Molecular Biology
BCH361

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Introduction

Course Main Objective

- To introduce the discipline of molecular biology and pivotal experiments that established the chemical nature of genetic material.
- To provide a comprehensive overview of the chemical composition and physical properties of DNA and RNA.
- To elucidate the biochemical processes underlying DNA replication and the maintenance of genomic integrity.
- To explore the molecular mechanisms governing the flow of genetic information from DNA to protein(central dogma), with an emphasis on the regulation of gene expression.
- To analyze the structural organization of the human genome and the mechanisms involved in its compaction within the nucleus.
- To provide an overview of the cell cycle regulation and its link to cancer etiology

Overview of syllabus and topics covered

1. Introduction to Molecular Biology and brief history
2. The Nobel Prize: Selected Winners who've contributed to the advancement of Molecular Biology
3. Early evidence of DNA as the carrier of genetic information
4. Chemical Structure of nucleotides
5. Chemical Structure of DNA (primary and secondary) and RNA
6. Physical properties of DNA and RNA
7. DNA packing; histones and histone modifications, DNA supercoiling
8. Central dogma that involved:

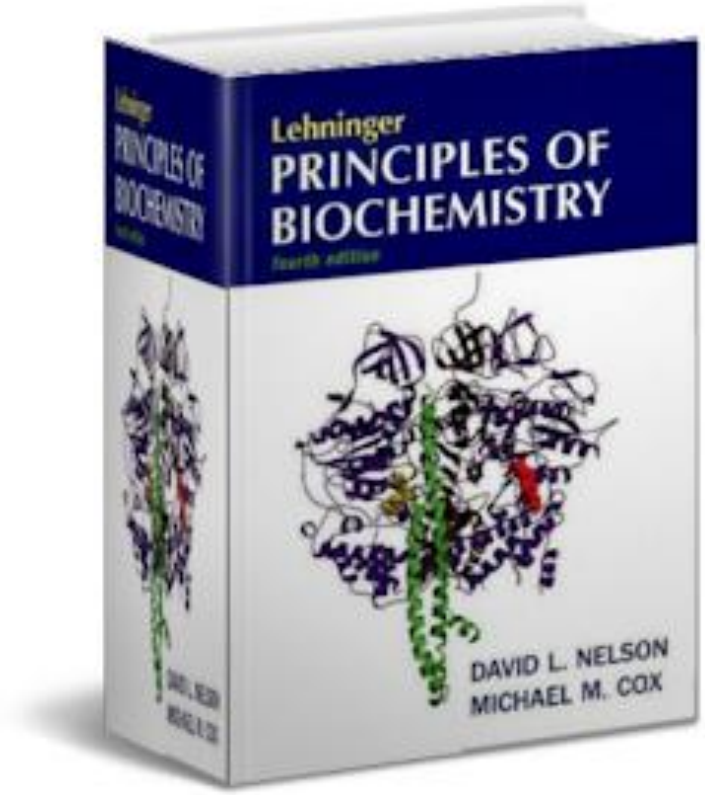
a) DNA Replication, DNA damage, and DNA repair

b) Transcription, and the regulation of gene expression

c) Translation

1. Human genome
2. Cell cycle
3. Application of molecular biology in medicine and industry

Recommended text books



Lehninger Principles of Biochemistry, David L Nelson ,Michael M Cox

The PowerPoint presentations are not intended to substitute for the lectures, nor will they include every detail discussed in class

Grade distribution

Requirements	Marks
1st midterm	12
2nd midterm	12
Presentation	6
Practical	30
Final exam	40

Introduction and Brief History of molecular biology

All Life depends on 3 critical molecules

DNAs

Contains the genetic instructions used in the development and functioning of living organisms

Proteins

The workhorses within cells , participating in all processes

RNAs

Provide templates to synthesize into protein

lecture outline

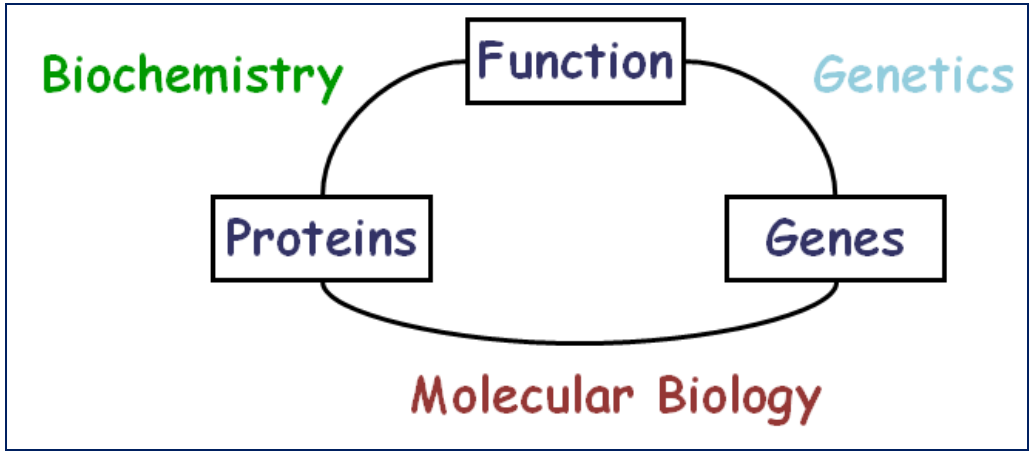
- Definition of Molecular Biology
- The central dogma
- Terminologies
- Brief History of Molecular Biology

Definition of Molecular Biology

- The science that studies biology at a molecular level.
- The field overlaps with genetics and biochemistry.
- Molecular biology focuses on understanding the interactions between the various systems of a cell, including the relationship between DNA, RNA, and protein synthesis, and learning how these interactions are regulated.

What is molecular biology?

