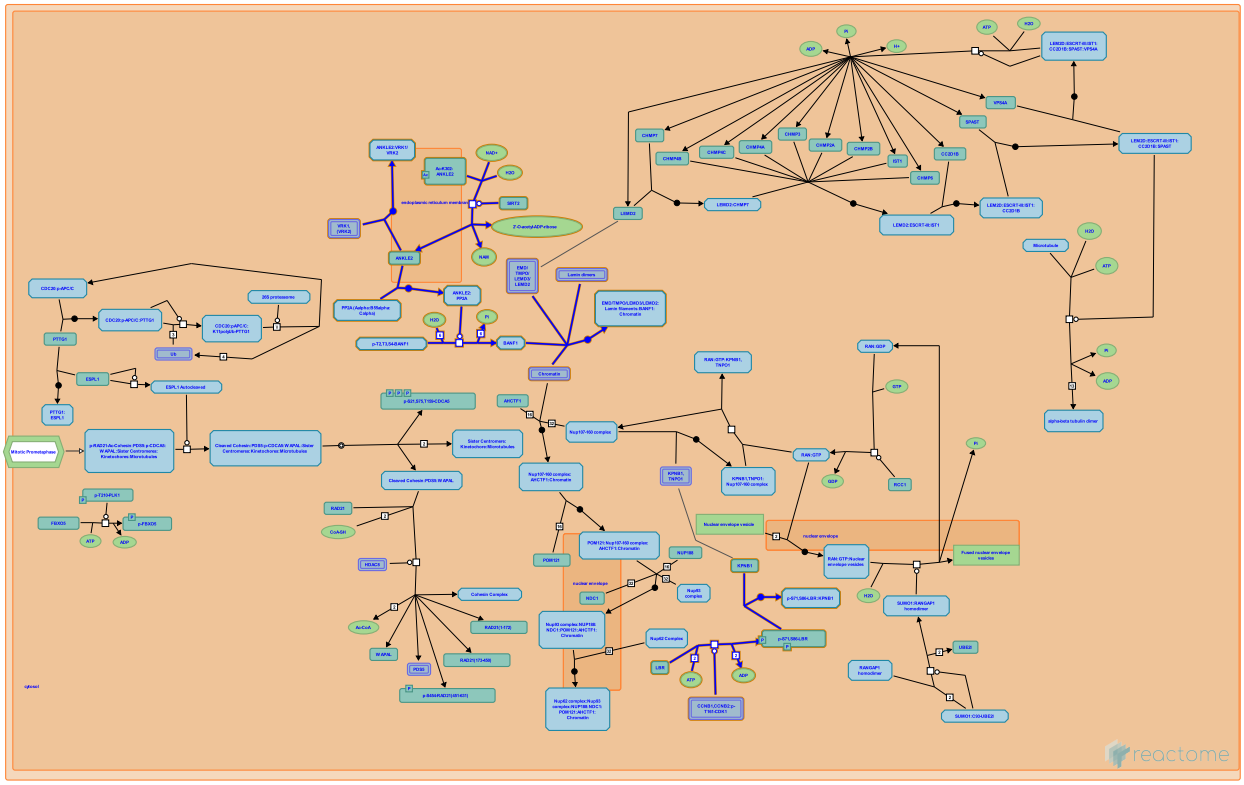
Initiation of Nuclear Envelope (NE) Reformation



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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. ↗

