Overview of DNA replication in prokaryotes

In prokaryotes, the initiator protein DnaA binds with the 9-mer motif and starts the unwinding from 13-mer motif. This unwinding may require a number of other factors like HU/IHF (integration host factor), FIS (factor for inversion stimulation) etc. which are DNA bending proteins. DnaA also recruits DNA helicase, DnaB and helicase loader, DnaC, in an inactive complex. Once bound to the appropriate site at the origin, DnaC directs the assembly of DnaB around the ssDNA formed by the action of initiator. This is followed bythe release of helicase loader DnaC. One helicase with different polarity is loaded at each of the two ssDNA formed at the origin.

The helicase then recruits primase, DnaG which synthesizes the primer. The complex of helicase and primase is known as primosome. Next, DNA pol III holoenzyme which is a large multiprotein complex is recruited and sliding clamps are assembled at primer:template junction resulting in the synthesis of leading strand. Each pol III holoenzyme has two copies of core DNA pol III and a copy of γ-complex. As helicase continues to unwind the duplex DNA more ssDNA is exposed, the primase synthesizes short primer and DNA pol III holoenzyme initiate the synthesis of lagging strand. The DNA pol III holoenzyme interacts with the DNA helicase, DnaB through τ-subunit of the clamp loader. The complex of helicase, primase and DNA pol III holoenzyme assembled at the replication fork is known as replisome. One of the pol III core enzymes is involved in the replication of leading strand while the other is involved in the replication of lagging strand. Once the core enzyme involved in the synthesis of lagging strand completes the synthesis of one Okazaki fragment, it is released from the sliding clamp. Then a new primer is synthesized by the primase and the clamp loader assembles a new sliding clamp which engages the core enzyme for synthesis of another Okazaki fragment. This view of DNA replication is commonly known as the Trombone model (Fig. 3) which suggests the coordinated activity of two DNA polymerases at the replication fork.

Sometimes there may be a premature termination of replication. So the whole replication machinery is reorganized and reassembled to continue DNA synthesis. Three different proteins, RecF, RecO and RecR together make a complex that help in the recruitment of the complete machinery back to the DNA to continue the process of DNA synthesis.

Due to circular double stranded DNA, the DNA replication of prokaryotes proceeds via bidirectional synthesis. As the replication forks move ahead, the synthesis of leading and lagging strands lead to the formation of θ shape. So, sometimes the replication of such circular DNA is also referred to as θ-replication (Fig. 4).

Once the replication of DNA is complete, it should be terminated. These termination sites have been well characterized in E. coli and are referred to as ter sites. A total of 6 ter sites have been recognized (terA, terB, terC, terD, terE and terF) which bind with ter binding protein (TBP) or Tus protein. The binding of these proteins inhibit the helicase and disrupts the process of DNA synthesis. However, it has been found that these termination zones are not essential to terminate DNA replication. Once the replication of the bacterial circular DNA molecule is completed, the resulting two DNA molecules remain linked together

as catenanes. Type II topoisomeraes break one of the dsDNA resulting in separation of the catenanes (Fig. 4) thus completing DNA replication.