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Mcm10 regulates DNA replication elongation by stimulating the CMG replicative helicase.

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Author information

Abstract

Activation of the Mcm2-7 replicative **DNA** helicase is the committed step in eukaryotic **DNA** replication initiation. Although Mcm2-7 activation requires binding of the helicase-activating proteins Cdc45 and GINS (forming the CMG complex), an additional protein, Mcm10, drives initial origin **DNA** unwinding by an unknown mechanism. We show that Mcm10 binds a conserved motif located between the oligonucleotide/oligosaccharide fold (OB-fold) and A subdomain of Mcm2. Although buried in the interface between these domains in Mcm2-7 structures, mutations predicted to separate the domains and expose this motif restore growth to conditional-lethal *MCM10* mutant cells. We found that, in addition to stimulating initial **DNA** unwinding, Mcm10 stabilizes Cdc45 and GINS association with Mcm2-7 and stimulates replication elongation in vivo and in vitro. Furthermore, we identified a lethal allele of *MCM10* that stimulates initial **DNA** unwinding but is defective in replication elongation and CMG binding. Our findings expand the roles of Mcm10 during **DNA** replication and suggest a new model for Mcm10 function as an activator of the CMG complex throughout **DNA** replication.

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KEYWORDS: Cdc45/Mcm2–7/GINS; **DNA** replication fork; S. cerevisiae; cell cycle; reconstituted **DNA** replication

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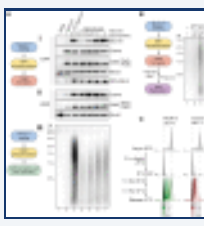

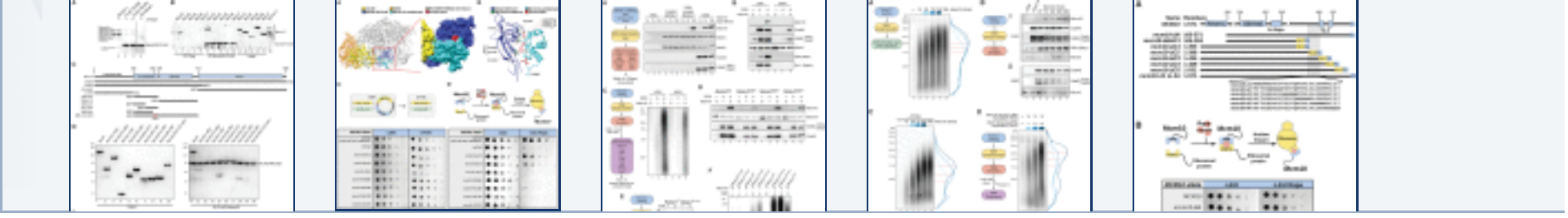

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