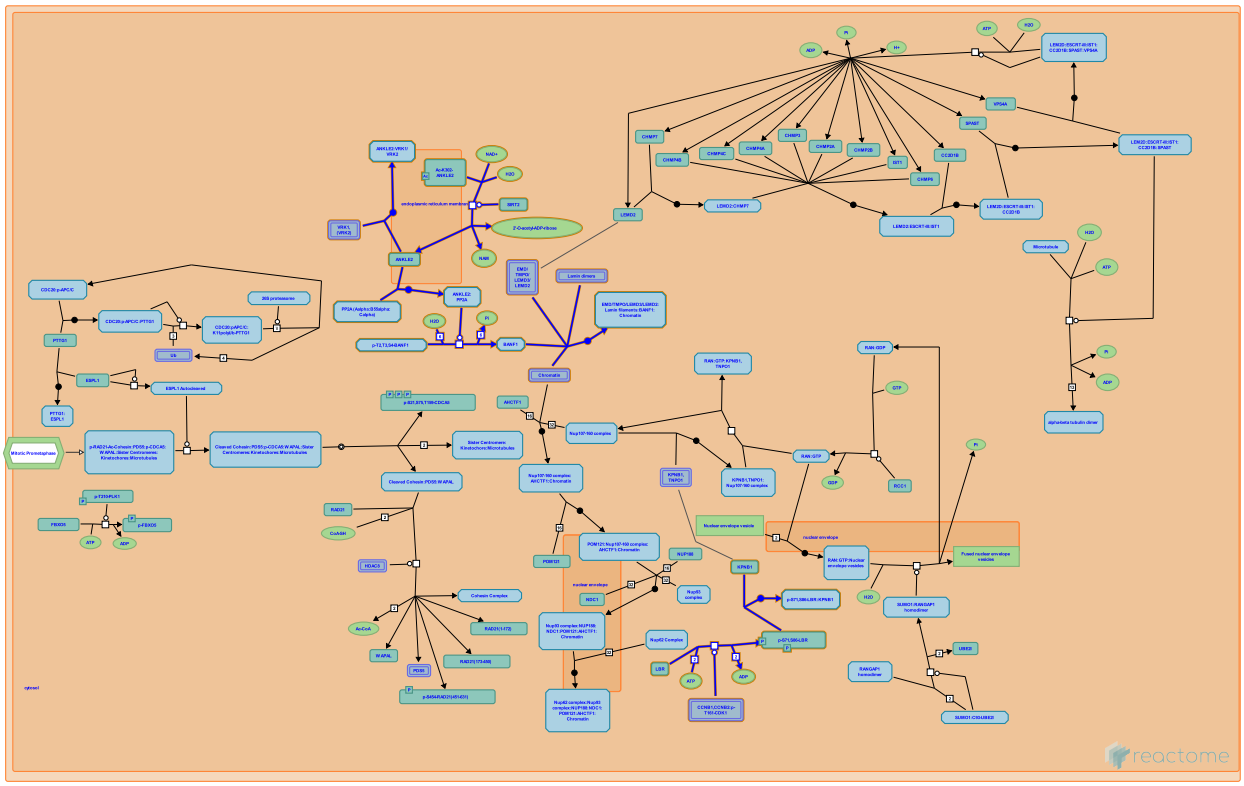
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Initiation of Nuclear Envelope (NE) Reformation ↗

Stable identifier: R-HSA-2995383



Reassembly of the nuclear envelope (NE) is initiated at late anaphase/early telophase when BANF1 (BAF), which is dispersed throughout the cytoplasm during metaphase, accumulates on the surfaces of coalesced chromosomes. This is coordinated with the chromatin association of membranes and inner nuclear membrane proteins that include EMD (emerin), TMPO (LAP2beta), LEMD3 (MAN1) and LEMD2 (LEM2), and lamins (Haraguchi et al. 2008, reviewed by Wandke and Kutay 2013). The DNA-cross-bridging activity of BANF1 is required for individual chromosomes to properly coalesce for enclosure in a single nucleus (Samwer et al. 2017).

