Principles of

MOLECULAR BIOLOGY

BURTON E. TROPP

Chapter 1
Introduction to Molecular Biology

105 Molecular Biology

Dr. Nabil Bashir

Second semester, 2023

- Molecular biology is one of the most rapidly advancing fields of medicine and is now **integral** to all aspects of biomedical sciences.
- Every physician who practices in the 21st century will require a **basic knowledge** of the principles of molecular biology and their application to a wide variety of clinical problems.
- The practice of modern medicine includes recognition of the **role of genetic factors in health and disease**.
- This requires knowledge of the structure, function, and transmission of genes and understanding of interactions both among genes, and between genes and the environment

- Objectives of this course are designed to understand the basic principles of molecular Biology .
- The structure of DNA and RNA as genetic material, DNA organization and its replication, mutation and repair in both prokaryotes and eukaryotes will be covered.
- Furthermore, transcription of information from DNA to RNA, and then to proteins as well as gene expression will also be discussed.
- Finally, the course will cover some molecular biology techniques.

- The Department of Biochemistry and physiology has the responsibility for teaching a major part of the Molecular biology curriculum at the University of Jordan. The following outline lists the objectives of the course material in Molecular biology:
- Students in Molecular biology should know and understand :

1. What genes are and how they are organized .
2. How genes are arranged in chromosomes and how chromosomes replicate.
3. The nature of mutations and how they are repaired, and how they contribute to human variability and disease .
4. What genes do: the flow of genetic information from DNA to RNA to protein.
5. How gene expression is controlled.
6. The significance of the Human Genome Project to medicine.

Introduction to Nucleic Acids

- DNA contains the sugar Deoxyribose
- RNA contains the sugar Ribose

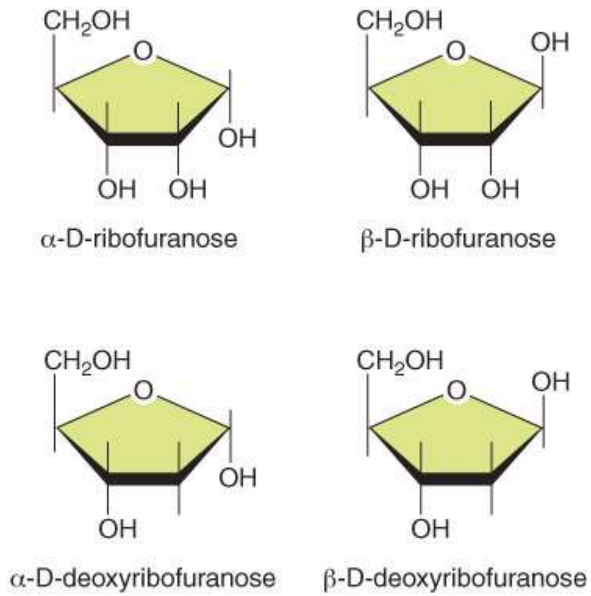

Figure 01.03: Haworth structures for ribofuranose and deoxyribofuranose.

Introduction to Nucleic Acids

- A nucleoside
  - Attachment of a purine or pyrimidine base to a sugar

Figure 01.04A: Pyrimidine and purine bases in DNA. (a) pyrimidine bases

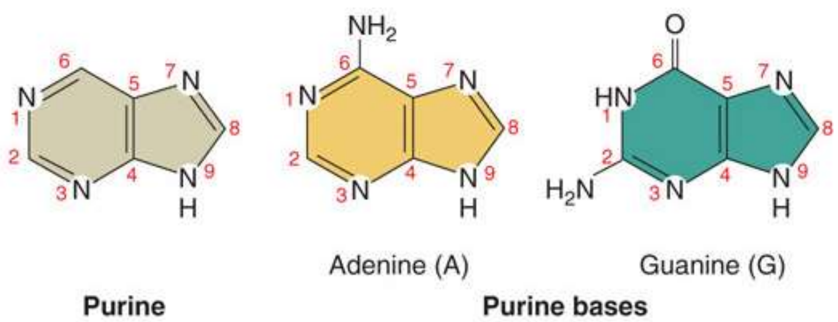

Figure 01.04B: Pyrimidine and purine bases in DNA. (b) purine bases

Introduction to Nucleic Acids

- Pyrimidine derivatives
  - Thymine (T)
  - Cytosine (C)

