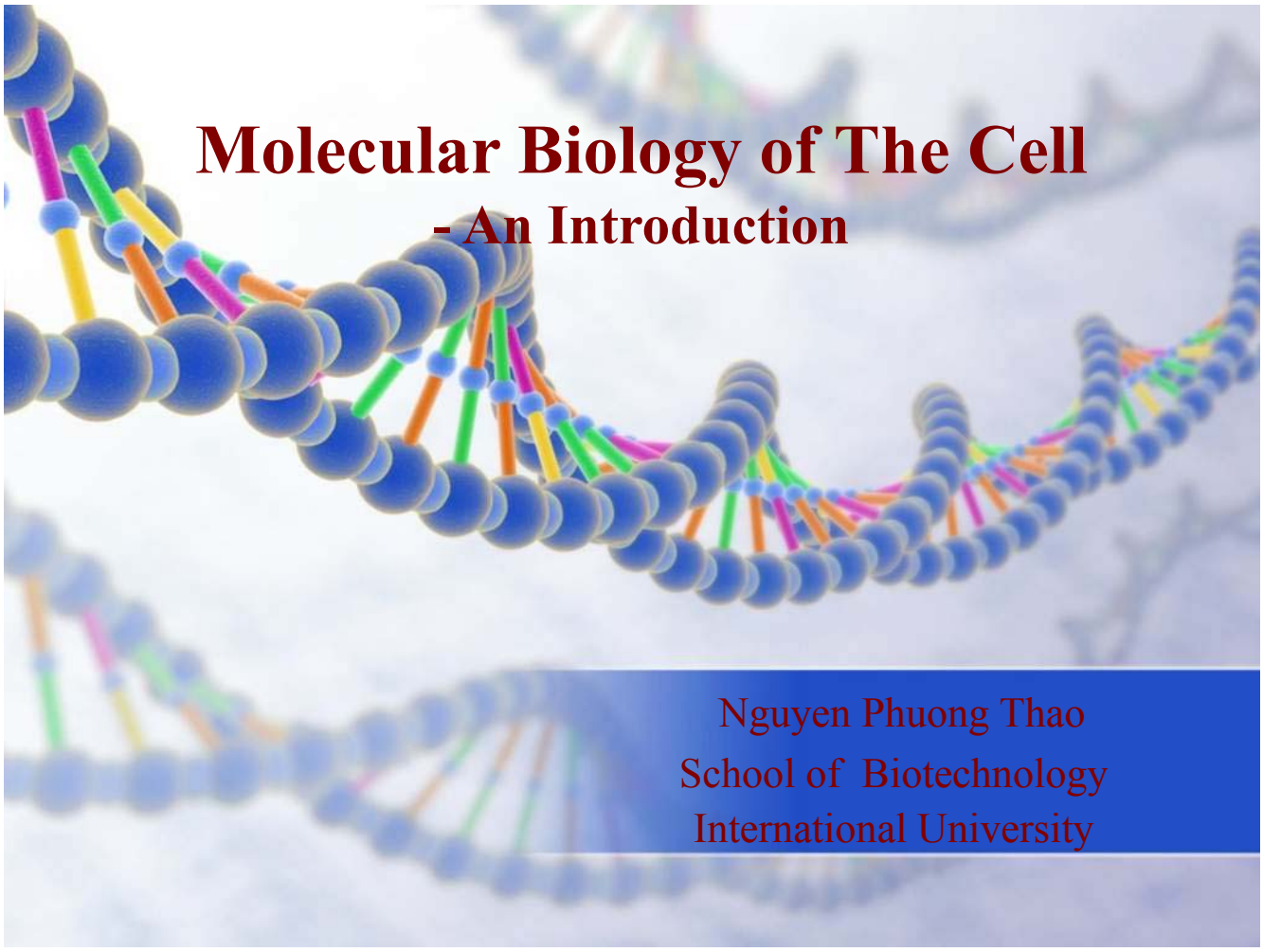


Molecular Biology of The Cell
- An Introduction

Nguyen Phuong Thao
School of Biotechnology
International University

Contents

Molecular Biology

- What is molecular biology?