Literature references

Wandke, C., Kutay, U. (2013). Enclosing chromatin: reassembly of the nucleus after open mitosis. *Cell, 152*, 1222-5. ↗

Hiraoka, Y., Haraguchi, T., Osakada, H., Koujin, T., Mori, C., Kojidani, T. et al. (2008). Live cell imaging and electron microscopy reveal dynamic processes of BAF-directed nuclear envelope assembly. *J. Cell. Sci., 121*, 2540-54. ↗

Zuber, J., Jude, JG., Hoefler, R., Samwer, M., Gerlich, DW., Schmalhorst, PS. et al. (2017). DNA Cross-Bridging Shapes a Single Nucleus from a Set of Mitotic Chromosomes. *Cell, 170*, 956-972.e23. ↗

Editions

2013-01-23	Edited	Gillespie, ME.
2013-01-23	Authored	Orlic-Milacic, M.
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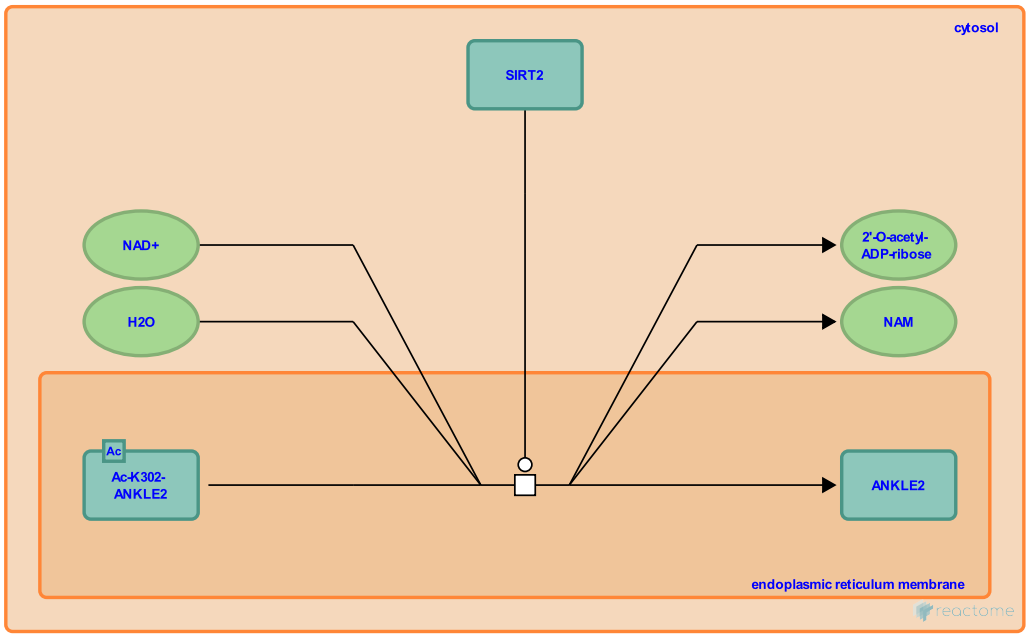
ANKLE2 is deacetylated by SIRT2 ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-9667952

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



ANKLE2 (LEM4) is required for normal nuclear envelope (NE) formation at the end of mitosis (Ascencio et al. 2012, Kaufmann et al. 2016). Deacetylation of ANKLE2 on residue K302 by SIRT2 promotes this process (Kaufman et al. 2016).

Followed by: ANKLE2 binds PP2A, ANKLE2 binds VRK1,(VRK2)

Literature references

Kostrhon, S., Kukolj, E., Opravil, S., Slade, D., Brachner, A., Kaufmann, T. et al. (2016). SIRT2 regulates nuclear envelope reassembly through ANKLE2 deacetylation. *J. Cell. Sci., 129*, 4607-4621. ↗

Wallenfang, MR., Mall, M., Davidson, IF., Santarella-Mellwig, R., Ly-Hartig, TB., Asencio, C. et al. (2012). Coordination of kinase and phosphatase activities by Lem4 enables nuclear envelope reassembly during mitosis. *Cell, 150*, 122-35. ↗

