

Replicative helicase, a key player of chromosome replication.

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DNA replication is an essential task to any living organism. In eukaryotes, multiple replication origins are used to replicate their large genomes. To achieve that any given origin is activated only once per cell cycle, the activation of the replicative helicase has been partitioned in two mutually exclusive steps along the cell cycle. During G1, origins are licensed and an inactive form of the helicase is loaded onto DNA, MCM2-7 double hexamer (DH). Upon entry into S-phase, origin activation takes place and a subset of the DH are converted into the active helicase or CMG. This activation allows the assembly of the replication machinery, known as a replisome, and DNA synthesis starts. These differentially regulated steps establish the replicative helicase as the main key player in chromosome replication regulation. Recently, both steps, origin licensing and helicase activation, have been reconstituted using purified proteins in budding yeast. These new powerful assays have just started to unveil the molecular mechanisms behind eukaryotic DNA replication. Recent advances on origin licensing in yeast and how these progress can be translated into new therapies will be presented.