

Cohesin-mediated chromatin folding constrains homology search during DNA repair

DNA break repair by homologous recombination (HR) entails a search for homology carried out by a specialized nucleoprotein filament (NPF). The search mechanism remains elusive, notably its interplay with the folding of chromatin in the nucleus. We show in the tractable model system *S. cerevisiae* that it takes place in the reorganized context of individualized metaphase-like chromosomes structured by cohesins into arrays of chromatin loops. Functionally, cohesin-mediated chromatin folding primarily constrains homology search intra-chromosomally, which provides a kinetic advantage for DNA strand invasion at intra- over inter-chromosomal donors. The sister chromatid plays a secondary inhibitory function. Using a *pds5* mutant to artificially enlarge cohesin loops, we further show that the DSB region acts as a cohesin (and thus directional loop expansion) barrier, which promotes donor identification in *cis*. Cohesin thus constrains homology search intra-chromosomally in multiple ways, inhibiting and orienting genome-wide homology search.

Auteurs principaux: THIERRY, AGNES (Régulation spatiale des génomes, Institut Pasteur, CNRS UMR3525, 75015 Paris, France); Dr PIAZZA, AURELE (Régulation spatiale des génomes, Institut Pasteur, CNRS UMR3525, 75015 Paris, France /Univ Lyon, ENS, UCBL, CNRS, INSERM, Laboratory of Biology and Modelling of the Cell, UMR5239, U 1210, F-69364, Lyon, France); FABIEN, GIRARD (Régulation spatiale des génomes, Institut Pasteur, CNRS UMR3525, 75015 Paris, France); Dr BORDELET, HELENE (Régulation spatiale des génomes, Institut Pasteur, CNRS UMR3525, 75015 Paris, France / Univ Lyon, ENS, UCBL, CNRS, INSERM, Laboratory of Biology and Modelling of the Cell, UMR5239, U 1210, F-69364, Lyon, France); Dr SAVOCCO, JEROME (Univ Lyon, ENS, UCBL, CNRS, INSERM, Laboratory of Biology and Modelling of the Cell, UMR5239, U 1210, F-69364, Lyon, France); Dr KOSZUL, ROMAIN (Régulation spatiale des génomes, Institut Pasteur, CNRS UMR3525, 75015 Paris, France)

Orateur: Dr BORDELET, HELENE (Régulation spatiale des génomes, Institut Pasteur, CNRS UMR3525, 75015 Paris, France / Univ Lyon, ENS, UCBL, CNRS, INSERM, Laboratory of Biology and Modelling of the Cell, UMR5239, U 1210, F-69364, Lyon, France)