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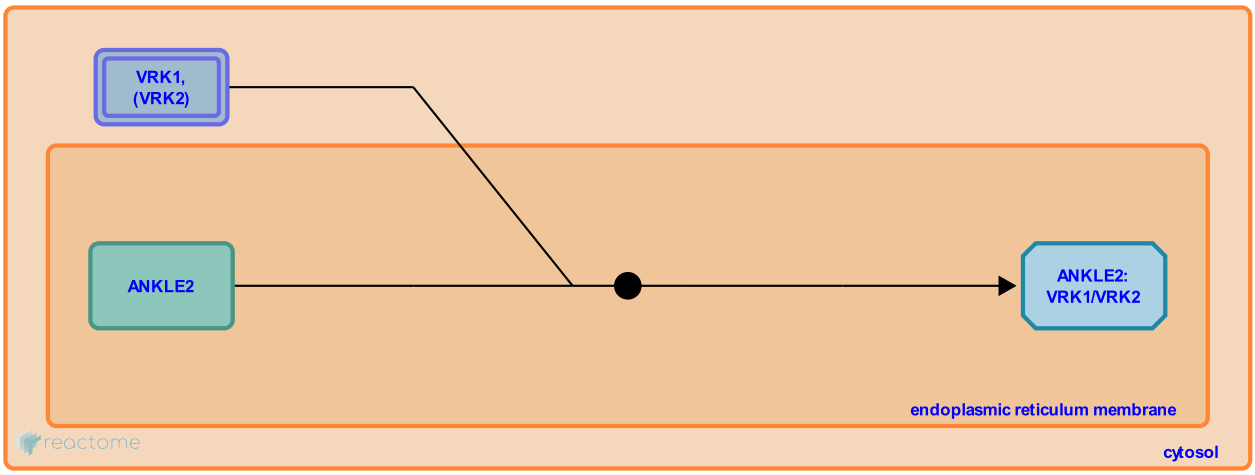
ANKLE2 binds VRK1,(VRK2) ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-2995389

Type: binding

Compartments: endoplasmic reticulum membrane, cytosol



Both human ANKLE2 and the C. elegans ortholog LEM4 bind VRK1 (and possibly VRK2), the kinase responsible for phosphorylation of BANF1 (BAF) in mitotic prophase, and inhibit VRK1 catalytic activity (Asencio et al. 2012).

Preceded by: ANKLE2 is deacetylated by SIRT2

Literature references

Wallenfang, MR., Mall, M., Davidson, IF., Santarella-Mellwig, R., Ly-Hartig, TB., Asencio, C. et al. (2012). Coordination of kinase and phosphatase activities by Lem4 enables nuclear envelope reassembly during mitosis. *Cell, 150*, 122-35. ↗

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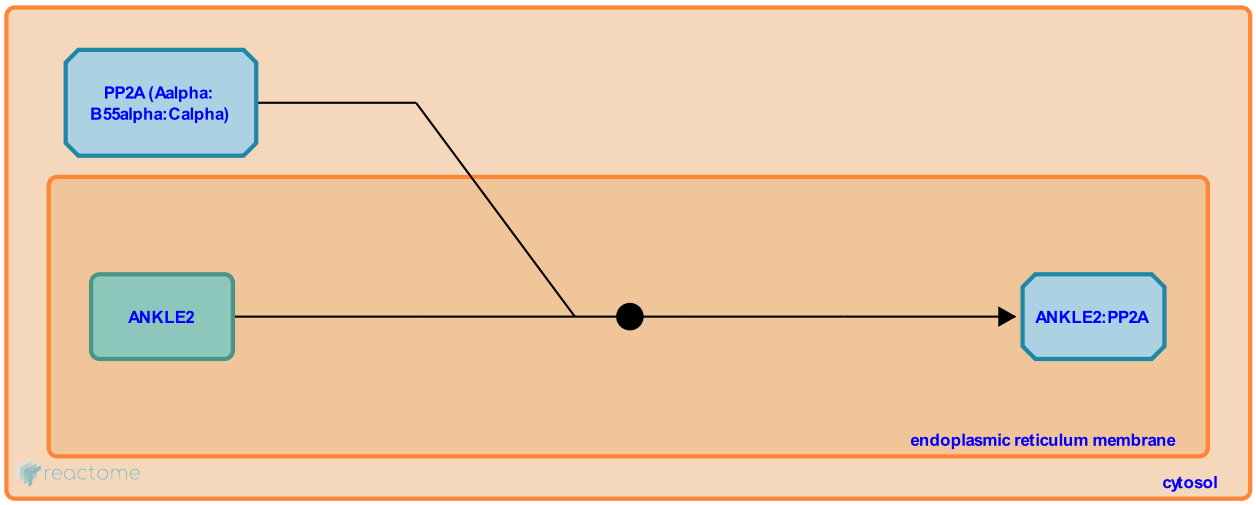
ANKLE2 binds PP2A ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-9667965

