BCH 204

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Pharmacology

DNA, short for deoxyribonucleic acid, is the self-replicating material which is present in nearly all living organisms as the main constituent of chromosomes. It is the fundamental carrier of genetic information, present in virtually every cell in your body.

Double-helix DNA is made of two asymmetrical strands. Each strand is made of nucleotides lined up one after the other, and these nucleotides are bound to corresponding ones on the other strand to create a ladder-like structure. DNA is made up of four nucleotides — the building blocks of nucleic acids — which are composed of a nitrogenous base, a five-carbon sugar (ribose or deoxyribose), and at least one phosphate group.

Adenine (A), Thymine (T), Guanine (G), and Cytosine (C) are called nucleotides. A and G are called Purines while T and C are called Pyrimidines. According to the rules of base pairing, A always pairs with T, and C always pairs with G.

Before a cell duplicates or divides, through either mitosis or meiosis, DNA must be replicated to ensure that each new cell receives the correct number of chromosomes.  This process occurs in all living organisms and is the basis for biological inheritance.

DNA replication occurs in several steps that involve multiple proteins called replication enzymes, as well as RNA. DNA replication is vital for cell growth, repair, and reproduction in organisms.

DNA replication steps

There are three main steps to DNA replication: initiation, elongation, and termination.

In order to fit within a cell’s nucleus, DNA is packed into tightly coiled structures called chromatin, which loosens prior to replication, allowing the cell replication machinery to access the DNA strands.

Step 1: Replication Fork Formation

Before DNA can be replicated, the double stranded molecule must be “unzipped” into two single strands. DNA has four bases called adenine (A), thymine (T), cytosine (C) and guanine (G) that form pairs between the two strands. Adenine only pairs with thymine and cytosine only binds with guanine. In order to unwind DNA, these interactions between base pairs must be broken. This is performed by an enzyme known as DNA helicase. DNA helicase disrupts the hydrogen bonding between base pairs to separate the strands into a Y shape known as the replication fork. This area will be the template for replication to begin.

DNA is directional in both strands, signified by a 5' and 3' end. This notation signifies which side group is attached the DNA backbone. The 5' end has a phosphate (P) group attached, while the 3' end has a hydroxyl (OH) group attached. This directionality is important for replication as it only progresses in the 5' to 3' direction. However, the replication fork is bi-directional; one strand is oriented in the 3' to 5' direction (leading strand) while the other is oriented 5' to 3' (lagging strand). The two sides are therefore replicated with two different processes to accommodate the directional difference.

Elongation

Enzymes known as DNA polymerases are responsible creating the new strand by a process called elongation. There are five different known types of DNA polymerases in bacteria and human cells. In bacteria such as E. coli, polymerase III is the main replication enzyme, while polymerase I, II, IV and V are responsible for error checking and repair. DNA polymerase III binds to the strand at the site of the primer and begins adding new base pairs complementary to the strand during replication. In eukaryotic cells, polymerases alpha, delta, and epsilon are the primary polymerases involved in DNA replication. Because replication proceeds in the 5' to 3' direction on the leading strand, the newly formed strand is continuous.

The lagging strand begins replication by binding with multiple primers. Each primer is only several bases apart. DNA polymerase then adds pieces of DNA, called Okazaki fragments, to the strand between primers. This process of replication is discontinuous as the newly created fragments are disjointed.

Step 4: Termination

Once both the continuous and discontinuous strands are formed, an enzyme called exonuclease removes all RNA primers from the original strands. These primers are then replaced with appropriate bases. Another exonuclease “proofreads” the newly formed DNA to check, remove and replace any errors. Another enzyme called DNA ligase joins Okazaki fragments together forming a single unified strand. The ends of the linear DNA present a problem as DNA polymerase can only add nucleotides in the 5′ to 3′ direction. The ends of the parent strands consist of repeated DNA sequences called telomeres. Telomeres act as protective caps at the end of chromosomes to prevent nearby chromosomes from fusing. A special type of DNA polymerase enzyme called telomerase catalyzes the synthesis of telomere sequences at the ends of the DNA. Once completed, the parent strand and its complementary DNA strand coils into the familiar double helix shape. In the end, replication produces two DNA molecules, each with one strand from the parent molecule and one new strand.

2.)

DNA replication would not occur without enzyme

Enzymes involved in DNA replication are:

\* Helicase (unwinds the DNA double helix)

\* Gyrase (relieves the buildup of torque during unwinding)

\* Primase (lays down RNA primers)

\* DNA polymerase III (main DNA synthesis enzyme)

\* DNA polymerase I (replaces RNA primers with DNA)

\* Ligase (fills in the gaps)

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