20.21: DNA Replication

According to the central dogma of molecular genetics, DNA is the genetically active component of the chromosomes of a cell. That is, DNA in the cell nucleus contains all the information necessary to control synthesis of the proteins, enzymes, and other molecules which are needed as that cell grows, carries on metabolism, and eventually reproduces. Thus when a cell divides, its DNA must pass on genetic information to both daughter cells. It must somehow be able to divide into duplicate copies. This process is called **replication**. Given the complementary double strands of DNA, it is relatively easy to see how DNA as a molecule is well structured for replication, as is show in Figure 20.21.1 Each strand serves as a template for a new strand. Thus, after DNA is replicated, each new DNA double helix will have one strand from the original DNA molecule, and one newly synthesized molecule. This is referred to as semiconservative replication.

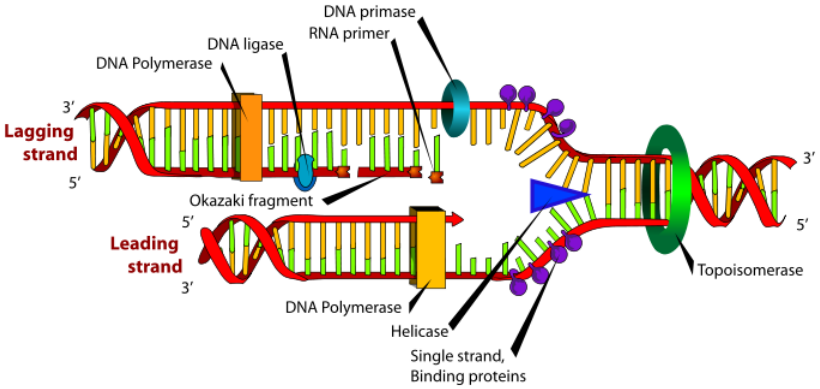

Figure 20.21.1: The replication of DNA. Replication occurs by means of partial unwinding of the two strands accompanied by synthesis of a new strand complementary to each of the originals.[1]

A rather complex mechanism exists for DNA replication, involving many different enzymes and protein factors. Let us consider some of the more important aspects of DNA replication. First, the double strand needs to be opened up to replicate each template strand. To do this, a set of proteins and enzymes bind to and open up the double helix at an origin point in the molecule. This forms replication forks, points where double stranded DNA opens up, allowing replication to occur. A helicase enzyme binds at the replication forks, with the function of further unwinding the DNA and allowing the replication fork to move along the double strand as DNA is replicated. Another enzyme, DNA gyrase, is also required to relieve stress on the duplex caused by unwinding the double strand. Further, single strand binding proteins are needed to prevent the single strands from reforming a double strand. Another essential enzyme in this initiation phase is primase, which creates an RNA primer on each single strand of DNA to begin replication from.

All of these initial functions are necessary to prepare the DNA for the main enzyme which builds then new strands, DNA polymerase. Multiple polymerase enzymes exist, but for the moment we will DNA polymerase III, the main DNA polymerase in *E. coli*. DNA polymerase III catalyzes the reaction by which a new nucleotide is added to a growing DNA strand. That reaction is seen in Figure 20.21.2 The DNA polymerase enzymes need a free 3' OH group in order to begin synthesizing a new strand, which explains the necesity of the RNA primer, which gives a 3'OH group for DNA polymerase III to start from. [2]

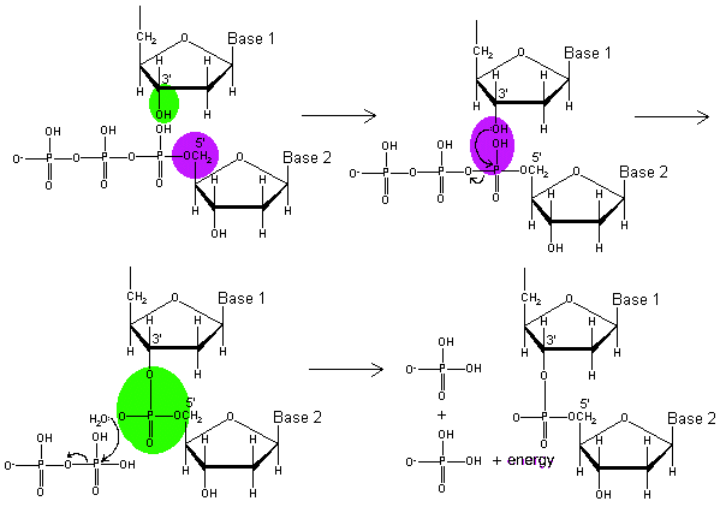

Figure 20.21.2 The polymerization of DNA nucleotides. The 3' hydroxyl group attacks the triphosphate group on the incoming nucleotide. A new phosphodiester bond is formed, and a pyrophosphate group leaves. This leaves two phosphates, the energy released from breaking down a the high energy phosphate group, and a elogated strand of DNA with a new 3' hydroxyl group to which another nucleotide may be added.

This leads to another constraint on DNA polymerase III. One strand, the **leading strand** can be polymerized continuously since the new strand being created goes 5' to 3' from the replication fork, but since the original strands are anti-parallel, the other strand, the **lagging strand** is going in the wrong direction for polymerization. In this case, the polymerzation reaction starts away from the replication fork and works back toward it. This means that the lagging strand is synthesized in disconnected segments, known as Okazaki fragments, instead of continuously. Later, another DNA polymerase, in the case of *E. coli*, DNA polymerase I, removes RNA primers and fills in the missing discontinuities. Then, *another* enzyme, DNA ligase, connects breaks between 3'OH groups and 5' phosphate groups in the newly synthesized strands that exist due to these discontinuities. While the enzymes of this process differ in eukaryotes, they fulfill similar mechanisms. Even with this complexity of this process, DNA polymerase III is able to add new nucleotides at a rate of 250-1,000 nucleotides per second.[3]

A number of advantages of the double-stranded structure held together by hydrogen bonds is evident in the process of replication. Complementary base pairing insures that the two new DNA molecules will be the same as the original. The large number of hydrogen bonds, each of which is relatively weak, makes complete separation of the two strands unlikely, but one hydrogen bond, or even a few, can be broken rather easily. The helicase portion of the replication complex can therefore separate the two strands in much the same way that a zipper operates. Like the teeth of a zipper, hydrogen bonds provide great strength when all work together, but the proper tool can separate them one at a time.

References

1. ↑ Mariana Ruiz. Wikimedia Commons. 24 January 2007. Retrieved: 11 August 2009.
2. ↑ Nelson, D.L., Cox, M.M. *Lehninger Principles of Biochemistry(5thed).* New York: W.H. Freeman and Company, 2008. pp. 985-991.
3. ↑ Nelson, D.L., Cox, M.M. *Lehninger Principles of Biochemistry(5thed).* New York: W.H. Freeman and Company, 2008. pp. 982-991.