Type: binding

Compartments: endoplasmic reticulum membrane, cytosol



ANKLE2 binds the PP2A complex that contains the B55-alpha regulatory subunit and facilitates BANF1 dephosphorylation (Asencio et al. 2012).

Preceded by: ANKLE2 is deacetylated by SIRT2

Followed by: PP2A dephosphorylates BANF1

Literature references

Wallenfang, MR., Mall, M., Davidson, IF., Santarella-Mellwig, R., Ly-Hartig, TB., Asencio, C. et al. (2012). Coordination of kinase and phosphatase activities by Lem4 enables nuclear envelope reassembly during mitosis. *Cell, 150*, 122-35. ↗

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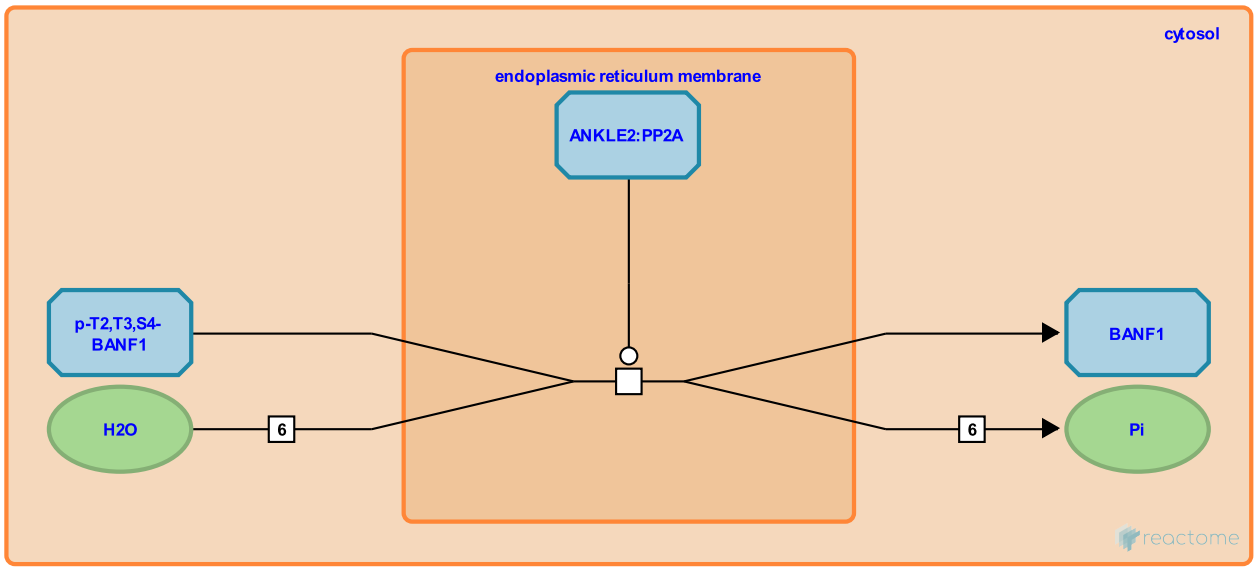
PP2A dephosphorylates BANF1 ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-2995388

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



The PP2A complex that contains the regulatory subunit PPP2R2A (B55-alpha) is the only phosphatase essential for mitotic exit (Schmitz et al. 2010). It is also necessary for BANF1 (BAF) dephosphorylation in anaphase/telophase. ANKLE2 binds the PP2A complex that contains the B55-alpha regulatory subunit and facilitates BANF1 dephosphorylation (Asencio et al. 2012).