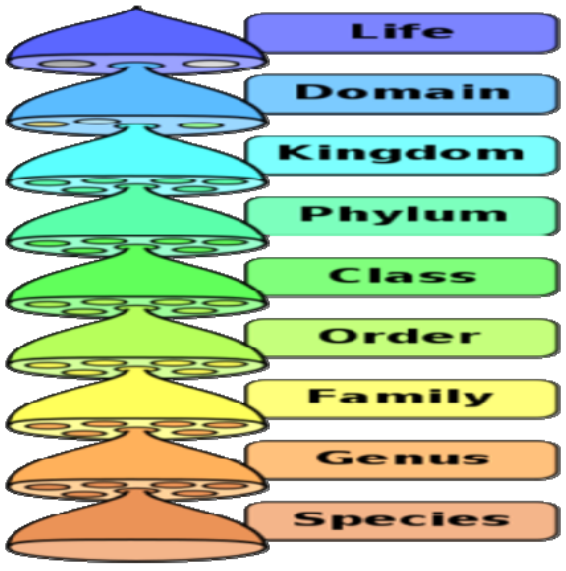
- The attempt to understand biological phenomena in molecular terms
- The study of gene structure and function at the molecular level

- Molecular biology is a melding of aspects of genetics and biochemistry.

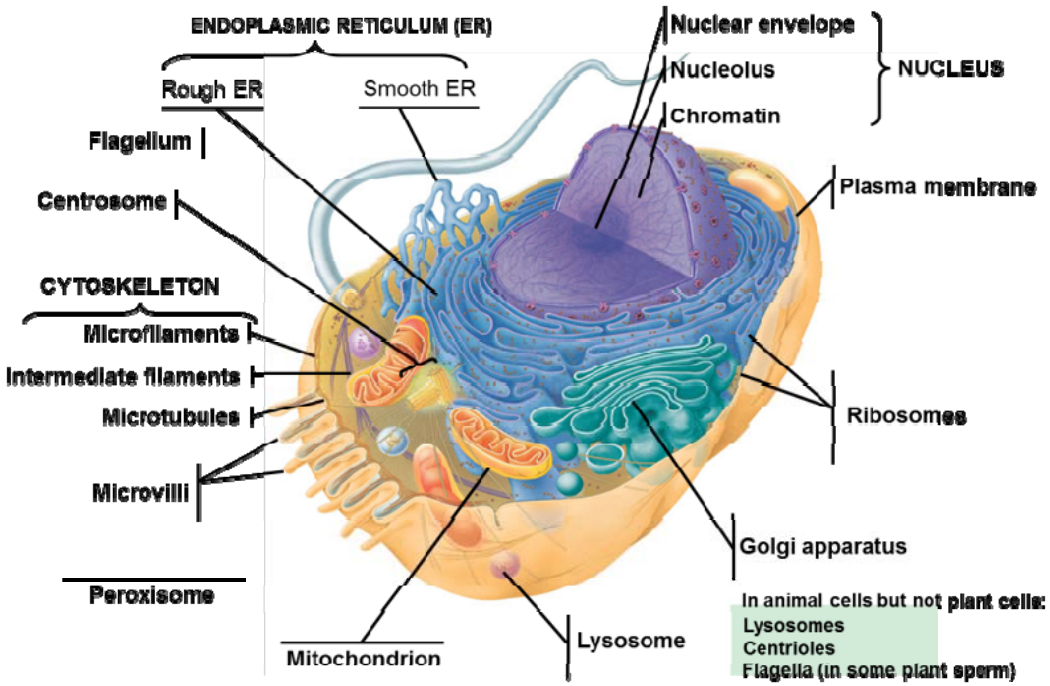
- The Molecular biology allows the laboratory to be predictive in nature; events that occur in the future.

