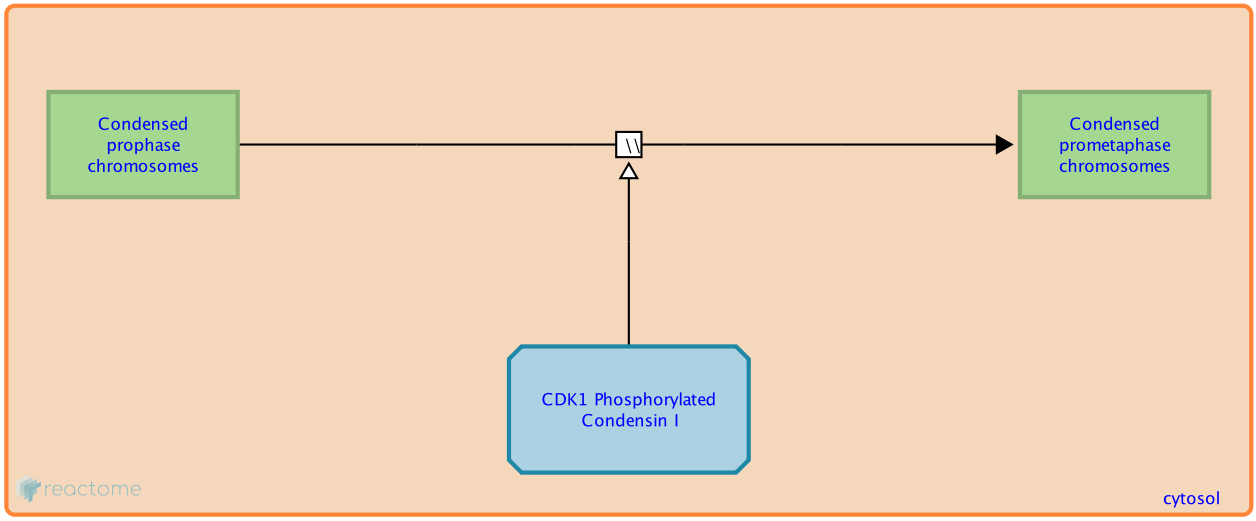
Phosphorylated condensin I promotes condensation of prometaphase chromosomes

Location: Condensation of Prometaphase Chromosomes

Stable identifier: R-HSA-2520883

Type: omitted

Compartments: cytosol



While condensin II complex (consisting of subunits SMC2, SMC4, NCAPD3, NCAPG2 and NCAPH2), responsible for condensation of chromosomes in prophase (Hirota et al. 2004, Abe et al. 2011), is nuclear, condensin I is cytosolic and gains access to chromosomes only after the nuclear envelope breakdown at the start of prometaphase (Ono et al. 2004). Condensin I, activated by CDK1 phosphorylation (Kimura et al. 1998, Kimura et al. 2001, Takemoto et al. 2006, Murphy et al. 2008), promotes further condensation of chromosomes in prometaphase and metaphase, visible as longitudinal chromosome shortening (Hirota et al. 2004). Besides CDK1-mediated phosphorylation, association of condensin I with chromosomes may be regulated by AURKB (Lipp et al. 2007). In budding yeast, condensin phosphorylation by Cdc2 (CDK1 ortholog) is followed by Cdc5-mediated phosphorylation (Cdc5 is PLK1 ortholog), which is important for the sustained mitotic activity of condensin complex (St-Pierre et al. 2009). Phosphorylation by PLK1 is also important for the activation of human condensin II complex (Abe et al. 2011).

Preceded by: CDK1 phosphorylates condensin I

Literature references

Abe, S., Nagasaka, K., Hirayama, Y., Kozuka-Hata, H., Oyama, M., Aoyagi, Y. et al. (2011). The initial phase of chromosome condensation requires Cdk1-mediated phosphorylation of the CAP-D3 subunit of condensin II. *Genes Dev., 25*, 863-74.

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Kimura, K., Hirano, M., Kobayashi, R., Hirano, T. (1998). Phosphorylation and activation of 13S condensin by Cdc2 in vitro. *Science, 282*, 487-90.

Ono, T., Fang, Y., Spector, DL., Hirano, T. (2004). Spatial and temporal regulation of Condensins I and II in mitotic chromosome assembly in human cells. *Mol. Biol. Cell, 15*, 3296-308.

Takemoto, A., Kimura, K., Yanagisawa, J., Yokoyama, S., Hanaoka, F. (2006). Negative regulation of condensin I by CK2-mediated phosphorylation. *EMBO J., 25*, 5339-48.

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