Figure 01.04A: Pyrimidine and purine bases in DNA.
(a) pyrimidine bases

Introduction to Nucleic Acids

- Purine derivatives
  - Adenine (A)
  - Guanine (G)

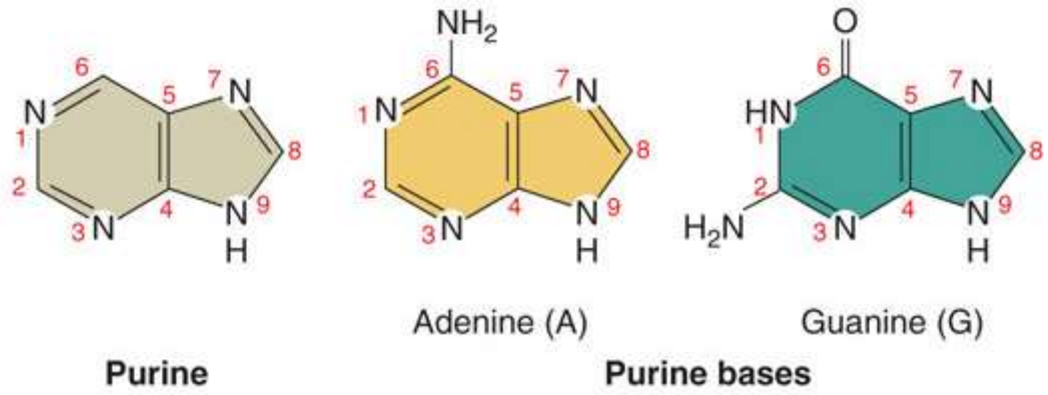

Figure 01.04B: Pyrimidine and purine bases in DNA.
(b) purine bases

Introduction to Nucleic Acids

- RNA
  - Uracil replaces Thymine

Figure 01.05: Uracil (U).

Introduction to Nucleic Acids

- Base is attached to the sugar by an N-glycosidic bond
  - Attached to the 1' C in the sugar

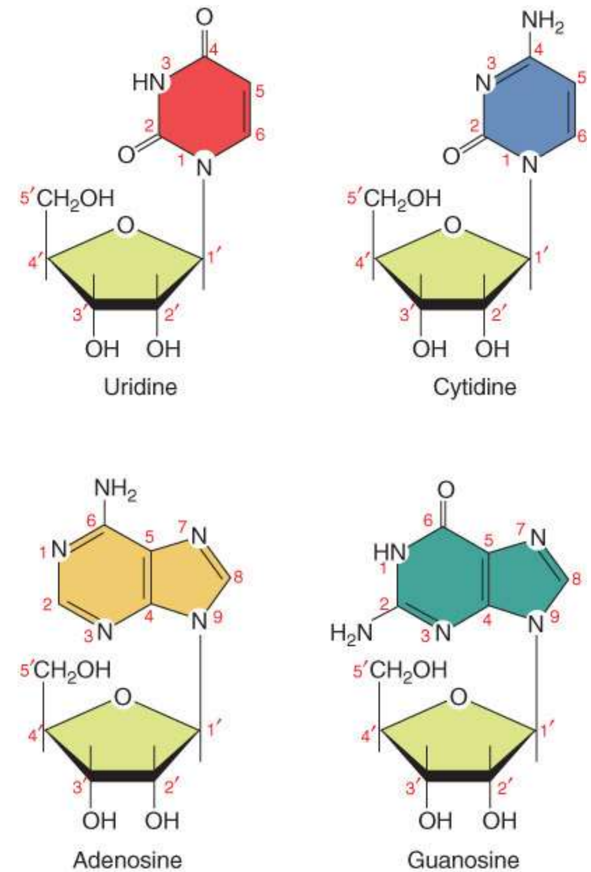

Figure 01.07: Ribonucleosides.

