MOLECULAR BIOLOGY NOTES (LECTURE 1)

➢ Introduction

There are two types of nucleic acids: DNA and RNA.

They are macromolecular polymers just like proteins and carbohydrates.

NOTE: Lipids also are macromolecular structures yet are not polymers, meaning they are not constituted of repeating subunits (monomers).

➢ Central Dogma of Molecular Biology

Molecular biology is basically biochemistry dealing specifically with DNA. Basically, it describes the molecular processes that occur in our cells. It primarily describes the processes of:

1. ***DNA Replication:*** Production of new copies of DNA using enzymes termed DNA Polymerases.
2. ***Transcription:*** Synthesis of copies of RNA from DNA using enzymes termed RNA Polymerases**.**
3. ***Translation:*** Synthesis of proteins using ribosomes and other molecular components.

Other DNA molecular processes that mainly take place in viruses known as **Retro Viruses** (coronavirus, HIV, etc.) were also discovered:

4. ***Reverse Transcription:*** A process that enables **DNA** production from an **RNA molecule** using it as a template. The enzyme used in this process is termed Reverse Transcriptase**.**
5. ***RNA Replication:*** A **reversible** process that enables **RNA** production form **another RNA molecule** using it as a template and vice versa. The enzyme used in this process is termed RNA Dependent RNA Polymerase**.**

Molecular Biology is not to be confused with **Genetics** which deals with inheritance of phenotypes and genetic diseases at chromosomal levels.

➢ Nucleic Acids

They are linear polymers of nucleotides bound to each other via Phosphodiester Bonds. DNA is primarily made of four distinct monomers: **Adenine, Guanine, Cytosine, Thymine.**

DNA is a double stranded molecule and can be packed or folded into coiled DNA that is associated with proteins (**histones**) forming chromosomes.

A nucleotide has three components:

1. **Ribose sugar**: in RNA it is ribose while deoxyribose in DNA. The difference is in the hydroxyl group at the 2' carbon. Pay attention to carbons numbered 3' and 5'.
2. **Nitrogenous Base:** Bound to 1' carbon in the pentose via a glycosidic bond, they are classified into two types:
    - **Purines:** Six membered ring fused with a five membered ring, they are larger and include Adenine and Guanine
    - **Pyrimidines:** Single six membered ring, they are smaller and include Cytosine, Thymine and Uracil (**<u>Present only in RNA</u>**)

IMPORTANT NOTE: Both the pentose and the nitrogenous bases have numbered rings **BUT** in the pentose the numbers are followed by the prime (') sign to differentiate between them.

3. **Phosphate Group**: Attached to 5' carbon of the pentose. It is negatively charged and gives DNA and RNA molecules their negative charges making them highly negatively charged molecules. To stabilize the structure, positively charged ions (Na^+ or Mg^{2+}) and peptides with positively charged side chains (Histones in DNA) are bound to the phosphate group.

➢ Differences between DNA and RNA

DNA	**RNA**
Double stranded	Generally single stranded
Deoxyribose (NO OXYGEN ON **3'** CARBON)	Ribose (HYDROXYL "**OH**" ON **3'** CARBON)
A, C, G, **<u>T</u>**	A, C, G, **<u>U</u>**

➢ Nucleotides VS. Nucleosides

Nitrogenous Base + Pentose = **NUCLEOSIDE**

NUCLEOSIDE + <u>one</u> phosphate group = **NUCLEOSIDE <u>MONO</u>PHOSPHATE**

NUCLEOSIDE + <u>two</u> phosphate groups = **NUCLEOSIDE <u>DI</u>PHOSPHATE**

NUCLEOSIDE + <u>three</u> phosphate groups = **NUCLEOSIDE <u>TRI</u>PHOSPHATE**

Simply, Nucleoside plus any number of phosphate groups would give a Nucleotide, but we use the above-mentioned method of naming to further differentiate between the nucleotides. **REFER TO SLIDES 13 AND 14 FOR EXAMPLES.**

➢ Nucleic Acid Polymers

The nucleotides are bound to one another by **Phosphodiester Linkages** and it is between the 3' carbon of one nucleotide and the 5' carbon on the other nucleotide mediated by the phosphate group.

