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Controlling origins of replication

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The number of replication origin sequences in the genome does not change during the lifespan of an organism, but it does vary according to the developmental stage. In the early embryo, the greater number of active origins may be supported by the higher density of origin recognition proteins and by the less constrained genomic regulation. In later stages, more concerned with differentiation than proliferation, epigenetic marking restrains most potential origins and restricts the speed of DNA replication and cell division, with the rate of replication fork movement remaining more or less constant. In the August 8 Cell, Mauro Anglana and colleagues at the Institut Curie show that the speed of replication fork movement varies depending on the size of the nucleotide pool, and it is this which determines the activity of origins within a cell and hence the speed of cell division (*Cell* 2003, **114:**385-394).

Using the dynamic molecular combing (DMC) procedure, Anglana *et al.* studied the replication pattern of three cell lines that acquired resistance to the inhibitor coformycin through amplification of a multigene locus including an origin already under study, oriGNAI3. Replication forks traveled across the amplified region at different speeds in different DNA fibers in the same cell. Seven repeatedly firing loci were visualized using the DMC technique, four of which were in an extensively analyzed region - including highly AT-rich matrix attachment regions - suggesting a role for these regions in DNA replication. The efficiency of firing of these four origins depended on culture conditions. A slower fork speed was compensated for by firing additional replication origins, while firing the predominant oriGNAI3 origin in this region resulted in the silencing of surrounding weaker origins.

"In mammalian cells, as in yeast models, not all the potential replication origins fire during S phase and the efficiency of some origins relies more on nucleotide availability and/or fork progression rate than on specific cis-sequences. Interestingly, the initiation sites identified within the sequenced part of the domain lie in intergenic regions and precisely co-map with previously identified A+T rich matrix attachment regions," conclude the authors.

References

1. Review: nuclear structure and DNA replication

2. *Cell*, [http://www.cell.com/]

3. Institut Curie, [http://www.curie.fr/recherche/index.cfm/lang/_gb.htm]

4. Dynamic molecular combing: stretching the whole human genome for high-resolution studies