- The attempt to understand biological phenomena in molecular terms
- The study of gene structure and function at the molecular level



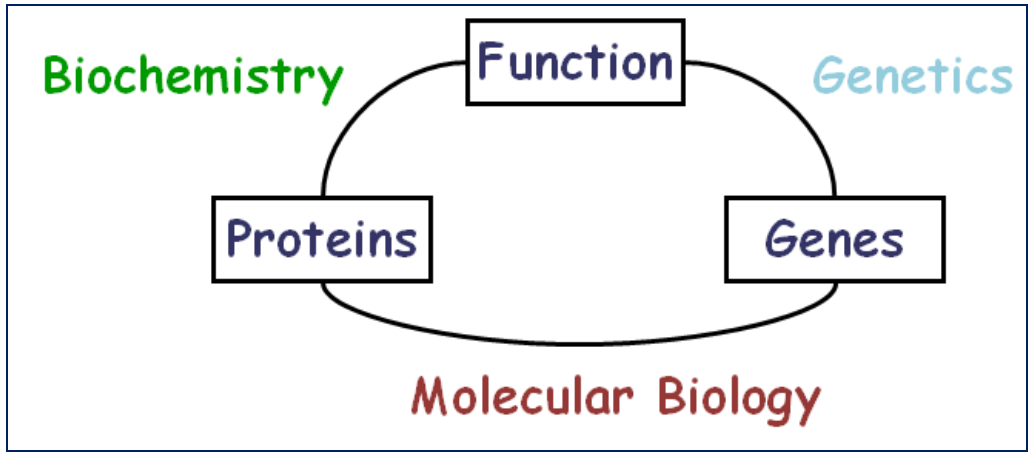
Molecular biology is a melding of aspects of genetics and biochemistry

Definition of Molecular Biology

Biochemistry showed that within one generation, proteins had a determining effect on phenotype.

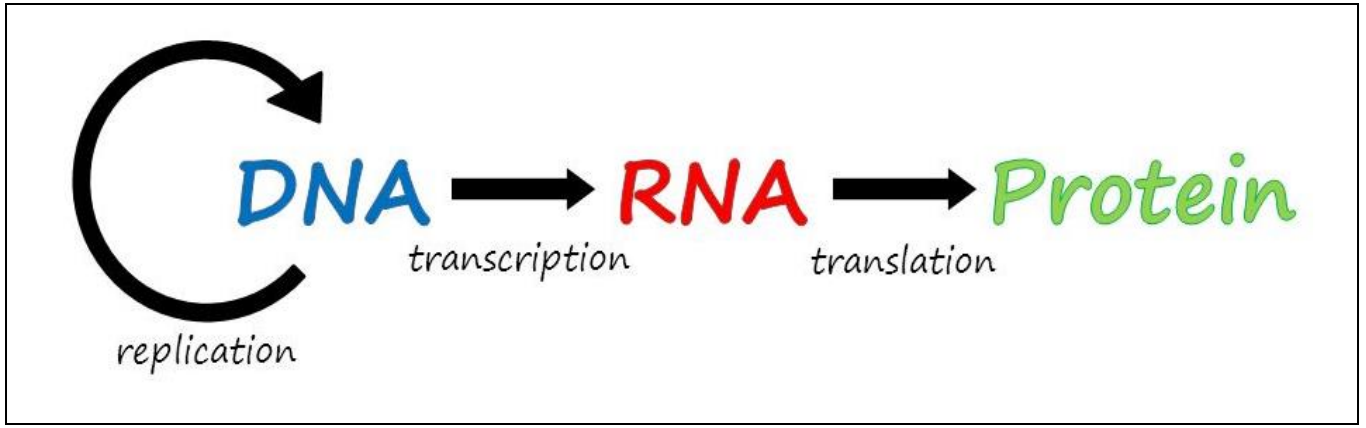
Molecular biology explains that hereditary information is passed between generations in codes.

Understanding how that code directs the creation of life is the goal of molecular biology.



Central Dogma of Molecular Biology

- The **Central Dogma of Molecular Biology** is a foundational concept that describes the directional flow of genetic information within a biological system from DNA to protein.
- Originally proposed by **Francis Crick in 1958.**