Three Domain of Life

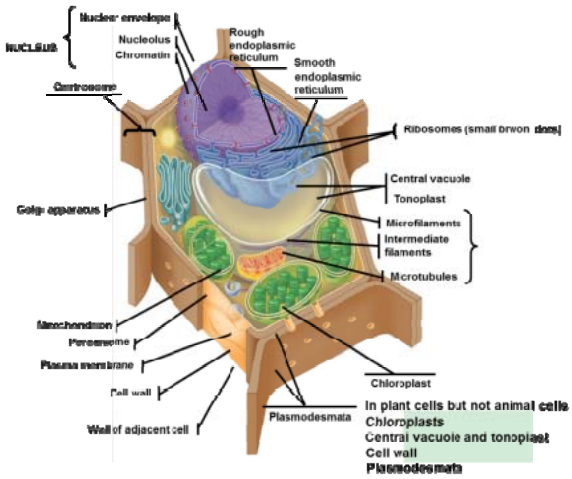
- Eukaryotic
- Prokaryotic
- Archaea
  - Thermophiles tolerate extremely high temperatures
  - Halophiles tolerate very high salt concentrations
  - Methanogens produce methane as a by-product of metabolism



Eukaryotic Cell

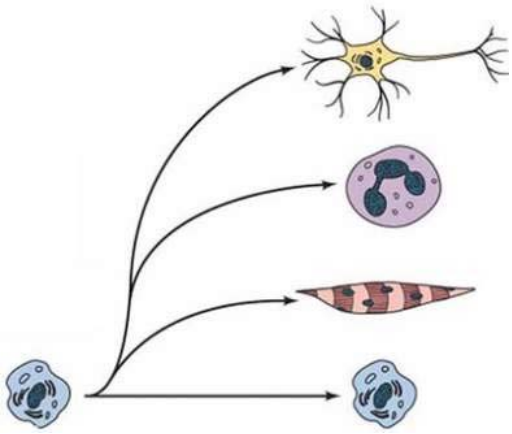


Eukaryotic Cell



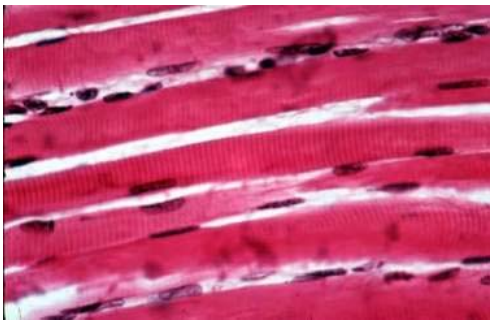
Cell Specialization

- **Cells in a multi-cellular organism become specialized by turning different genes on and off**
- **This is known as DIFFERENTIATION**



