Experimental/theoretical approach for chromosome conformation changes in response to an internal chemical cue

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Abstract:

In this JC, I focus on an experimental/mathematical study for chromosome conformation changes in response to an internal chemical cue. Chromosomes are folded into cells in a nonrandom fashion, with particular genomic loci occupying distinct spatial regions, whereas it still remains unclear how the spatial organization of a chromosome governs its functions, such as recombination or transcription. In budding yeast *Saccharomyces cerevisiae*, mating-type switching [1] is induced by a DNA double-strand break (DSB) at the *MAT* locus on chromosome III, followed by homologous recombination between the cut *MAT* locus and one of two donor loci (*HMLα* and *HMR**a***). Previous studies have suggested that after the DSB induction chr III undergoes refolding in *MAT**a*** cells, and the chromosome refolding directs the *MAT* locus to recombine with *HMLα* [2]. In the paper by B. Avsaroglu, *et al*., *PNAS (2016)*, http://www.pnas.org/content/113/45/E6929.abstract [3], they propose a quantitative model of mating-type switching predicated on the assumption of DSB-induced chromosome refolding, which also takes into account the previously measured stochastic dynamics and polymer nature of yeast chromosomes. Using quantitative fluorescence microscopy, they measured changes in the distance between the donor (*HMLα*) and *MAT* loci after the DSB and found agreement with the theory. Their results provide an example of functional organization of chromosomes so as to direct homology search during recombination.

References:

[1] Lee C-S, Haber JE, *Mating-type gene switching in Saccharomyces cerevisiae. Microbiol Spectr* **3**, A3–A0013, 2014, (2015).

[2] Coïc E, Richard GF, Haber JE, *Saccharomyces cerevisiae donor preference during mating-type switching is dependent on chromosome architecture and organization. Genetics* **173**, 1197–1206 (2006).

[3] B. Avsaroglu, *et al*., *Chromosome-refolding model of mating-type switching in yeast. PNAS* http://www.pnas.org/content/113/45/E6929.abstract , (2016).