The Mcm2-7 family is a group of six proteins that are highly conserved in all eukaryotes, with homologs having also been identified in Archaea. They are required for cell cycle progression and DNA replication initiation and elongation. Three of the geneswere originally identified as Cell Division Cycle mutants. In S. cerevisiae, each of the six Mcm2-7 proteinsis essential for viability. Mcm2-7pform a ring-shaped heterohexamerthat binds chromosomal replication origins and assembles as part of the prereplicative complexduring the G1 phase of the cell cycle. Other components of the pre-RC include the origin recognition complex, Cdc6p, and Tah11p. ORC activation of the origin DNA leads to the binding of the MCM proteins to the unwound origin. At the G1-S transition, ORC and the MCM proteins are phosphorylated by S-phase-specific cyclin-dependent kinaseswhich transform the pre-RC into an active replication complex. The MCM complex translocates along the DNA with the replication fork during S phase. Other S- and M-phase Cdks block the rebinding of MCMs to origin chromatin and prevent reinitiation of replication until mitosis is complete.Mcm2-7p undergo cell cycle-regulated cellular localization, accumulating in the nucleus during G1, only to be excluded from the nucleus later in the cell cycle. Tah11p exhibits this same cell cycle-regulated cellular localization pattern, and the nuclear accumulation of these proteins during G1 is interdependent. The MCM complex appears to interact with Tah11p prior to binding replication origin chromatin during pre-RC assembly. Each MCM protein is a member of the AAA+ class of ATPases and has an ATP binding site, although no individual MCM protein alone contains significant ATPase activity. ATPase activity is produced only by a combination of at least two MCM proteins, requiring a catalytic residue from one subunit and an ATP binding site from another, consistent with the location of ATP sites at the interfaces of AAA+ protein complexes. Pairwise studies of the six subunits have revealed ATPase activity in only three pairs: Mcm2/6p, Mcm4/7p, and Mcm3/7p. The majority of ATPase activity, however, is produced by the MCM complex as a whole. DNA helicase activity is associated only with Mcm4p, Mcm6p, and Mcm7p, which can also form a doughnut-shaped heterohexamer. This replicative DNA helicase complexbinds the leading strand and unwinds DNA in an ATP-dependent manner with 3' to 5' polarity.