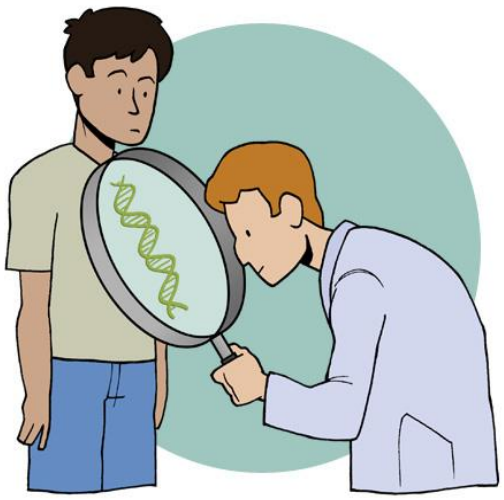
M.Sc Mazin Eidan Hadi
mazin.eidan@uomus.edu.iq

1- Basic of genetics



The laws of inheritance are investigated by genetics. The different nucleic acids (DNA and RNA) in the living organism play a central role in the inheritance of the different features. The information in the DNA molecule is inherited from one generation to the next generation through reproduction. It means that the hereditary material is the DNA (in some viruses the RNA), more exactly the genes which are the functional units which determine the nature of the features.

Gene definition: ***Genes are the units of inheritance***. Genes are pieces of DNA that contain information for synthesis of ribonucleic acids (RNAs) or polypeptides. Earlier only those units were regarded genes, which coded proteins. Nowadays, genes are also those, which code functional RNAs, which are not transcribed to proteins. These are called non-coding RNAs. In the so-called RNA-viruses (e.g. influenza, HIV1) genes are coded only in the form of RNA. The appearance of an organism which results from the expression of an organism's genes as well as the influence of environmental factors and the interactions between the two is called **phenotype.** The genetic background of an organism is called **genotype**. The majority of the DNA content of the cells is packaged in chromosomes and DNA can be also found in mitochondria. In diploid cells a couple of homologous chromosomes are a set of one maternal chromosome and one paternal chromosome that pair up with each other inside a cell during meiosis. These copies have the same genes in the same **locations, or loci.** In the nature a given gene can have different variations, these are called **alleles**. In a given population the most frequent allele of a gene is called wild type. If in a diploid cell the same alleles occur in a given locus of the homologous chromosomes then the organism is homozygous, if the alleles are different, it is heterozygous at this locus.

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1-2 Basics of molecular biology

The central dogma in molecular biology can be described as "DNA makes RNA and RNA makes protein," a positive statement which was originally termed the sequence hypothesis by Crick (Figure 1.2). However, this simplification does not make it clear that the central dogma as stated by Crick does not preclude the reverse flow of information from RNA to DNA, only ruling out the flow from protein to RNA or DNA.

