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Eukaryotic DNA replication: Orchestrated Action of Multi-subunit Protein Complexes

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Abstract

Genome duplication is an essential process to preserve genetic information between generations. The eukaryotic cell cycle is composed of functionally distinct phases: G1, S, G2, and M. One of the key replicative proteins that participate at every stage of DNA replication is the Mcm2-7 complex, a replicative helicase. In the G1 phase, inactive Mcm2-7 complexes are loaded on the replication origins by replication-initiator proteins, ORC and Cdc6. Two kinases, S-CDK and DDK, convert the inactive origin-loaded Mcm2-7 complex to an active helicase, the CMG complex in the S phase. The activated CMG complex begins DNA unwinding and recruits enzymes essential for DNA synthesis to assemble a replisome at the replication fork. After completion of DNA synthesis, the inactive CMG complex on the replicated DNA is removed from chromatin to terminate DNA replication. In this review, we will discuss the structure, function, and regulation of the molecular machines involved in each step of DNA replication.

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