DNA Catenation Maintains Structure of Human Metaphase Chromosomes - DTU Orbit

DNA Catenation Maintains Structure of Human Metaphase Chromosomes

Mitotic chromosome structure is pivotal to cell division but difficult to observe in fine detail using conventional methods. DNA catenation has been implicated in both sister chromatid cohesion and chromosome condensation, but has never been observed directly. We have used a lab-on-a-chip microfluidic device and fluorescence microscopy, coupled with a simple image analysis pipeline, to digest chromosomal proteins and examine the structure of the remaining DNA, which maintains the canonical 'X' shape. By directly staining DNA, we observe that DNA catenation between sister chromatids (separated by fluid flow) is composed of distinct fibres of DNA concentrated at the centromeres. Disrupting the catenation of the chromosomes with Topoisomerase IIa significantly alters overall chromosome shape, suggesting that DNA catenation must be simultaneously maintained for correct chromosome condensation, and destroyed to complete sister chromatid disjunction. In addition to demonstrating the value of microfluidics as a tool for examining chromosome structure, these results lend support to certain models of DNA catenation organization and regulation: in particular, we conclude from our observation of centromere-concentrated catenation that spindle forces could play a driving role in decatenation and that Topoisomerase IIa is differentially regulated at the centromeres, perhaps in conjunction with cohesin.

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