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Sequential Binding of SeqA Protein to Hemi-methylated GATC Sequences Maintains Chromosome Integrity

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GATC sequences of *E. coli* chromosome is methylated by Dam methyltransferase at the 6-amino group of the adenine residue. Following replication, GATC sites are in a hemi-methylated state; the parent strand retains its methylation while the nascent strand lacks methylation. Discrimination of the newly synthesized unmethylated strand from the parental methylated strand is necessary for methyl-directed mismatch repair system composed of MutH, L and S proteins. Binding of SeqA protein to the hemimethylated origin of chromosomal replication (*oriC*) inhibits chromosomal initiation as well as conversion to fully-methylated *oriC*. This sequestration by SeqA prevents re-initiation of chromosomal replication at *oriC*. SeqA stimulates topoisomerase IV that is responsible for the segregation of replicated chromosomes. Also, *seqA* mutant phenotype suggests that the interaction of SeqA with toppoisomerase IV regulates chromosome superhelicity. Therefore, the conversion of fully-methylated to hemi-methylated DNA and vice versa exerted by Dam and SeqA proteins participate in methyl-directed mismatch repair, inhibition of re-initiation of replicated chromosomes, segregation of replicated chromosomes and maintenance of chromosome superhelicity, which are necessary for achieving chromosome integrity.