

Bottom-up engineering of extra artificial chromosomes reveal principles of genome folding

Cohesin-dependent chromatin loops bring together distal regulatory elements and gene promoters in mammals and compact metaphase chromosome during budding yeast mitosis. Loop extrusion is a ubiquitous model that stipulates that SMC rings organize genomes by gradually enlarging small DNA loops into larger structures. Transcription and specific DNA-binding proteins were shown to be involved, but current investigations are hindered by the complex nature of chromosomes that display an intertwined, multi-scale network of structures resulting from metabolic processes, protein binding, supercoiling, loops, cohesion and compaction. We developed a bottom-up approach to investigate chromosome folding using an artificial, non-coding Mb long chromosome implanted into the yeast genome. HiC experiments show that a DNA with a low GC content (20%) can compact in mitosis in the absence of positioned loops and stripes. These features appear on a chromosome that contains a 40% GC content and correlate with an enrichment at specific sites of cohesin and polymerase II, respectively. Introduction of inducible transcription units create DNA stripes that do not depend on cohesin binding nor contribute to cohesin dependent DNA loop borders.

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