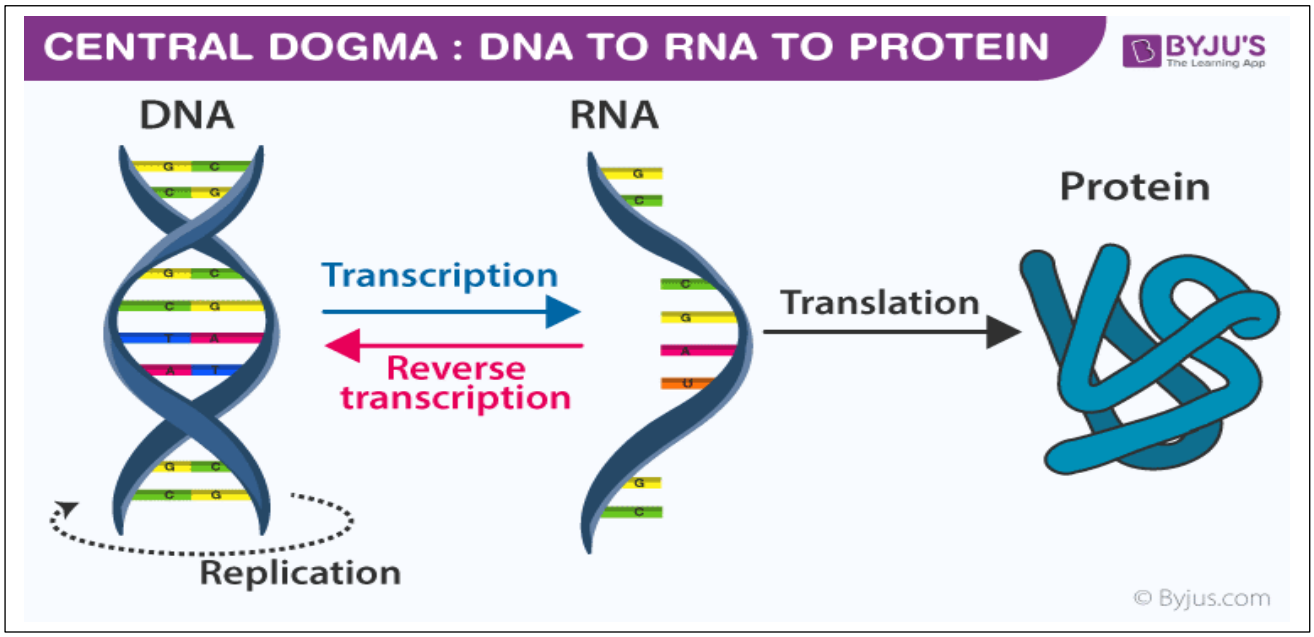

Figure 1.2. (The central dogma of molecular biology).

1-3 Some characteristics of the human DNA

The proteins coded by the DNA in our cells determine the structures and functions of the cells. If there is a mutation in the DNA, it can change the structure and function of the protein, which can have consequences on the function of the cell and can lead to diseases. Let's see the structure of the DNA in our cells. The backbone of the DNA strand is made from alternating phosphate and sugar residues (Figure 1.3). The sugar in DNA is 2-deoxyribose, which is a pentose (five-carbon) sugar. The sugars are joined together by phosphate groups that form phosphodiester bonds between the third and fifth carbon atoms of adjacent sugar rings. These asymmetric bonds mean a strand

of DNA has a direction. In a double helix the direction of the nucleotides in one strand is opposite to their direction in the other strand: the strands are antiparallel.