Preceded by: ANKLE2 binds PP2A

Followed by: BANF1 binds chromatin, EMD/TMPO/LEMD3/LEMD2 and lamins

Literature references

Hyman, AA., Poser, I., Hudecz, O., Peters, JM., Held, M., Hutchins, JR. et al. (2010). Live-cell imaging RNAi screen identifies PP2A-B55alpha and importin-beta1 as key mitotic exit regulators in human cells. *Nat. Cell Biol., 12*, 886-93. ↗

Wallenfang, MR., Mall, M., Davidson, IF., Santarella-Mellwig, R., Ly-Hartig, TB., Asencio, C. et al. (2012). Coordination of kinase and phosphatase activities by Lem4 enables nuclear envelope reassembly during mitosis. *Cell, 150*, 122-35. ↗

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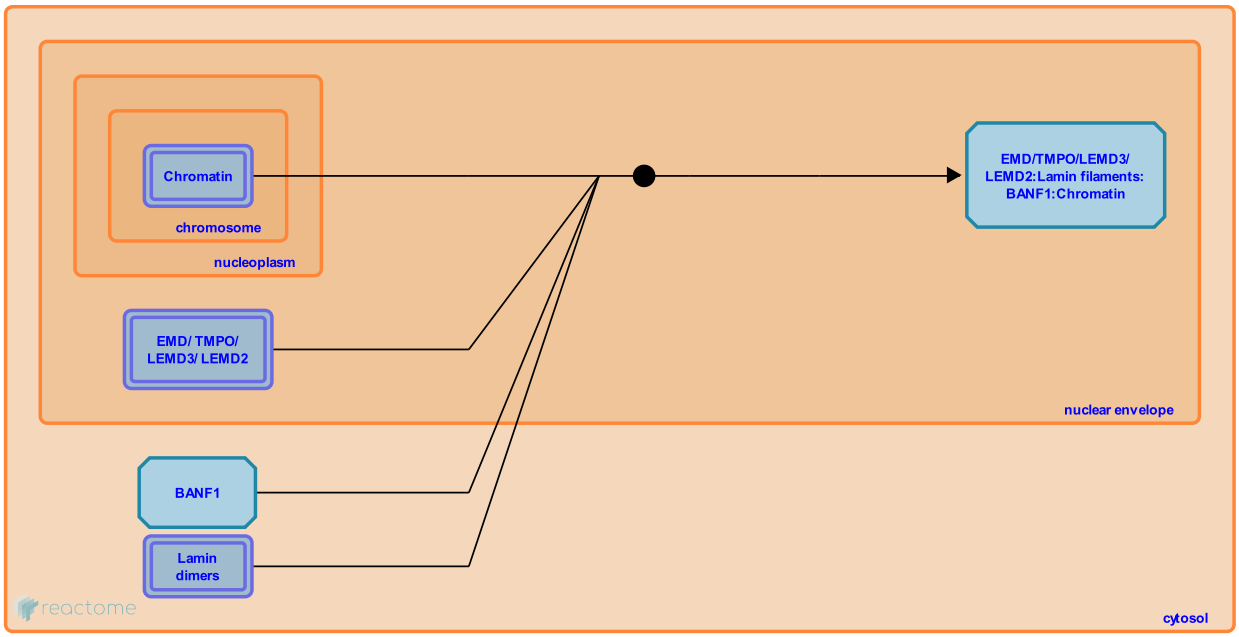
BANF1 binds chromatin, EMD/TMPO/LEMD3/LEMD2 and lamins ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-2995376

