1.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.

Before DNA replication can begin, the double helix structure of the DNA molecules has to be ‘unzipped.’ Helicase, an enzyme, is integral to this process, breaking the hydrogen bonds that hold the complementary bases of DNA together (A with T and C with G). The separation creates a ‘Y’ shape called a replication fork and the two single strands of DNA now act as templates for making new strands of DNA.

Next, the Single-Stranded DNA Binding Protein (SSB Protein) binds to the now single-stranded DNA, preventing the separating strands from joining again.

The two strands of the double-helix DNA are joined together by cross-bars, twisted around. For this to work, each DNA strand runs in opposite direction.

Replication of leading and lagging strands of DNA. Credit: Genome Research Limited.

One of the strands is oriented in the 3’ to 5’ direction (towards the replication fork), this is the leading strand. The other strand is oriented in the 5’ to 3’ direction (away from the replication fork), this is the lagging strand.

Because the enzyme that carries out the replication, DNA polymerase, only functions in the 5' to 3' direction, this means that the daughter strands synthesize through different methods, one adding nucleotides one by one in the direction of the replication fork, the other able to add nucleotides only in chunks. The first strand, which replicates nucleotides one by one is the leading strand; the other strand, which replicates in chunks, is the lagging strand.

The notations 5' and 3' mean “five prime” and “three prime,” which indicate the carbon numbers in the DNA’s sugar backbone. These numbers indicate end-to-end chemical orientation, with the numbers 5 and 3 representing the fifth and third carbon atom of the sugar ring respectively. The 5' carbon has a phosphate group attached to it and the 3' carbon a hydroxyl (-OH) group. It’s this asymmetry that gives a DNA strand a “direction,” allowing for easy binding between nucleotides of the opposite strands.

It’s important to note that the two sides are replicated through two different processes in order to accommodate the directional difference.

Leading strand Lagging Strand

A short piece of RNA called a primer, which is produced by an enzyme called primase, binds to the end of the leading strand in the 5’ to 3’ direction. The primer acts as the starting point for DNA synthesis.

Enzymes called DNA polymerases generate new complementary nucleotide bases (the A,C, G, and T) and are responsible for creating the new strand by a process called elongation. In eukaryotic cells, polymerases alpha, delta, and epsilon are the primary polymerases involved in DNA replication.

This sort of replication is called ‘continuous.’

The lagging strand begins the replication process by binding with multiple RNA primers, tgenerated by the primase enzyme, at various points along the lagging strand.

Chunks of DNA, called Okazaki fragments, are added to the lagging strand between the primers, also in the 5’ to 3’ direction.

This type of replication is called ‘discontinuous’, as the Okazaki fragments will need to be joined up later.

After the formation of both the continuous and discontinuous strands, an enzyme called exonuclease removes all RNA primers from the original strands. The gaps where the primer(s) had been are then filled by yet more complementary nucleotides.

Another enzyme “proofreads” the newly formed strands in order to make sure there are no errors.

The enzyme DNA ligase then joins Okazaki fragments together, forming a single unified strand.

A special type of DNA polymerase enzyme called telomerase catalyzes the synthesis of telomere sequences at the ends of the DNA. Telomeres are regions of repetitive nucleotide sequences at each end of a chromatid, which protect the end of the chromosome from deterioration or from fusion with neighboring chromosomes. Think of shoelace caps. Telomeres are also a biomarker of aging, with telomeres shortening with each cellular division or, in other words, as you advance in age. As a cell’s telomeres shorten, it loses its ability to function normally. Basically, shorter telomeres make you more susceptible to a number of diseases, such as cancer or cardiovascular disease.

Finally, the parent strand and its complementary DNA strand coils into the familiar double helix shape. The result is two DNA molecules consisting of one new and one old chain of nucleotides. Each of these two daughter helices is a nearly exact copy of the parental helix (it is not 100% the same due to mutations).

The human genome — meaning the complete set of genes present in a cell’s nucleus — is comprised of 3 billion base pairs. Remarkably, it takes very little time for our biological machinery to copy something this exceedingly long. Every cell completes the entire process in just one hour.

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.

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).