Specialized Animal Cells

Muscle cells

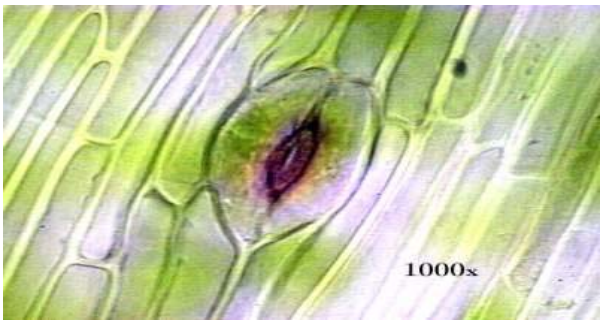


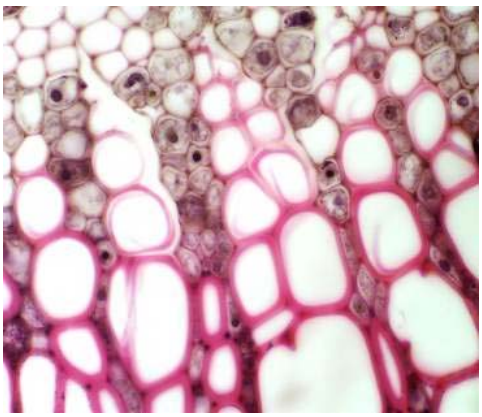
Red blood cells

Cheek cells

Specialized Plant cells

Guard Cells





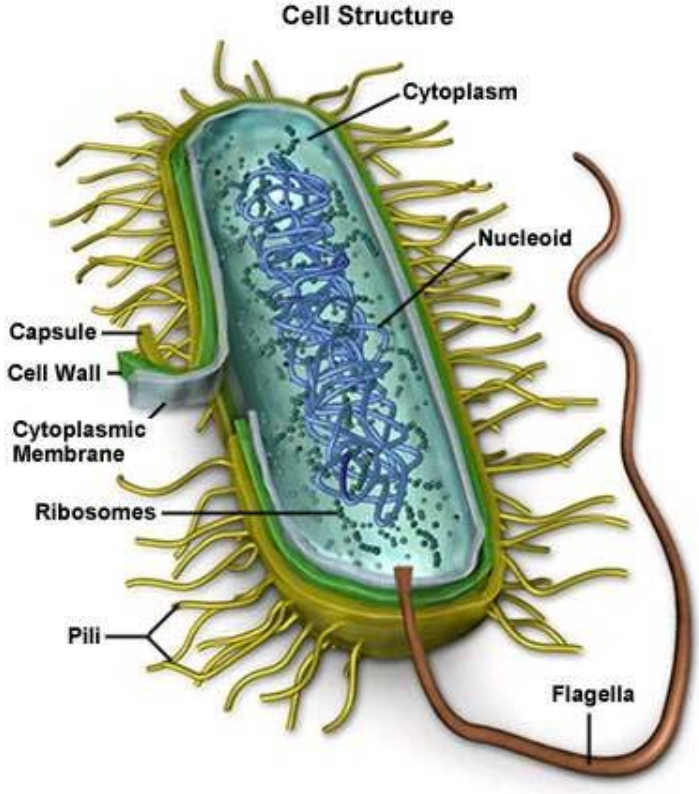
Pollen

Xylem cells

Eukaryotic Cell

- Eukaryotes include protists, fungi, animals and plants;
- Cell with a true nucleus, where the genetic material is surrounded by a membrane;
- Eukaryotic genome is more complex than that of prokaryotes and distributed among multiple chromosomes;
- Eukaryotic DNA is linear;
- Eukaryotic DNA is complexed with proteins called histones;
- Numerous membrane-bound organelles;
- Complex internal structure;
- Cell division by mitosis.

Prokaryotic Cell



Prokaryotic Cell

- Unicellular organisms, found in all environments. These include bacteria and archaea;
- Without a nucleus; no nuclear membrane (genetic material dispersed throughout cytoplasm;
- No membrane-bound organelles;
- Cell contains only one circular DNA molecule contained in the cytoplasm;
- DNA is naked (no histone);
- Simple internal structure; and
- Cell division by simple binary fission.

Archaea

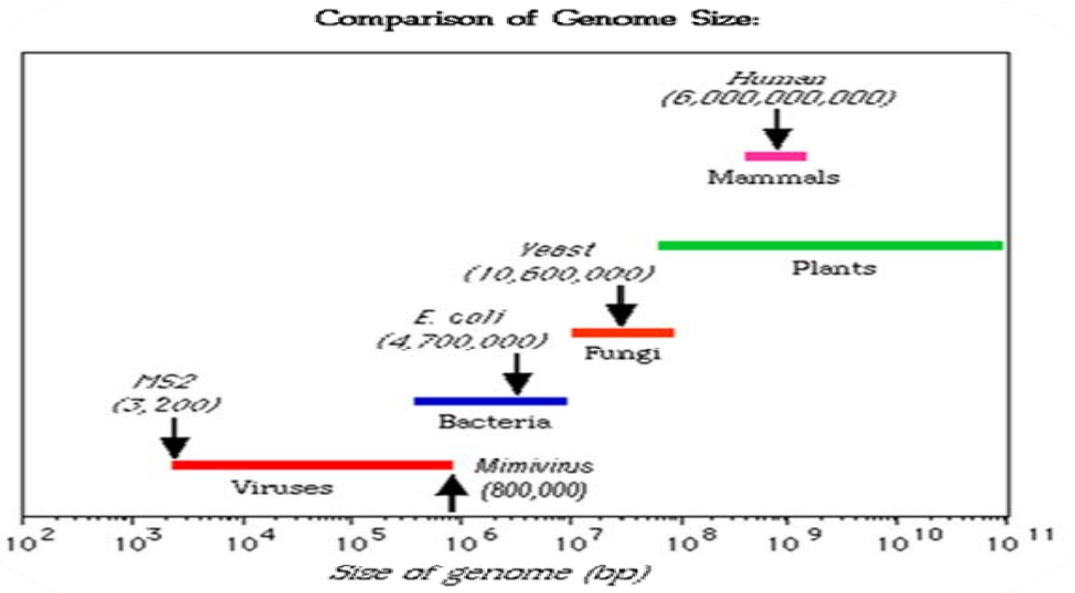
Archaea is prokaryotes; organisms without nucleus but some aspects of their molecular biology are more similar to those of eukaryotes.