Introduction to Nucleic Acids

- A nucleotide is formed by attaching a phosphate group to the nucleoside sugar

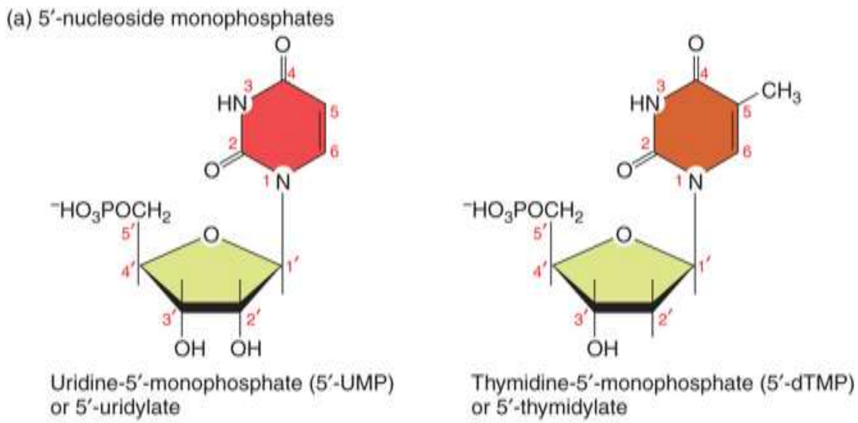

Figure 01.08A: Nucleotides. (a) Nucleotides formed by adding a phosphate group to the 5′-hydroxyl group in uridine or thymidine.

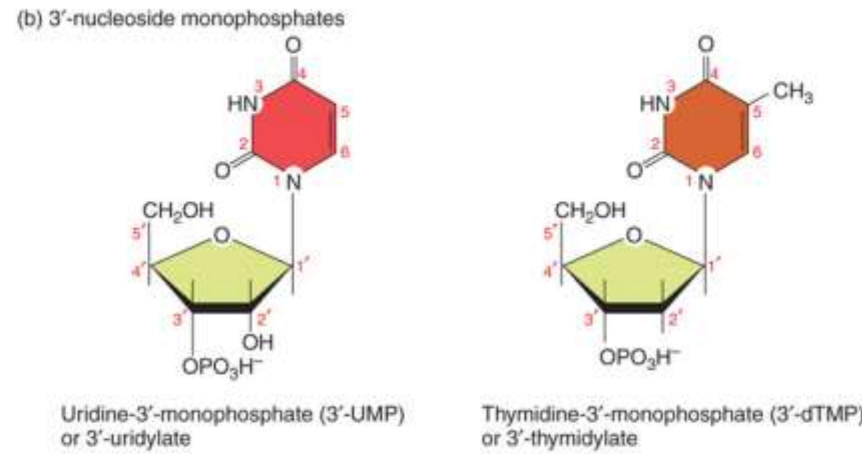

Figure 01.08B: Nucleotides. (b) Nucleotides formed by adding a phosphate group to the 3′-hydroxyl group in uridine or thymidine.

Introduction to Nucleic Acids

- DNA is a linear chain of deoxyribonucleotides
- All DNA and RNA chains have a 5’ and 3’ terminus
- Phosphodiester bond joins neighboring nucleosides

Introduction to Nucleic Acids

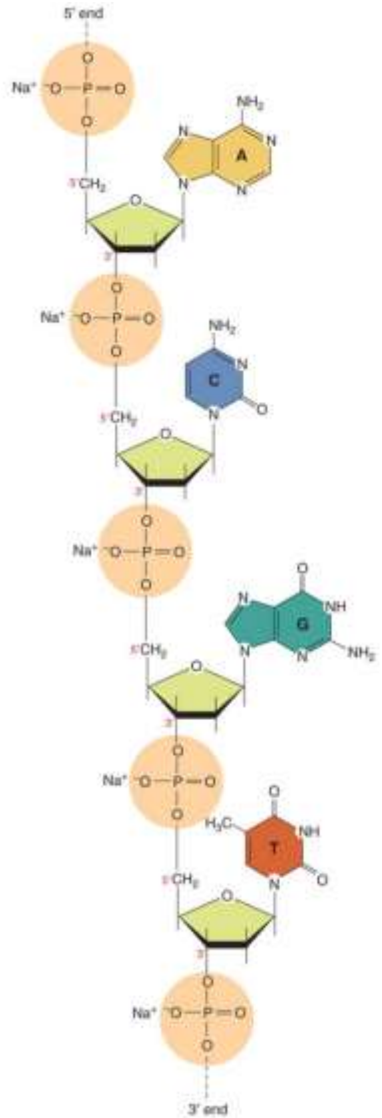

Figure 01.09A: Segment of a polydeoxyribonucleotide. (a) Extended structure as a sodium salt

DNA: Hereditary Material

Transforming Principle

1928 - Fred Griffith

- S. pneumoniae bacteria

- S (smooth) bacteria - **lethal**
- Mutant R (rough) bacteria and heat killed S bacteria - **non lethal**
- Mix of live R and heat killed S - **lethal**

