Evidence that nucleosome arrays antagonise the folding of genomic DNA into condensed mitotic chromosomes by loop-extruding condensin

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Résumé

DNA-translocases of the SMC family, such as condensin and cohesin, shape the 3D genome by extruding DNA into loops, but how such a loop-extrusion reaction is achieved in the context of a crowded chromatinized genome remains poorly understood. Particularly unclear is the impact of tightly packed nucleosome arrays on DNA binding and loop-extrusion by SMC protein complexes. Using a combination of Hi-C, quantitative ChIP-seq, reconstituted nucleosome arrays, proteomics and chromosome imaging, we found that nucleosome arrays antagonize the chromatin-folding activity of the condensin SMC complex in vivo. Condensin loads onto DNA upon mitotic entry and drives mitotic chromosome condensation by extruding chromatin into arrays of loops. Using in vitro reconstituted nucleosome arrays we show that condensin purified from fission yeast cells fails to bind nucleosomal DNA, suggesting therefore that condensin must rely on auxiliary factors to access genomic DNA in the context of chromatin. In agreement, we further show that fission yeast condensin associates with the histone chaperone FACT and the ATP-dependent nucleosome remodeler ChD1 in vivo. We found that depleting FACT during mitosis causes a general loss of nucleosomes, which correlates with an enhancement of both metaphase chromatin folding and mitotic chromosome condensation. Consistent with a causal relationship, reducing histone gene dosage and thereby nucleosome occupancy phenocopies the mitotic depletion of FACT. Thus, nucleosome integrity hinders mitotic chromosome assembly. We provide evidence that condensin occupancy is not increased upon depletion of FACT, and that FACT impinge on mitotic chromosome condensation independently of RNA Pol II or cohesin. We therefore propose that while nucleosomes compact the genome they hinder the folding of chromatin and the condensation of mitotic chromosomes. The impact of nucleosome arrays and the role played by chromatin remodelers on the extrusion of a chromatinized DNA by condensin will be discussed.

Mots-Clés: condensin, fact, chd1

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