Saperaud. Source: Wikipedia

The Genome

- Totality of genetic information of an organism.
- Encoded in the DNA (for some viruses, RNA).

The Genome Size



Species/ Number of Chromosomes

Species	Number of chromosomes
Human	46
Mouse	40
Rat	42
Fruit flies	8
Bacteria	1

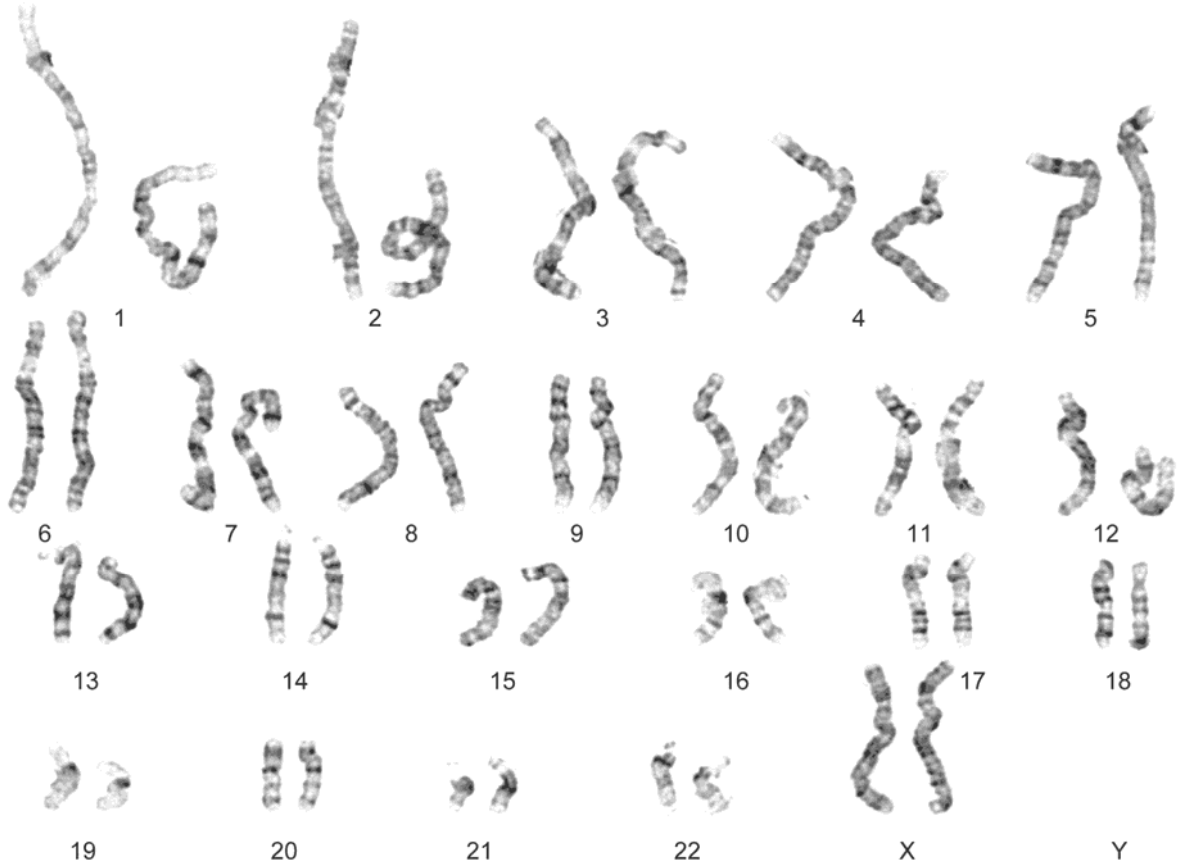
Human Genome

Human Genome; Arranged on multiple chromosomes; twenty three pairs of chromosomes;