Example of Central Dogma of Molecular Biology

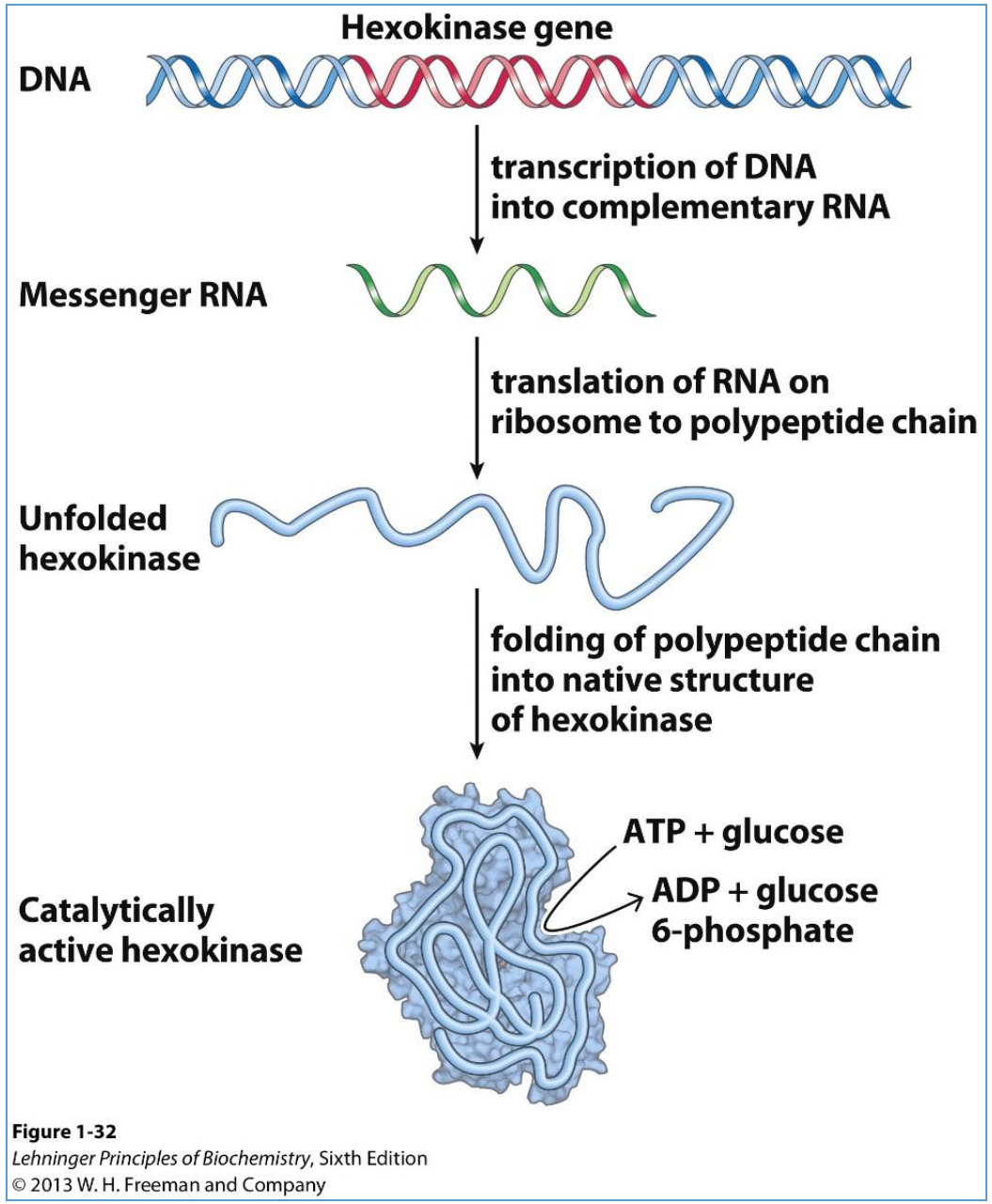


Figure 1-32
Lehninger Principles of Biochemistry, Sixth Edition

Protein Function

Proteins:

1- Serve as enzymes that catalyze hundreds of chemical reactions

2- Provide the structure that helps give cells integrity and shape

3- Serve as hormones carrying signals from one cell to another

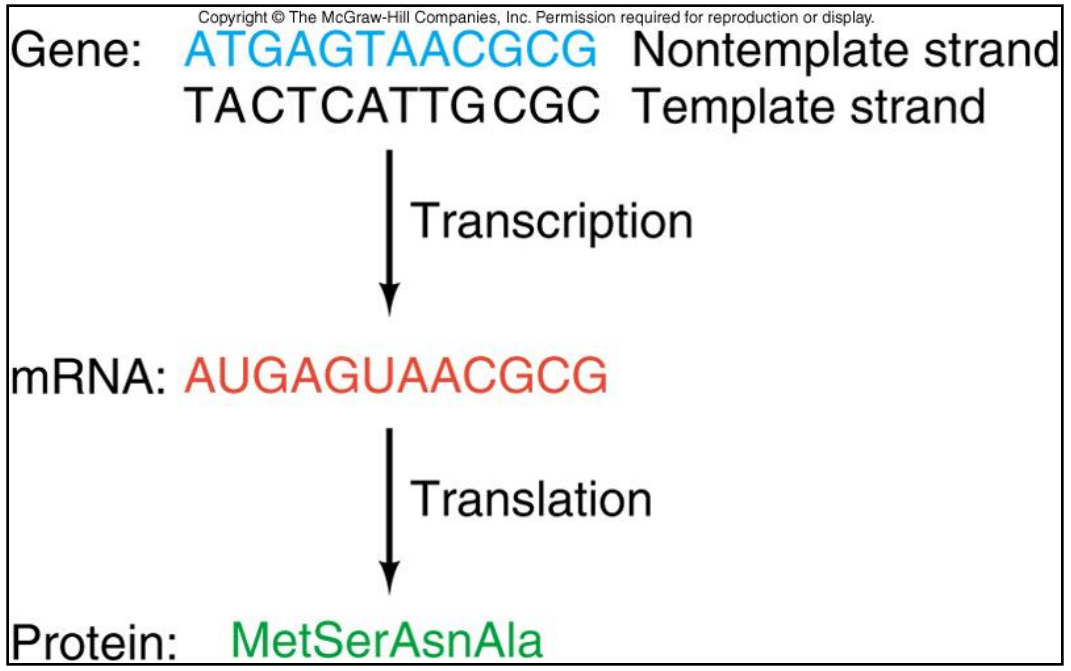
4- Immunity

5- Control the activities of genes

Storing Information

Producing a protein from DNA information involves both transcription and translation

- **Template strand** is the complementary DNA strand that is used to generate the mRNA
- **Non-template strand** is a strand not used in RNA transcription



Terminologies

A codon is the 3 base sequence that determines what amino acid is used

For instance:

