DNA replication: from origin recognition to cell identity

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In multicellular eukaryotes, 30 000 to 50 000 DNA replication origins are activated at each cell division to permit the accurate duplication of our genome. Until very recently, only a very few of them were identified and they did not share a consensus sequence like in S. cerevisiae. We have proposed that they should be plastic and selected in connection with to the establishment of functional chromatin domains during cell differentiation and development. During the years, we analyzed their regulation during Xenopus development as well as in differentiating mouse cells. More recently we used a genome wide approach to identify and characterize them both in mouse and drosophila cells. Mouse embryonic stem cells were analyzed and the position of replication origins mapped both in the pluripotent or differentiating stage. We will describe the different characteristics of these origins, including their positioning, flexibility, CpG content, clustering, association with transcriptional units as well as their organization in domains during differentiation. Experiments aimed to reprogram DNA replication origins on chromosomes were also carried out. These results will be discussed in relationship with both genetic and epigenetic features of chromosome structure.

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