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Single-cell DNA replication profiling identifies spatiotemporal developmental dynamics of chromosome organization

Hisashi Miura, Saori Takahashi, Rawin Poonperm, Akie Tanigawa, Shin-Ichiro Takebayashi & Ichiro Hiratani⊠

Nature Genetics (2019) | Download Citation ± 14 Accesses

Abstract

In mammalian cells, chromosomes are partitioned into megabase-sized topologically associating domains (TADs). TADs can be in either A (active) or B (inactive) subnuclear compartments, which exhibit early and late replication timing (RT), respectively. Here, we show that A/B compartments change coordinately with RT changes genome wide during mouse embryonic stem cell (mESC) differentiation. While A to B compartment changes and early to late RT changes were temporally inseparable, B to A changes clearly preceded late to early RT changes and transcriptional activation. Compartments changed primarily by boundary shifting, altering the compartmentalization of TADs facing the A/B compartment interface, which was conserved during reprogramming and confirmed in individual cells by single-cell Repli-seq. Differentiating mESCs altered single-cell Repli-seq profiles gradually but uniformly, transiently resembling RT profiles of epiblast-derived stem cells (EpiSCs), suggesting that A/B compartments might also change gradually but uniformly toward a primed

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