

Process of DNA replication and their applications.

Zhiqiang Wei*

Department of Life Science, Beijing Key Laboratory of DNA Damage Responses and College of Life Sciences, Capital Normal University, Beijing, China

Abstract

DNA replication is probably one of the most amazing tricks that DNA does. If you think about it, each cell contains all of the DNA you need to make the other cells. And we start out from a single cell and we end up with trillions of cells. And during that process of cell division, all of the information in a cell has to be copied, and it has to be copied perfectly. And so DNA is a molecule that can be replicated to make almost perfect copies of itself. Which is all the more amazing considering that there are almost three billion base pairs of DNA to be copied. And replication uses DNA polymerases which are molecules specifically dedicated to just copying DNA.

Keywords: DNA replication, DNA, Single human cell.

Introduction

Replicating all of the DNA in a single human cell takes several hours of just pure copying time. At the end of this process, once the DNA is all replicated, the cell actually has twice the amount of DNA that it needs, and the cell can then divide and parcel this DNA into the daughter cell, so that the daughter cell and the parental cell in many case are absolutely genetically identical [1].

The elucidation of the structure of the double helix by James Watson and Francis Crick in 1953 provided a hint as to how DNA is copied during the process of DNA replication. Separating the strands of the double helix would provide two templates for the synthesis of new complementary strands, but exactly how new DNA molecules were constructed was still unclear. In one model, semiconservative replication, the two strands of the double helix separate during DNA replication, and each strand serves as a template from which the new complementary strand is copied. After replication in this model, each double-stranded DNA includes one parental or “old” strand and one daughter or “new” strand [2].

DNA replication has been well studied in bacteria primarily because of the small size of the genome and the mutants that are available. *E. coli* has 4.6 million base pairs (Mbp) in a single circular chromosome and all of it is replicated in approximately 42 minutes, starting from a single origin of replication and proceeding around the circle bidirectionally (i.e., in both directions). This means that approximately 1000 nucleotides are added per second. The process is quite rapid and occurs with few errors. *E. coli* has a single origin of replication, called *oriC*, on its one chromosome [3].

As noted above, the replication of the bacterial chromosome is initiated at *oriC* where the initiator protein, DnaA, binds to start the assembly of the enzymatic replisome machine. The early stages of this process involve the assembly of a primosome, that functions to unwind the two strands of DNA at the replication forks and add RNA primers to the DNA templates that will be used by the DNA Polymerase enzymes to begin replication. Subsequent to the remodelling of the replication origin induced by DnaA, the assembly of the bacterial loader-dependent primosome occurs in discrete steps and involves at least four different proteins (initiator protein, helicase, helicase loader protein, and primase) that act in a coordinated and sequential manner [4].

The *oriC* region of prokaryotes contains highly conserved sequence motifs that include an AT-rich box domain that serves as the recognition sequence for the binding of the DnaA initiator protein. Initial binding of DnaA to *oriC* promotes the melting of the DNA double helix and the recruitment of multiple DnaA subunits that form a helical oligomer along the newly opened single stranded DNA (ssDNA). The DnaA protein contains four major domains. Domains III and IV are integral to binding the ssDNA, while domain I is involved with protein-protein interactions. Domain II forms a flexible linker between the protein interaction domain and the DNA binding domains [5].

Conclusion

The two strands of DNA unwind at the origin of replication. Helicase opens the DNA and replication forks are formed. The DNA is coated by the single-strand binding proteins around the replication fork to prevent rewinding of DNA. Topoisomerase prevents the supercoiling of DNA.

*Correspondence to: Zhiqiang Wei Department of Life Science, Beijing Key Laboratory of DNA Damage Responses and College of Life Sciences, Capital Normal University, Beijing, China, E-mail: wei.zhiqiang@usask.ca

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