Phe: UUU

UUC

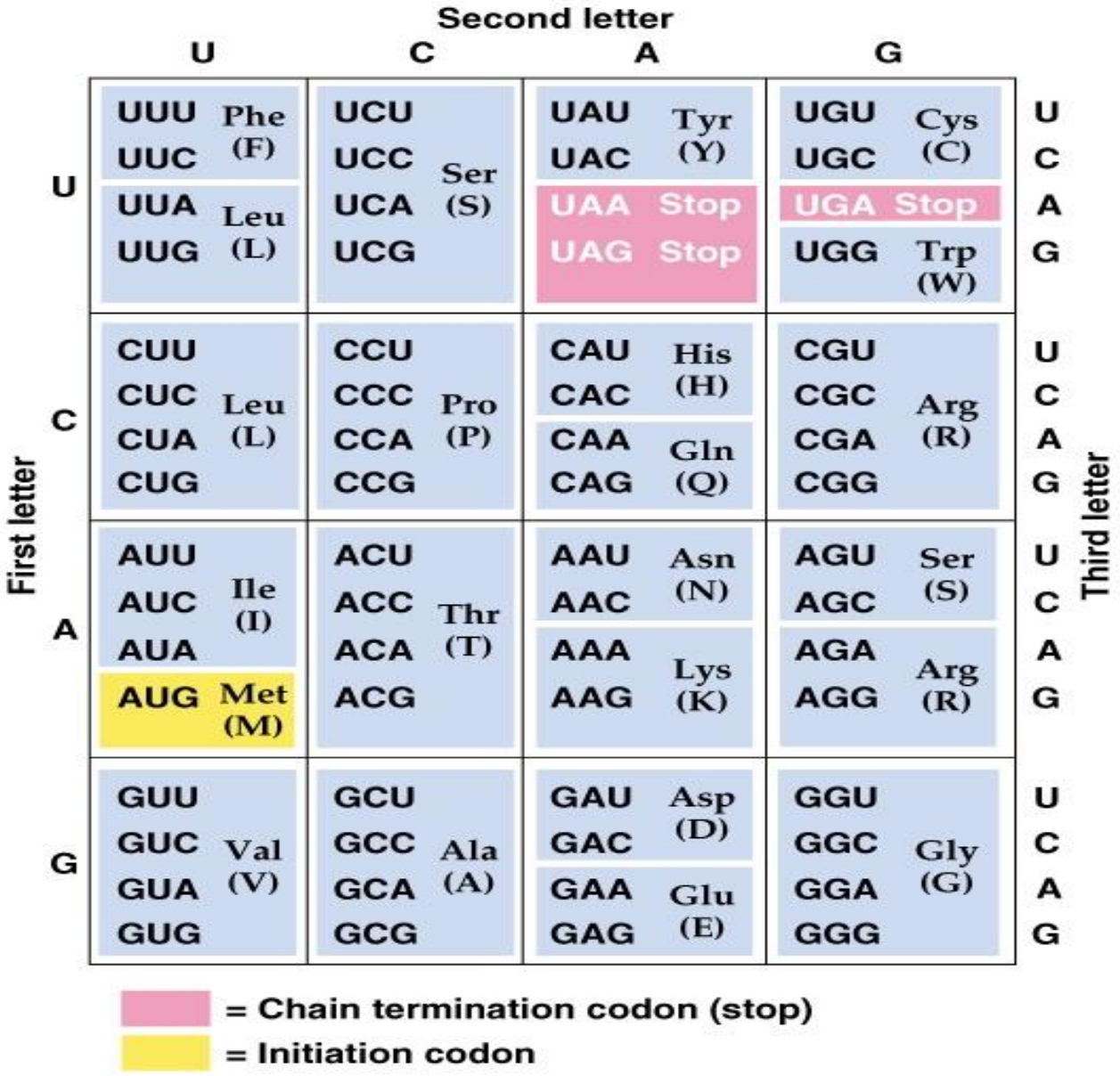
TRAY IT .....YOUR TURN

Please recognize the genetic condone of the following amino acid ?

Met.....

His.....

Gly.....