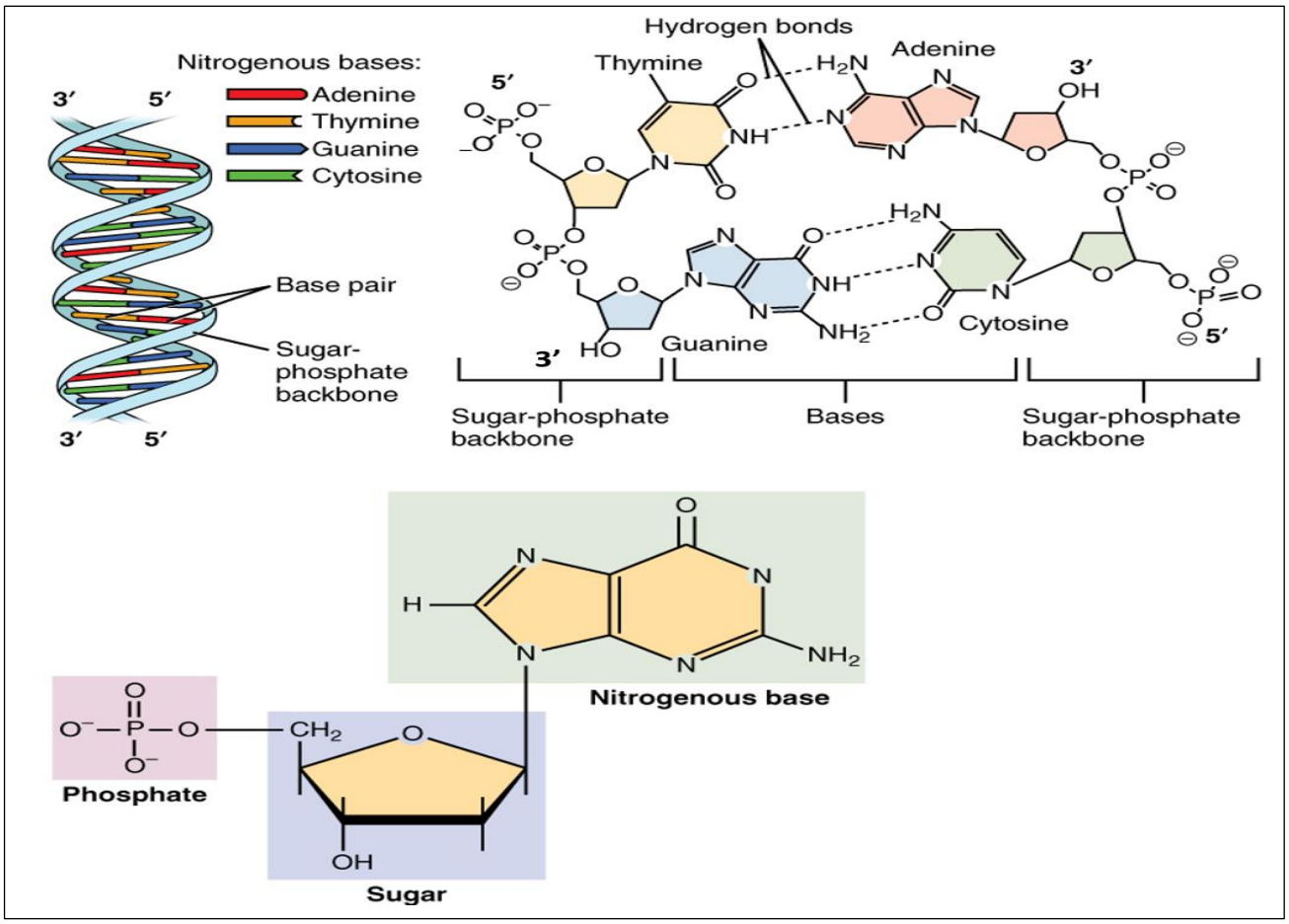

Figure 1.3 (The backbone of the DNA structure)

The asymmetric ends of DNA strands are called the 5′ (five prime) and 3′ (three prime) ends, with the 5′ end having a terminal phosphate group and the 3′ end a terminal hydroxyl group. One major difference between DNA and RNA is the sugar, with the 2-deoxyribose in DNA being replaced by the alternative pentose sugar ribose in RNA. The four bases found in DNA are adenine (abbreviated A), cytosine(C), guanine (G) and thymine (T). These four bases are attached to the sugar/phosphate to form the complete nucleotide, as shown for adenosine monophosphate. The nucleobases are classified into two types: the purines, A and G, being fused five- and six-membered heterocyclic compounds, and the pyrimidines, the six-membered rings C and T. A fifth pyrimidine nucleobase, uracil (U), usually takes the place of thymine in RNA and differs from thymine by lacking a methyl group on its ring. Uracil is not usually found in DNA, occurring only as a breakdown product of cytosine.

In a DNA double helix, each type of nucleobase on one strand bonds with just one type of nucleobase on the other strand. This is called complementary base pairing. Here, purines form hydrogen bonds to pyrimidines, with adenine bonding only to thymine in two hydrogen bonds, and cytosine bonding only to guanine in three hydrogen bonds. This arrangement of two nucleotides binding together across the double helix is called a base pair. As hydrogen bonds are not covalent, they can be broken and rejoined relatively easily. The two strands of DNA in a double helix can therefore be pulled apart like a zipper, either by a mechanical force or high temperature. As a result of this complementarity, all the information in the double-stranded sequence of a DNA helix is duplicated on each strand, which is vital in DNA replication. Indeed, this reversible and specific interaction between complementary base pairs is critical for all the functions of DNA in living organisms. A DNA sequence is called "sense" if its sequence is the same as that of a messenger RNA copy that is translated into protein. The sequence on the opposite strand is called the "antisense" sequence. Both sense and antisense sequences can exist on different parts of the same strand of DNA (i.e. both strands can contain both sense and antisense sequences).

In human cells DNA is in two compartments. Nuclear DNA, or nuclear deoxyribonucleic acid (nDNA), is DNA contained within a nucleus of the cell. Nuclear DNA encodes for the majority of the genome, with DNA located in mitochondria coding for the rest. Nuclear DNA adheres to Mendelian inheritance, with information coming from two parents, one male and one female. The other DNA containing compartment is the mitochondria. Mitochondria are cellular organelles within eukaryotic cells that convert chemical energy from food into a form that cells can use, adenosine triphosphate (ATP). In most multicellular organisms, including humans the mitochondrial DNA (mtDNA) is inherited from the mother (maternally inherited). Nuclear DNA and mitochondrial DNA differ in many ways. The structure of nuclear DNA chromosomes is linear with open ends and includes 46 chromosomes containing more than 3 billion nucleotides ($3.38 *10^9$). Mitochondrial DNA chromosomes have closed, circular structures, and contain 16,569 nucleotides. Nuclear DNA is located within the nucleus of eukaryote cells and usually has two copies per cell while mitochondrial DNA is located in the mitochondria and contains 100-1,000 copies per cell. Nuclear DNA contains more than 20 thousands protein coding and more than 23 thousands non-coding genes. The mitochondrial DNA contains 37 genes. Of the 37 genes 13 are protein coding, 2 rRNA and 22 tRNA coding genes. The

mutation rate for nuclear DNA is less than 0.3% while that of mitochondrial DNA is generally higher. As mitochondria is the "powerhouse of the cell", mutations of its DNA will effect on the power production processes of the cell, and will have serious consequences especially in tissues with large power need, like liver, neurons and muscle. As the mutation rate in the mitochondrial DNA higher, the mitochondrial diseases usually deteriorate with age, and can play also a role in the aging processes.