DNA: Hereditary Material

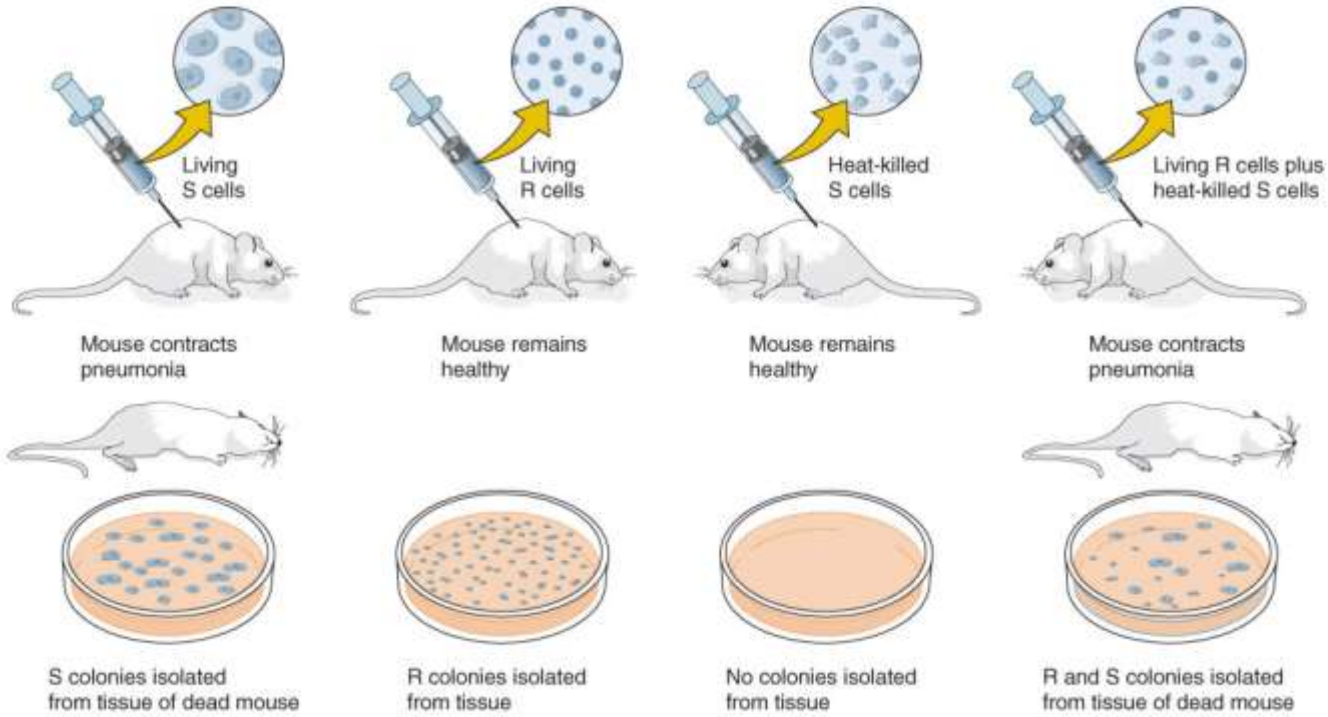

Figure 01.11: Griffith's experiment demonstrating bacterial transformation.

DNA: Hereditary Material

The Chemical Nature of the Transforming Principle

1944 - Avery, Mcleod and McCarty

- The Transforming Principle was a viscous mix of DNA, protein and polysaccharides

DNA: Hereditary Material

- Purified polysaccharides from S cells did not transform R cells
- Transforming Principle not destroyed by proteolytic enzymes or RNase
- DNase inactivated the Transforming Principle
    - DNA is the Transforming Factor

DNA: Hereditary Material

Chargaff's Rules

- Double stranded DNA has equimolar adenine and thymine concentrations as well as equimolar guanine and cytosine concentrations
- DNA composition varies from one genus to another

Watson – Crick Model

- Rosalind Franklin and Maurice Wilkins
  - Generated X-ray diffraction patterns that lead to the solution of DNA's structure

Watson – Crick Model

- Watson and Crick built a model consistent with X-ray diffraction data
  - Double helix
  - Adenine pairs with Thymine
  - Guanine pairs with Cytosine
  - Held together by Hydrogen Bonds

Watson – Crick Model

Key Features

- 2 DNA strands twist about each other to form a double helix
- Phosphate and sugar groups form backbone on the outside
- Base pairs stack inside the helix
- Helix diameter of 2.0 nm

