GETTY

Cycling through acetylation

The cohesin complex, the core components of which are structural maintenance of chromosomes 1 (Smc1), Smc3 and sister chromatid cohesion 1 (Scc1), holds sister chromatids together from their replication in S phase until their separation in mitosis, and the establishment of cohesion depends on the acetylation of Smc3 by the acetyltransferase establishment of cohesion 1 (Eco1). Smc3 is deacetylated at anaphase, but the importance of this, and the deacetylase responsible, were unknown. Two groups now identify Hos1 as the enzyme that deacetylates Smc3 in *Saccharomyces cerevisiae*, and reveal an important role for the Smc3 acetylation–deacetylation cycle in establishing sister chromatid cohesion.

To identify the Smc3 deacetylase, Borges *et al.* and Beckouët *et al.* screened 11 *S. cerevisiae* strains, each of which had one of the 11 known deacetylase genes deleted, for acetylated Smc3. Increased levels of acetylated Smc3 were observed in extracts from *Hos1*-null cells under various conditions, including in G1-arrested cells (which do not normally have acetylated Smc3), indicating that Hos1 is the Smc3 deacetylase.

So, why is Smc3 deacetylation triggered at anaphase? At the onset of anaphase Scc1 is cleaved by separase, which releases cohesin from chromosomes to trigger chromosome segregation. Expression of a Scc1 variant that cannot be cleaved by separase prevents Smc3 deacetylation, whereas cells expressing a Scc1 variant that is cleaved when the tobacco etch virus protease is expressed undergo Smc3 deacetylation. These data suggest that Scc1 cleavage is necessary to trigger deacetylation. To confirm this *in vitro* Beckouët *et al.* reconstituted Smc3 deacetylation and found that it is effective in the presence of Hos1 and active separase. Borges *et al.* showed that Smc3 deacetylation also occurs *in vitro* in the presence of a nuclease that fragments chromosomal DNA but not cohesin. This suggests that the cohesin complex is protected from deacetylation when it is bound to chromosomes and that its dissociation from chromosomes at anaphase enables Smc3 deacetylation.

But why is Smc3 deacetylation important? To investigate this, both groups expressed a version of Eco1 that can be depleted from cells in a temperature-sensitive manner. Beckouët *et al.* found that depletion of Eco1 causes cohesion defects and that these cells inherit little or no acetylated Smc3 from the previous cell cycle in the presence of Hos1, as expected. Although acetylated Smc3 persists in the next cell cycle in the absence of Eco1 and Hos1, this does not rescue cohesion defects. Borges *et al.* also show that depletion of Hos1, which results in increased levels of acetylated Smc3, does not compensate for reduced Eco1 function. These data suggest that it is the *de novo* acetylation of unacetylated Smc3 that is essential for establishing cohesion during S phase.

In short, these papers show that Hos1 deacetylates Smc3 at anaphase, after cohesin has been released from the chromosomes, to ensure that there is a pool of unacetylated Smc3 available for *de novo* Eco1-mediated acetylation, and thus efficient cohesion, in the next cell cycle.

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ORIGINAL RESEARCH PAPERS Borges, V. *et al.* Hos1 deacetylates Smc3 to close the cohesin acetylation cycle. *Mol. Cell* **39**, 677–688 (2010) | Beckouët, F. *et al.* An Smc3 acetylation cycle is essential for establishment of sister chromatid cohesion. *Mol. Cell* **39**, 689–699 (2010)

FURTHER READING Hirano, T. At the heart of the chromosome: SMC proteins in action. *Nature Rev. Mol. Cell Biol.* **7**, 311–322 (2006)