CELL DIVISION

Repo-Man's extra exit strategy

Repo-Man actually has two distinct anaphase functions

Protein phosphatase 1 γ (PP1 γ) is recruited to mitotic chromatin at anaphase by its regulatory subunit Repo-Man (also known as CDCA2), where it promotes dephosphorylation of histone H3 and chromosome decondensation. Vagnarelli *et al.* now confirm these results and show that Repo-Man actually has two distinct anaphase functions that are mediated by opposite ends of the protein: chromatin remodelling and coordination of nuclear envelope reformation.

The authors previously showed that Repo-Man is phosphorylated *in vitro* by cyclin-dependent kinase 1 (CDK1)–cyclin B. Here, they identify Thr412 as a key residue for this reaction: mutating Thr412 to Ala led to premature localization

of Repo-Man to chromosomes. However, this early chromosomal localization was blocked if the PP1 γ -binding site was mutated, suggesting that PP1 γ is also required for this localization. Therefore, they conclude that CDK1–cyclin B phosphorylates Repo-Man at multiple sites to prevent PP1 γ binding and keep it off chromosomes until anaphase.

They then identified factors that interact with Repo-Man during mitotic exit. Pull-down experiments detected not only the expected PP1 γ subunits and histones but also importin- β and nucleoporin 153, factors that are important for nuclear envelope reassembly. Repo-Man partially colocalized with importin- β at the periphery of chromosomes in anaphase. Moreover, importin- β bound directly to an amino-terminal domain of Repo-Man (residues 1–135). This interaction was specific to anaphase, independent of the PP1 γ -binding site and negatively controlled by CDK-mediated phosphorylation of Repo-Man.

The idea that Repo-Man might regulate not only chromosome organization but also early steps in nuclear envelope reassembly at the chromosome periphery was supported by analysis of its dynamic localization. A carboxy-terminal (403–1023) fragment of Repo-Man localized to bulk chromatin rapidly after anaphase but was not at the periphery of chromosomes, whereas an N-terminal (1–397) region accumulated exclusively at the periphery a few minutes later.

Moreover, Repo-Man was required for both normal chromatin reorganization in G1 and nuclear reassembly. RNA interference-mediated depletion of Repo-Man interfered with normal histone H3 dephosphorylation and reduced heterochromatin protein 1 α accumulation on chromatin and subsequent assembly of heterochromatin foci during mitotic exit. It also resulted in irregular nuclear morphology, which the authors attributed to defective importin- β localization.

The authors propose that the N-terminal section of Repo-Man is important for organizing components needed early on for nuclear reassembly, whereas the C-terminal section is required for PP1 γ -mediated modification of histone H3 to promote chromatin remodelling. Further work is needed to determine the mechanisms by which the N-terminal and C-terminal domains of Repo-Man control its different anaphase functions. However, this study highlights the importance of having a common regulator coordinating chromosome condensation and nuclear envelope reassembly.

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ORIGINAL RESEARCH PAPER Vagnarelli, P. *et al.* Repo-Man coordinates chromosomal reorganization with nuclear envelope reassembly during mitotic exit. *Dev. Cell* **21**, 328–342 (2011)
FURTHER READING Qian, J. *et al.* PP1/Repo-Man dephosphorylates mitotic histone H3 at T3 and regulates chromosomal Aurora B targeting. *Curr. Biol.* **21**, 766–773 (2011) | Wurzenberger, C. & Gerlich, D. W. Phosphatases: providing safe passage through mitotic exit. *Nature Rev. Mol. Cell Biol.* **12**, 469–482 (2011)