Watson – Crick Model

Key Features

- Adenine - Thymine base pairs
  - 2 hydrogen bonds
- Guanine – Cytosine base pairs
  - 3 hydrogen bonds

Explains Chargaff's Rule

Watson – Crick Model

Key Features

- Antiparallel strands
  - One strand 3' to 5'
  - Other strand 5' to 3'
- Sequence is always written by convention from 5' to 3'
- Major groove and Minor groove wind about outer face

Watson – Crick Model

Implications of the Watson – Crick Model

- Each strand serves as the template for the synthesis of the complimentary strand

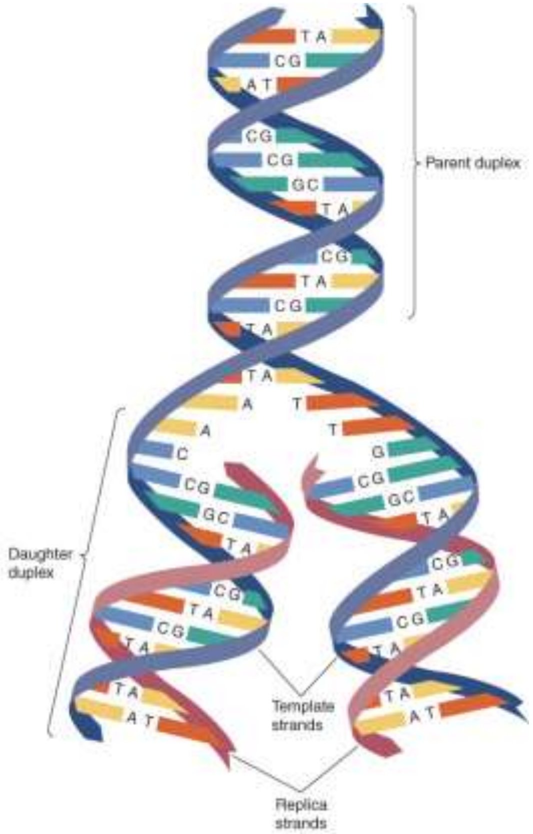

Figure 01.16: Replication of DNA. Replication of a DNA duplex as originally envisioned by Watson and Crick.

The Central Dogma of Molecular Biology

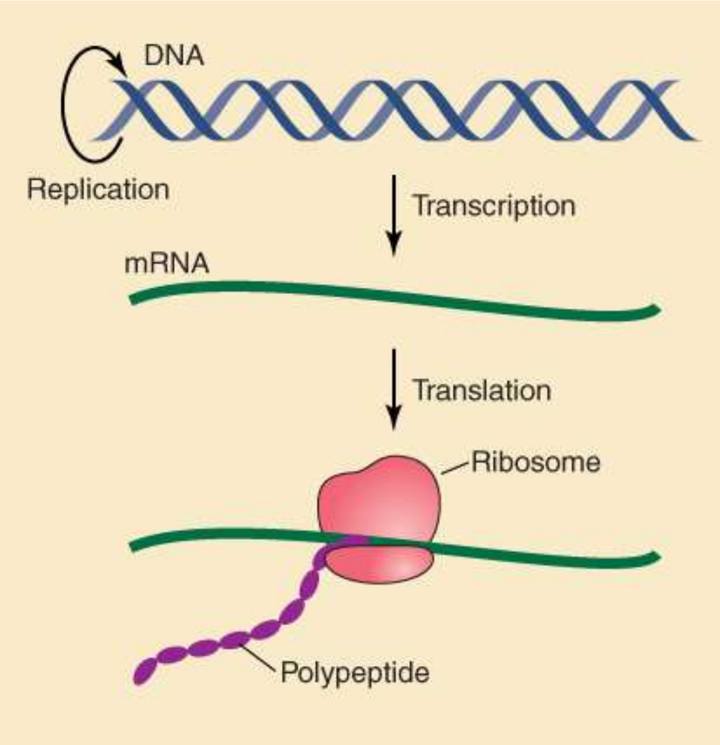

Figure 01.17: The "central dogma." The central dogma as originally proposed by Francis Crick postulated information flow from DNA to RNA to protein.

Central Dogma

- Genetic information flows from:
  - DNA to DNA (**Replication**)
  - DNA to RNA (**Transcription**)
  - RNA to polypeptide (**Translation**)