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1.The three steps in the process of DNA replication are initiation, elongation and termination.

Replication Basics. Replication depends on the pairing of bases between the two strands of DNA. ...

Initiation

Elongation.

Termination

2. The process of DNA replication is catalyzed by a type of enzyme called DNA polymerase (poly meaning many, mer meaning pieces, and –ase meaning enzyme; so an enzyme that attaches many pieces of DNA). Observe Figure 1: the double helix of the original DNA molecule separates (blue) and new strands are made to match the separated strands. The result will be two DNA molecules, each containing an old and a new strand. Therefore, DNA replication is called semiconservative. The term semiconservative refers to the fact that half of the original molecule (one of the two strands in the double helix) is “conserved” in the new molecule. The original strand is referred to as the template strand because it provides the information, or template, for the newly synthesized strand.

Stylized DNA replication fork with nucleotides matched, 5'->3' synthesis shown, no enzymes in diagram.

Figure 1. By Madprime(wikipedia) (DNA replication split horizontal) CC BY-SA 2.0

Diagram of a primer moving along the template strand of DNA.

Figure 2. Primer and Template

DNA replication relies on the double-stranded nature of the molecule. One double stranded DNA molecule, when replicated, will become two double-stranded molecules, each containing one original strand and one newly synthesized strand. You remember that the two strands of DNA run antiparallel: one from the 5′ to the 3′, and the other from the 3′ to the 5′. The synthesis of the new DNA strand can only happen in one direction: from the 5′ to the 3′ end. In other words, the new bases are always added to the 3′ end of the newly synthesized DNA strand. So if the new nucleotide is always added to the 3′ end of an existing nucleotide, where does the first nucleotide come from? In fact, DNA polymerase needs an “anchor” to start adding nucleotides: a short sequence of DNA or RNA that is complementary to the template strand will work to provide a free 3′ end. This sequence is called a primer (Figure 2).

How does DNA polymerase know in what order to add nucleotides? Specific base pairing in DNA is the key to copying the DNA: if you know the sequence of one strand, you can use base pairing rules to build the other strand. Bases form pairs (base pairs) in a very specific way. Figure 3 shows how A (adenine) pairs with T (thymine) and G (guanine) pairs with C (cytosine). It is important to remember that this binding is specific: T pairs with A, but not with C. The molecular recognition occurs because of the ability of bases to form specific hydrogen bonds: atoms align just right to make hydrogen bonds possible. Also note that a larger base (purine, A or G) always pairs with a smaller base (pyrimidine, C or T).

Diagram showing the hydrogen bonds between nucleotides. Adenine is bound to thymine, and cytosine is bound to guanine.

Figure 3. DNA chemical structure. Modification of DNA chemical structure by Madeleine Price Ball; CC-BY-SA-2.0

Now that you understand the basics of DNA replication, we can add a bit of complexity. The two strands of DNA have to be temporarily separated from each other; this job is done by a special enzyme, helicase, that helps unwind and separate the DNA helices (Figure 4). Another issue is that the DNA polymerase only works in one direction along the strand (5′ to 3′), but the double-stranded DNA has two strands oriented in opposite directions. This problem is solved by synthesizing the two strands slightly differently: one new strand grows continuously, the other in bits and pieces. Short fragments of RNA are used as primers for the DNA polymerase.

Replication in eukaryotes starts at multiple origins of replication. A primer is required to initiate synthesis, which is then extended by DNA polymerase as it adds nucleotides one by one to the growing chain. The leading strand is synthesized continuously, whereas the lagging strand is synthesized in short stretches called Okazaki fragments. The RNA primers are replaced with DNA nucleotides; the DNA remains one continuous strand by linking the DNA fragments with DNA ligase. Below is a summary table of the major enzymes addressed in this reading, listed in rough order of activity during replication.

Important Enzymes in DNA Replication

Enzyme Function

Topoisomerase Relaxes the super-coiled DNA

DNA helicase Unwinds the double helix at the replication fork

Primase Provides the starting point for DNA polymerase to begin synthesis of the new strand

DNA polymerase Synthesizes the new DNA strand; also proofreads and corrects some errors

DNA ligase Re-joins the two DNA strands into a double helix and joins Okazaki fragments of the lagging strand