Type: binding

Compartments: nuclear envelope, cytosol, chromosome



In late anaphase/early telophase, the separated sister chromatids usually coalesce into a single "chromatin disc". At the surface of the chromatin disc, there is an accumulation of dephosphorylated BANF1 (BAF) (Kaufmann et al. 2016), as well as proteins EMD (emerin), TMPO (LAP2beta), LEMD3 (MAN1), LEMD2 (LEM2) and lamins (Haraguchi et al. 2008, Asencio et al. 2012). Collectively, these interactions promote enclosure of the separated sister chromatids with nuclear membranes (Anderson et al. 2009).

Preceded by: PP2A dephosphorylates BANF1

Literature references

Kostrhon, S., Kukolj, E., Opravil, S., Slade, D., Brachner, A., Kaufmann, T. et al. (2016). SIRT2 regulates nuclear envelope reassembly through ANKLE2 deacetylation. *J. Cell. Sci., 129*, 4607-4621. ↗

Hiraoka, Y., Haraguchi, T., Osakada, H., Koujin, T., Mori, C., Kojidani, T. et al. (2008). Live cell imaging and electron microscopy reveal dynamic processes of BAF-directed nuclear envelope assembly. *J. Cell. Sci., 121*, 2540-54. ↗

Hetzer, MW., Hsiao, JP., Vargas, JD., Anderson, DJ. (2009). Recruitment of functionally distinct membrane proteins to chromatin mediates nuclear envelope formation in vivo. *J. Cell Biol., 186*, 183-91. ↗

Wallenfang, MR., Mall, M., Davidson, IF., Santarella-Mellwig, R., Ly-Hartig, TB., Asencio, C. et al. (2012). Coordination of kinase and phosphatase activities by Lem4 enables nuclear envelope reassembly during mitosis. *Cell, 150*, 122-35. ↗

Editions

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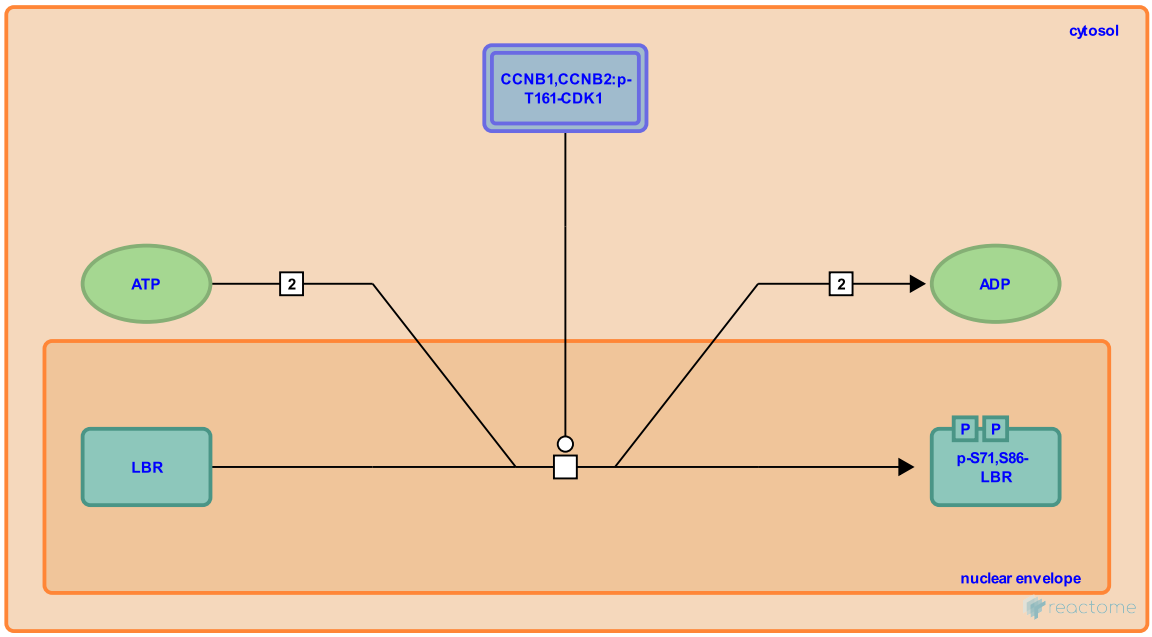
CDK1 phosphorylates LBR ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-9624800