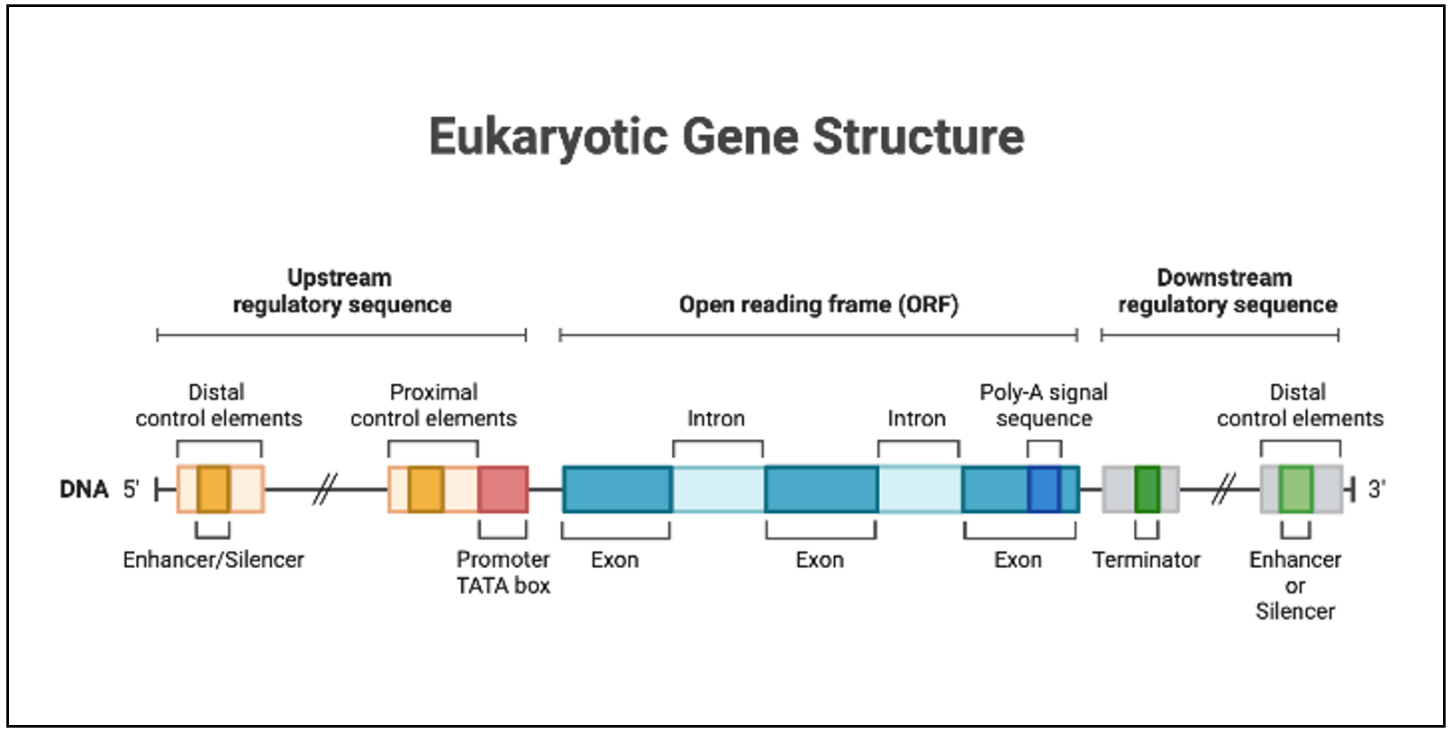


Terminologies

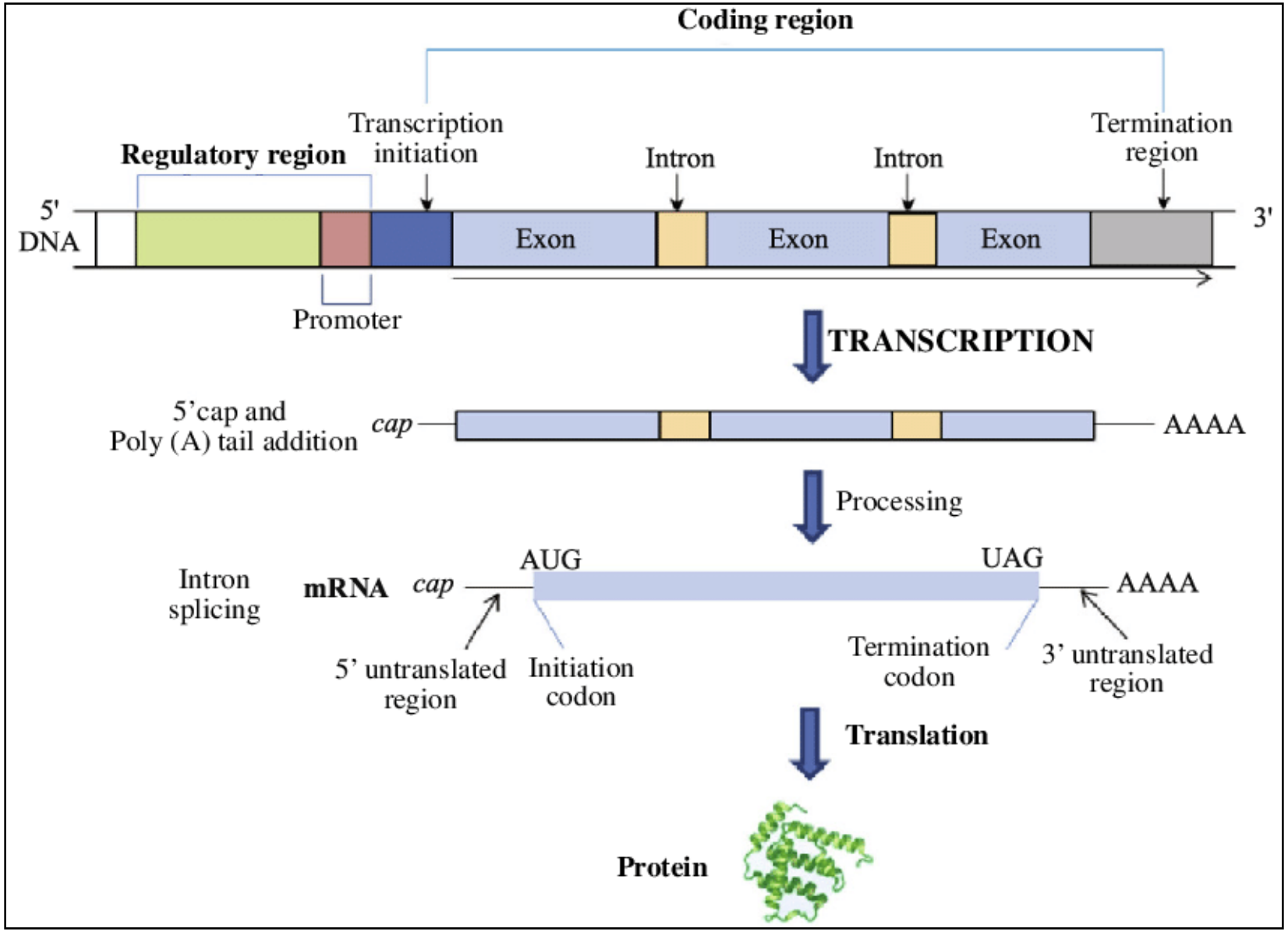
Gene A discrete unit of hereditary information located on the chromosomes and consists of DNA. Which contains coded information that directs the synthesis of proteins.

(i.e. It is the basic physical and functional units of heredity.

Contains specific sequences of DNA bases that encode instructions on how to make proteins.)



Eukaryotic gene organization



•Biotechnology and Plant Breeding (pp.179-199)
•Edition: 1ed
•Chapter: 8
•Publisher: Elsevier
•Editors: Aluízio Borém, Roberto Fritsche-Neto

Terminologies

Nucleic acid Biological molecules (RNA and DNA) that allow organisms to reproduce

Genetics showed that genes control the transmission of phenotype from one generation to the next.

Proteins Make up the cellular structure. Are large, complex molecules made up of smaller subunits called **amino acids.**

Genotype The genetic makeup of an organism

Phenotype the physically expressed traits of an organism.

An organism denotes its external appearance (size, color, intelligence, etc.)

Molecular Biology Timeline table

Year	Discovery/Advancement	Significance
1869	Discovery of "nuclein" by Friedrich Miescher	First isolation of DNA from cell nuclei
1902	Chromosome theory of Inheritance	Linked genes to chromosomes
1928	Griffith’s transformation experiment	Suggested genetic traits can be transferred between bacteria
1944	Avery, MacLeod, and McCarty identify DNA as the genetic material	Demonstrated DNA as the carrier of genetic information
1952	Hershey-Chase experiment	Confirmed DNA (not protein) is the genetic material in viruses
1953	Watson and Crick model of DNA	Described the double-helix structure of DNA
1958	Meselson-Stahl experiment	Demonstrated semiconservative DNA replication
1958	Crick’s Central Dogma	Proposed the flow of genetic information: DNA → RNA → Protein
1961	Discovery of mRNA	Identified mRNA as the intermediary between DNA and protein
1966	Genetic code deciphered	Established the correspondence between codons and amino acids
1970	Discovery of reverse transcriptase	Showed RNA can be reverse-transcribed into DNA

Molecular Biology Timeline table

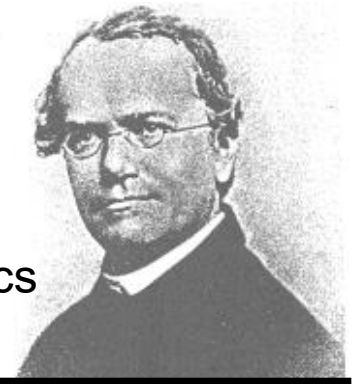
Year	Discovery/Advancement	Significance
1977	Discovery of introns and RNA splicing	Revealed gene structure in eukaryotes is discontinuous
1983	Invention of PCR (Kary Mullis)	DNA amplification
2001	Draft of the Human Genome Project completed	First complete mapping of the human genome
2012	Development of CRISPR-Cas9 genome editing	Revolutionized genetic engineering
2015	Base and prime editing techniques introduced	Allowed precise DNA edits without double-strand breaks
2020	Nobel Prize for CRISPR; mRNA COVID-19 vaccines	Validated genome editing and RNA-based therapeutics
2021	AlphaFold predicts nearly all known protein structures	Solved a 50-year protein-folding problem using AI
2022	First FDA-approved CRISPR therapy for sickle cell disease	Marked clinical success of gene editing
2023	Further CRISPR approvals; microbiome inheritance insights	Expanded applications in genetic therapy and developmental biology
2024	Nobel Prize for AlphaFold protein folding AI	Recognition of AI's impact on molecular biology
2025	cryo-electron tomography is a Nobel Prize-winning technology was awarded in 2017, and research into newer CRISPR-associated integrases is an ongoing area of scientific advancement	Advanced structural biology and precision gene insertion methods

Brief history of Molecular Biology

Major events in the history of Molecular Biology ***1800 - 1870***

In the 19th century, two studies performed in the **1860s** provided the foundation for molecular biology.