In the polymer, the 5'-Terminus has a phosphate group bound and 3'-Terminus has no phosphate group attached so addition of nucleotides would occur at the 3'-Terminus by a phosphodiester bond.

By convention, nucleic acid polymers are written in a *5' to 3'* direction only similar to how amino acid sequence in a protein begins with the N-terminus and ends with the C-terminus.

NOTE: If specified that the given molecule is that of a DNA, there is NO NEED to use deoxy when naming the nucleotide. **OTHERWISE IT IS NECESSARY TO SPECIFY WHETHER THE PENTOSE IS DEOXY OR NOT.**

➢ DNA Structure

- It is a double stranded molecule **(Double Helix):** It is made of two intertwining stranded of nucleotides.
- The winding of the DNA molecule is not perfect, there is an angle to it.
- **It has a phosphate-sugar backbone and side chains** (Nitrogenous Bases) are bound to it almost **Perpendicularly.**
- There are **hydrogen bonds** between side chains of apposing molecules**.** This base pairing is **specific**: A always pairs with T, G always pairs with C.
- **Complementary base pairing.** Since it is specific, wherever there is A, there is T, and wherever there is G, there is C. This means that from knowing only one strand, we can know the complementary strand to it.
- The base pairs face inward while the backbone lies outward.
- The strands run **Antiparallel** to each other; one runs from 5' to 3' while the complementary runs from 3' to 5'
- A=T. G=C always **(Chargaff's Rules).**
- **It is flexible, yet stable.**
- **The presence of DNA grooves.** This is due to the imperfect winding of the helix. There are **Major Grooves** and opposite to them are **Minor Grooves.** Major grooves are important for enabling protein access to the DNA for interactions via **noncovalent bonding** (Hydrogen bonds, Electrostatic

interactions, Van Der Waals interactions and hydrophobic interactions) between the amino acids of proteins and the bases of DNA.

In Prokaryotes, DNA is a circular single loop that is not enclosed by a nucleus. **In Eukaryotes,** DNA is composed of different strands of different lengths that are enclosed by a nucleus. The length of DNA is a single eukaryotic cell is approximately 1.8 meters long yet due to high coiling is able to be packaged in the nucleus. This is achieved by wrapping DNA around histones, since they are positively charged, they are able to interact with the phosphate groups of DNAs forming the **Chromatin** molecule.

➢ Nucleosomes

The histone protein core is an octamer (two copies of each subunit; H2A, H2B, H3, H4) and has DNA (146-nucleotide-pair DNA double helix) wrapped around it**.** Sealing this octamer-DNA complex is an H1 molecule. Connecting these octamer-DNA complexes is **Linker DNA.** A **Nucleosome** is composed of the octamer-DNA complex plus the linker DNA.

Further packing of Nucleosomes results in structures called **Chromatosomes** with very little linker DNA between these structures. When you have a single large molecule of DNA and histones in a single unit it is called **Chromosome.**

A **Gene** is region of DNA (a sequence of nucleotides) that encodes for a certain polypeptide through the processes of transcription and translation. We all have the same genes on every single chromosome in the same order and location.

Humans are **Diploid (2n).** Every cell contains two copies of every chromosome (a maternal copy and a paternal one) which are called **Homologous Chromosomes.**

Germ cells (Sperm and Eggs) are **Haploid (1n),** containing only one copy of each chromosome.

➢ RNA

It consists of a single stranded long, unbranched chains of nucleotides joined by phosphodiester bonds. It has the base uracil instead of cytosine. An RNA molecule doesn’t have a precise structure as DNA does, but it can fold on itself forming hydrogen bonds between complementary bases within the same molecule. Multiple types of RNA have been discovered. We have coding RNAs such as mRNA. We also have non-coding RNAs having different functions such as rRNA, tRNA, small ncRNA, etc.