The Origin Recognition Complexis a six-subunit ATP-dependent DNA-binding protein encoded in yeast by ORC1-6. ORC is a central component for eukaryotic DNA replication, and binds chromatin at replication origins throughout the cell cycle. ORC directs DNA replication throughout the genome and is required for its initiation. ORC bound at replication origins serves as the foundation for assembly of the pre-replicative complex, which includes Cdc6p, Tah11p, and the Mcm2-7p complex. Pre-RC assembly during G1 is required for replication licensing of chromosomes prior to DNA synthesis during S phase. Cell cycle-regulated phosphorylation of Orc2p, Orc6p, Cdc6p, and MCM by the cyclin-dependent protein kinase Cdc28p regulates initiation of DNA replication, including blocking reinitiation in G2/M phase. In yeast, ORC also plays a role in the establishment of silencing at the mating-type loci HML and HMR. ORC participates in the assembly of transcriptionally silent chromatin at HML and HMR by recruiting the Sir1p silencing protein to the HML and HMR silencers. Both Orc1p and Orc5p bind ATP, though only Orc1p has ATPase activity. The binding of ATP by Orc1p is required for ORC binding to DNA and is essential for cell viability. The ATPase activity of Orc1p is involved in formation of the pre-RC. ATP binding by Orc5p is crucial for the stability of ORC as a whole. Only the Orc1p-5p subunits are required for origin binding; Orc6p is essential for maintenance of pre-RCs once formed. Interactions within ORC suggest that Orc2p-3p-6p may form a core complex. ORC homologs have been found in various eukaryotes, including fission yeast, insects, amphibians, and humans.