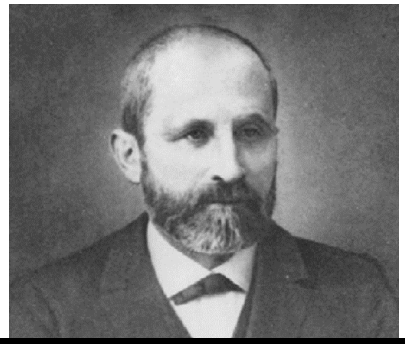
- **1865** Gregor Mendel discover the basic rules of heredity of garden pea.
  - An individual organism has two alternative heredity units for a given trait (dominant trait v.s. recessive trait)



Mendel
The Father of Genetics

Gregor Mendel's (1865) Three Laws of Inheritance

- **1869** Johann Friedrich Miescher discovered DNA and named it nuclein.

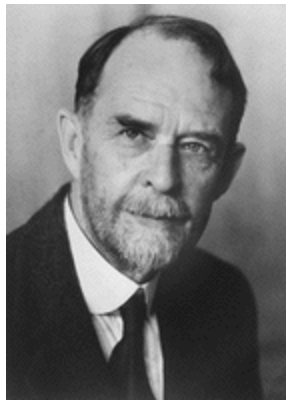


Friedrich Miescher (1869) identified DNA & called it nuclein

Major events in the history of Molecular Biology 1900-1911

- **1902** - Emil Hermann Fischer wins Nobel prize: showed amino acids are linked and form proteins
  - Postulated: protein properties are defined by amino acid composition and arrangement, which we nowadays know as fact
- **1902-**Walter Sutton created term **"gene"** to describe "factors" located on chromosomes
- **1911 –** Thomas Hunt Morgan discovers genes on chromosomes are the discrete units of heredity (Nobel prize 1933)
- **1911** Phoebus Aaron Theodor Levene discovers RNA

Fischer


Thomas Morgan

Major events in the history of Molecular Biology 1940 - 1950

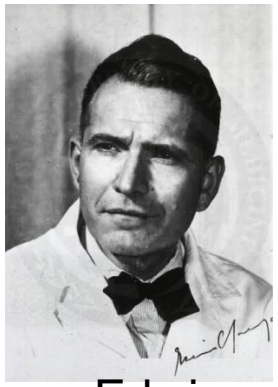
- **1944**- Avery showed that the transforming material (or genetic material) was pure DNA, not protein, lipid, or carbohydrate

George Beadle

Edward Tatum

- **1946** –**HERMANN JOSEPH MULLER** was awarded the noble prize for the discovery of the production of mutations (physical changes in genes) using X-ray irradiation

- **1950** – Edwin Chargaff finds **C** = **G** and **A** = **T** **in DNA**



Edwin Chargaff

Major events in the history of Molecular Biology 1952 - 1960

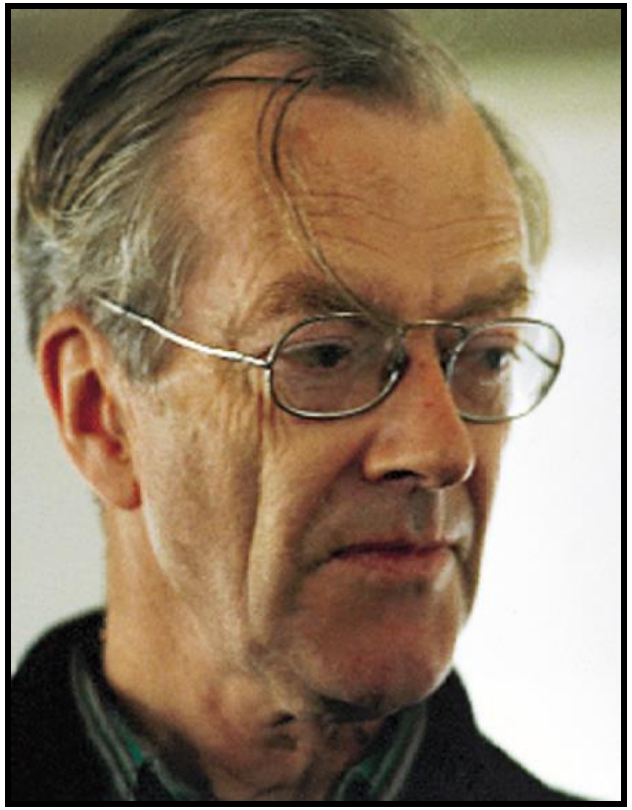
- **1952-1953** James D. **Watson** and Francis H. C. **Crick** deduced the double helical structure of DNA. In **1962** –The noble prize was awarded jointly to **CRICK**, **WATSON,** and **WILKINS** for their discoveries concerning the molecular structure of nuclear acids and its significance for information transfer in living material

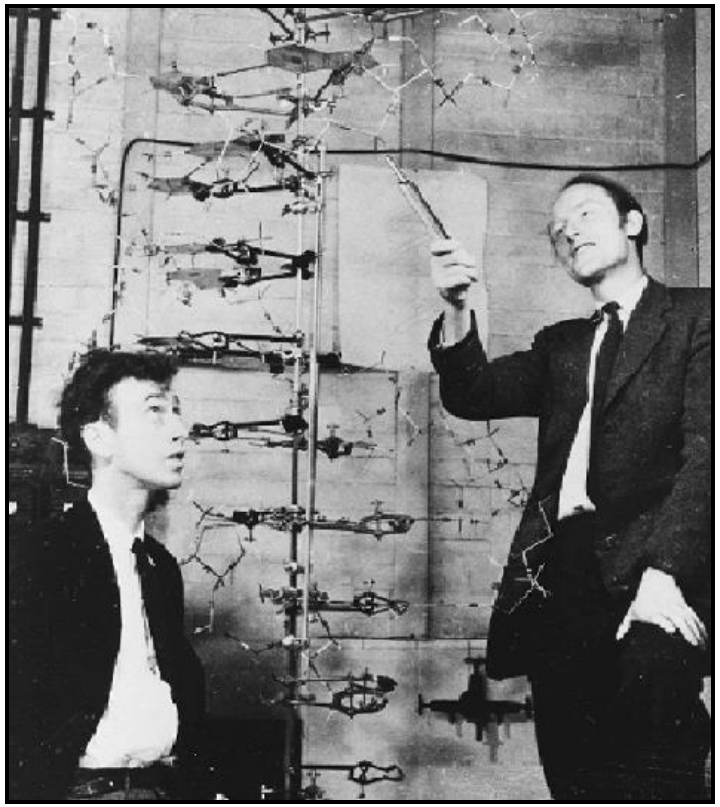
James Watson and Francis Crick

- **1956-Francis Crick and George Gamow** worked out the **"Central Dogma"** to explain protein synthesis from DNA

