Choosing replication origins

After mitosis, cells prepare for the next round of DNA replication by assembling complexes of proteins on chromatin that will carry out the task of copying the genome. Pre-replication complexes (preRCs) assemble during telophase, but studies of the dihydrofolate reductase locus in mammalian cells have indicated that, during G1, genome. Prereplication complexes (preRCs) assemble during telophase, but studies of the dihydrofolate reductase locus in mammalian cells have indicated that, during G1, only a subset of preRCs are designated for use as origins of replication. On page 257, Li et al. demonstrate that the same is true for origins throughout the genome.

Li et al. compared origins used by mammalian cells in vivo with those chosen in isolated mammalian nuclei undergoing premature replication in frog cytoplasmic extracts. Comparison of the two sets of origins revealed that, soon after mitosis, few of the sites used matched. About two hours after mitosis, the sites used in vitro were clustered into domains surrounding in vivo sites, but the actual sites fired still did not necessarily correspond. This domain selection was previously suggested by examinations of the timing of replication of whole chromosomal domains and is known as the timing decision point.

Five hours after mitosis, the sites chosen in vitro were more likely to be the same sites used in vivo. This site selection is known as the origin decision point. Thus, as for the DHFR locus, the general choice of origins used is not random, but why origin selection should be regulated is unclear. Perhaps origins are placed near genes that encode replication proteins so that they are activated early by passage of the replication fork. Alternatively, origins may be regulated to prevent collision of RNA and DNA polymerases. If the latter is true, origin choice may change during differentiation to accommodate transcriptional differences.