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Genome stability: Interplay between DSB, chromatin mobility and SMC complexes

The genome is susceptible to multiple damages, including DNA double-strand breaks (DSBs) and replication stress. Chromosome configuration of the Saccharomyces cerevisiae plays a critical role in maintaining genome integrity upon damage, as only DSBs near pericentromeres cause an increase in global mobility, protective for the genome (1). Here, we want to understand what makes the pericentromere a special region. An interesting candidate is the conserved Smc5/6 complex that is part of the SMCs (structural maintenance complexes). This complex is enriched at centromeres, is recruited to DSBs and in yeast interacts with both microtubules and DNA (2,3). The interaction with microtubules is mediated by three lysines in the Smc5 protein (K624, K631 and K667). We hypothesized that mutations in these residues would impact chromatin mobility around the pericentromere. We chose to mutate the two lysines (K624 and K631), present in the characteristic hinge of Smc5. These mutations lead to increased chromatin mobility near the pericentromere, even in the absence of damage, in a microtubule-dependent manner. Microtubules are involved in genome mobility as well as maintaining the tension between kinetochores, which is essential for the error-free chromosome segregation. Interestingly, we show that the distances between spindle pole bodies in dividing cells, but not the distance between the spindle pole and the centromere, increase in the mutant. Moreover, the mutant presents a declustering of centromeres. These last observations suggest that mutations may cause a tension defect. Altogether, our results suggest a possible role of Smc5/6 in maintaining the tension when chromosomes segregate that could be correlated with the increase in chromosome mobility.

References:
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