George Emil Palade

Watson, Crick, Franklin, Wilkins(1953)
Structure of DNA





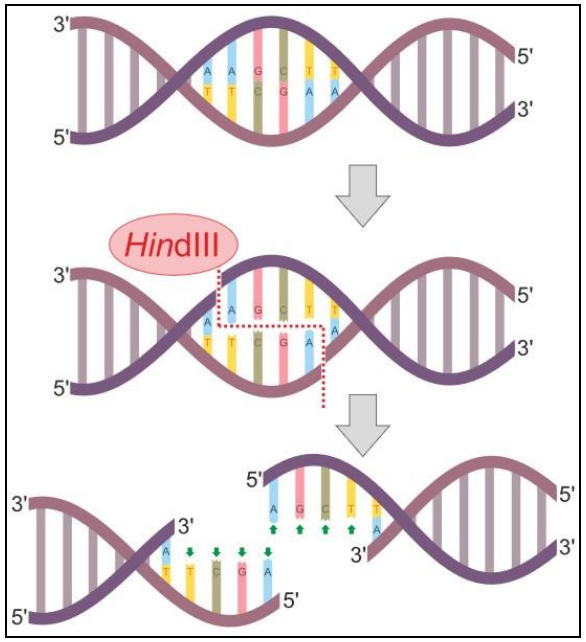
Crick laid out: the central dogma, which gave the relationship between DNA, RNA, and proteins,

.

- **1961-**Marshall Nirenberg, Heinrich Mathaei and Severo Ochoa cracked the **"Genetic Code"**: a sequence of three nucleotide bases (codon) determine each of amino acids
- **1965-**The noble prize was awarded jointly to: **FRANÇOIS JACOB** , **ANDRÉ LWOFF** and **JACOUES MONOD** for their discoveries concerning the regulation of gene expression

Major events in the history of Molecular Biology 1970

- **1970** Howard Temin and David Baltimore independently isolate the first restriction enzyme
- DNA can be cut into reproducible pieces with site-specific endonuclease called restriction enzymes;
  - the pieces can be linked to bacterial vectors and introduced into bacterial hosts. (gene cloning or recombinant DNA technology)



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- **1972** -Paul Berg used a restriction enzyme to cut DNA and ligase to paste two DNA strands together to form hybrid circular molecule. This was the first recombinant DNA molecule and First successful DNA cloning experiment.

- **1974-** Allan Maxam and Walter Gilbert (Harvard) and Frederick Sanger (U.K. Medical Research Council) independently developed different methods for **sequencing DNA**

Major events in the history of Molecular Biology 1970- 1977

- **1977** Phillip Sharp and Richard Roberts demonstrated that pre-mRNA is processed by the excision of introns and exons are spliced together.

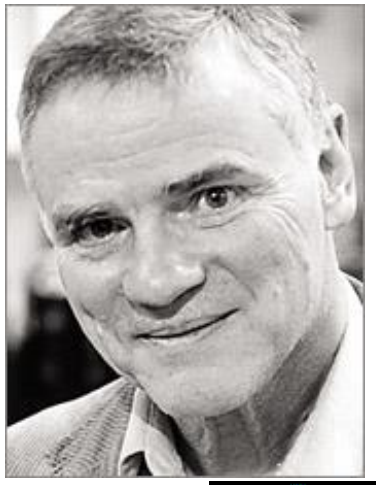
Phillip Sharp

Richard Roberts

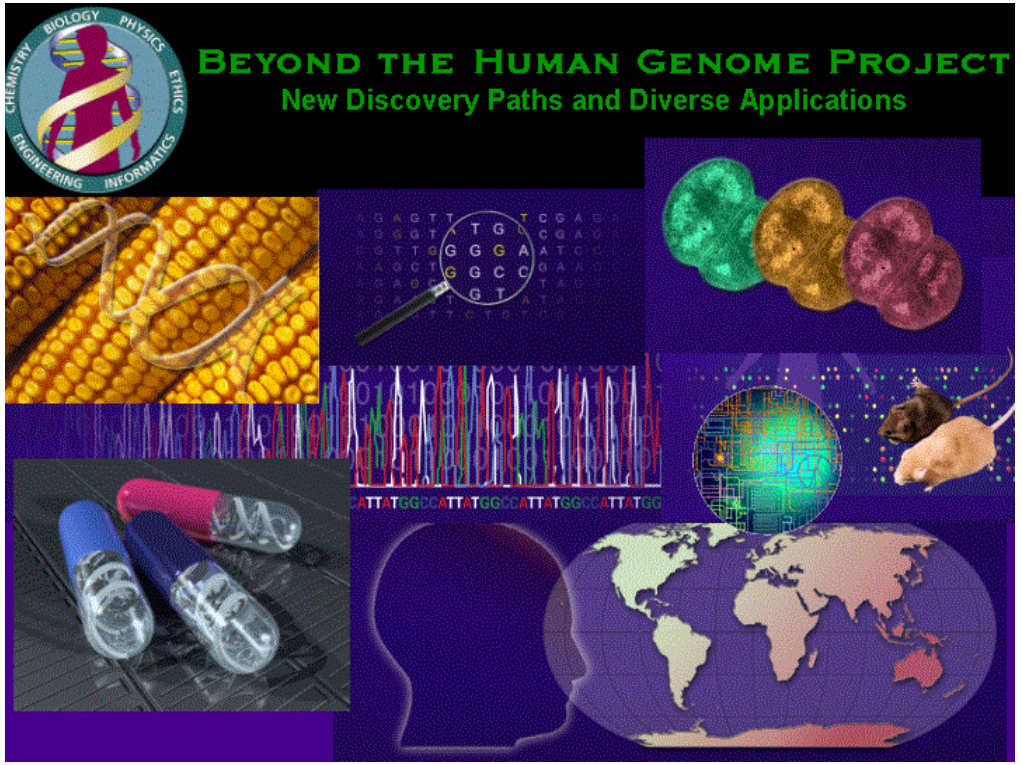
Joan Steitz

Major events in the history of Molecular Biology 1986 - 1995

- **1986** Leroy Hood: Developed automated sequencing mechanism
- **1986** Human Genome Initiative announced
- **1990** The 15-year Human Genome Project is launched by congress



