Compartmentalization of an artificial bacterial chromosomes in budding yeast

Léa Meneu[1,2,Ψ], Christophe Chapard[1,Ψ], Jacques Serizay[1,Ψ] ,Myriam Ruault[3], Amaury Bignaud[1,2], Géraldine Gourgues[4], Carole Lartigue[4], Aurèle Piazza[1], Angela Taddei[3], Frédéric Beckouët[5], and Romain Koszul[1]

[1] Institut Pasteur, CNRS UMR 3525, Université Paris Cité, Unité Régulation Spatiale des Génomes, 75015 Paris, France
[2] Sorbonne Université, College Doctoral, 75005 Paris, France
[3] Institut Curie, PSL University, Sorbonne Université, CNRS, Nuclear Dynamics, 75005 Paris, France
[4] Univ. Bordeaux, INRAE, Biologie du Fruit et Pathologie, UMR 1332, F-33140 Villenave d'Ornon, France
[5] Intégrative (CBI), Université de Toulouse, CNRS, UPS, 31062, Toulouse, France

DNA transfer is often considered as a key driver of evolution, promoting higher levels of genetic complexity. The integration of exogenous sequences into a genome raises immediate questions regarding its potential impact on essential DNA-related processes such as genetic regulation, DNA repair, 3D chromosome organization and segregation. Indeed, these sequences are processed and organized by transcription factors and chromatin-associated proteins of the host genome, obeying new rules under which they have not co-evolved, and which cast them in a different light.

To directly explore the causal relationships between the DNA sequence composition and the spontaneous loading and activity of these DNA-associated complexes in the absence of co-evolution, we characterized chromatin assembly and activity in yeast strain carrying exogenous *Mycoplasma mycoides mycoides* chromosome that diverged from eukaryotic sequences over 1.5 billion years ago. We have fused this bacterial chromosome with chromosome XVI to study the relationships between DNA sequence, chromatin composition, activity, folding and compartmentalization. Using targeted translocations, Hi-C, RNA-seq, FISH imaging and ChIP-seq, we explore the behavior of these "hybrid" chromosomes at different stages of the cell cycle. In particular, we show how inactive AT-rich regions of *M. mycoides* self-associate in 3D, leading to the spontaneous formation of inactive chromosome compartments by an unknown mechanism.