Type: transition

Compartments: nuclear envelope, cytosol



During mitosis, CDK1 phosphorylates LBR (lamin B receptor) on N-terminal serine residues S71 and S86. S71 is the major CDK1 phosphorylation site in LBR (Tseng and Chen 2011).

Followed by: LBR binds KPNB1

Literature references

Tseng, LC., Chen, RH. (2011). Temporal control of nuclear envelope assembly by phosphorylation of lamin B receptor. *Mol. Biol. Cell, 22*, 3306-17. ↗

Editions

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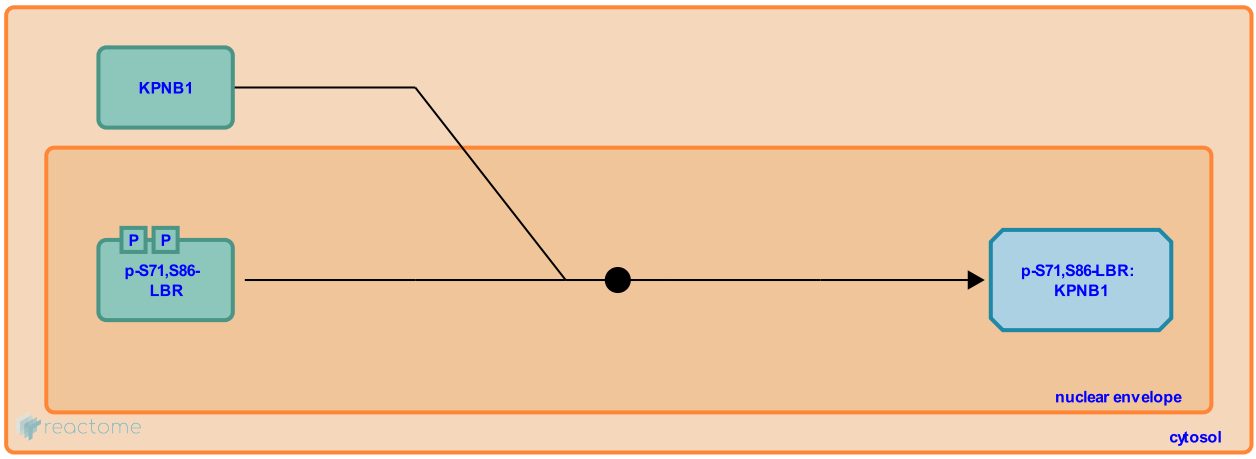
LBR binds KPNB1 ↗

Location: Initiation of Nuclear Envelope (NE) Reformation

Stable identifier: R-HSA-9624798

Type: binding

Compartments: nuclear envelope, cytosol



Phosphorylation of LBR (lamin B receptor) at serine residue S71 drives binding of LBR to KPNB1 (importin beta) (Lu et al. 2010). This prevents premature association of nascent nuclear membranes with chromatin in anaphase (Tseng and Chen 2011). Dephosphorylation of this site is suggested to promote NE reassembly (Tseng and Chen 2011).

Preceded by: CDK1 phosphorylates LBR

Literature references

Lu, X., Ji, J., Lu, Q., Shi, Y., Jiang, Q., Ma, Y. et al. (2010). Requirement for lamin B receptor and its regulation by importin {beta} and phosphorylation in nuclear envelope assembly during mitotic exit. *J. Biol. Chem., 285*, 33281-93. ↗

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