Leroy Hood



Major events in the history of Molecular Biology 1995-1996

- **1995** John Craig Venter: First bactierial genomes sequenced
- **1995** Automated fluorescent sequencing instruments and robotic operations
- **1996** First eukaryotic genome-yeast-sequenced

John Craig Venter

Major events in the history of Molecular Biology 1997 - 1999

- **1997** E. Coli sequenced
- **1998** PerkinsElmer, Inc.. Developed 96-capillary sequencer
- **1998** Complete sequence of the Caenorhabditis elegans genome
- **1999** First human chromosome (number 22) sequenced

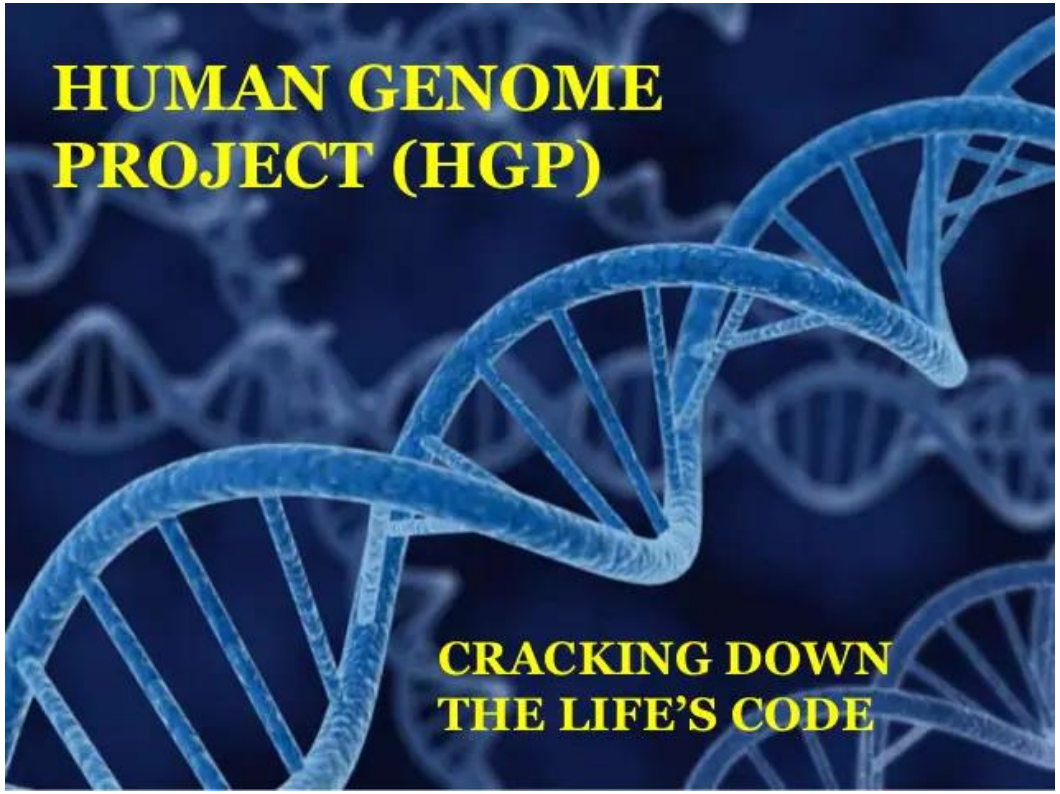
Major events in the history of Molecular Biology 2001

- **2001** International **Human Genome Sequencing**: first draft of the sequence of the human genome published

Selected major events in the history of Molecular Biology 2003-2004

- **April 2003** Human Genome Project. Mouse genome is sequenced.

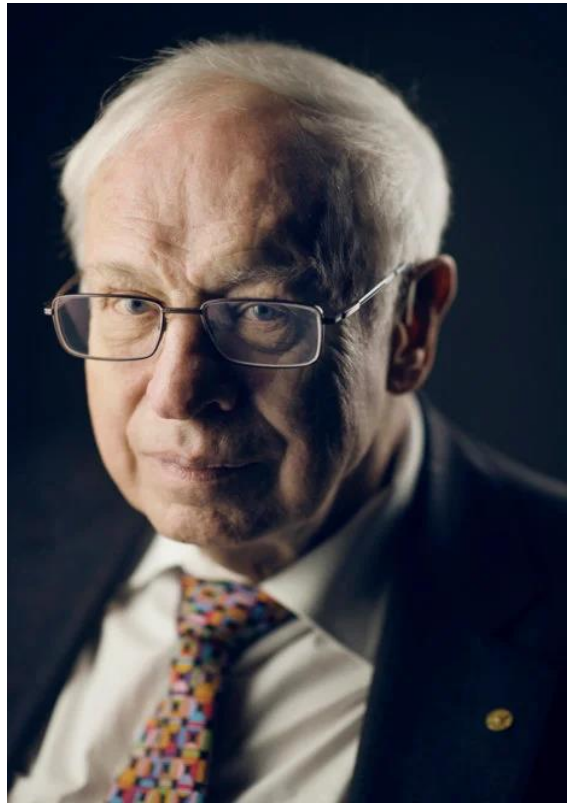
- **April 2004** Rat genome sequenced.



The Nobel Prize in Chemistry 2015

- was awarded jointly to Tomas Lindahl, Paul Modrich and Aziz Sancar

  "for mechanistic studies of DNA repair"



Nobel prize in Medicine and Physiology 2018

- was awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation

The Nobel Prize in Chemistry 2020

- Was awarded to Emmanuelle Charpentier and Jennifer A. Doudna for the development of a method for genome editing

Nobel prize in Medicine and Physiology 2023

- was awarded jointly to Katalin Karikó and Drew Weissman "for their discoveries concerning nucleoside base modifications that enabled the development of effective mRNA vaccines against COVID-19"

Nobel prize in Medicine and Physiology 2024

- was awarded jointly to Victor Ambros and Gary Ruvkun "for the discovery of microRNA and its role in post-transcriptional gene regulation"