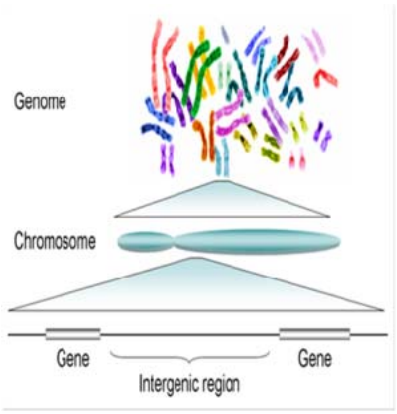
- Twenty two pairs (autosomes).
- One pair (sex chromosome) (XX) (female) or (XY) (male).

Humans have 23 pairs of chromosome in every cell (except mature red blood cells..); Gametes or sex cells (sperm and eggs) have half the normal complement of chromosomes.

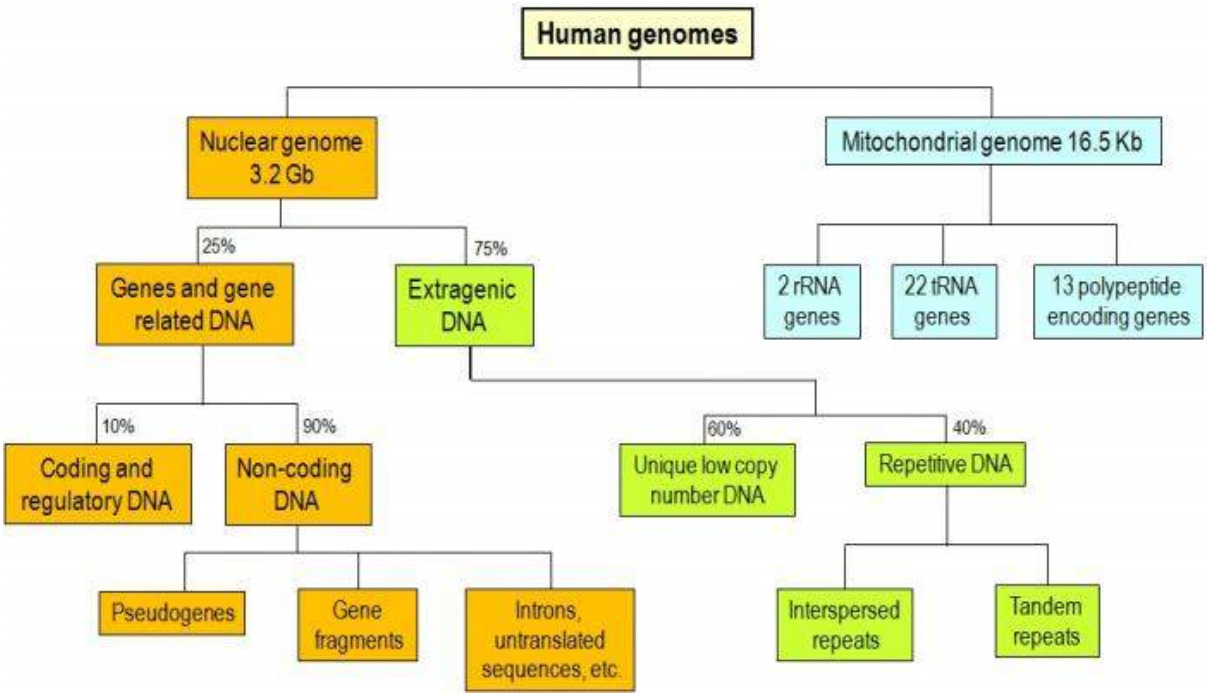
Each human cell contains 46 chromosomes (except sperm or egg cells)



Human Genome



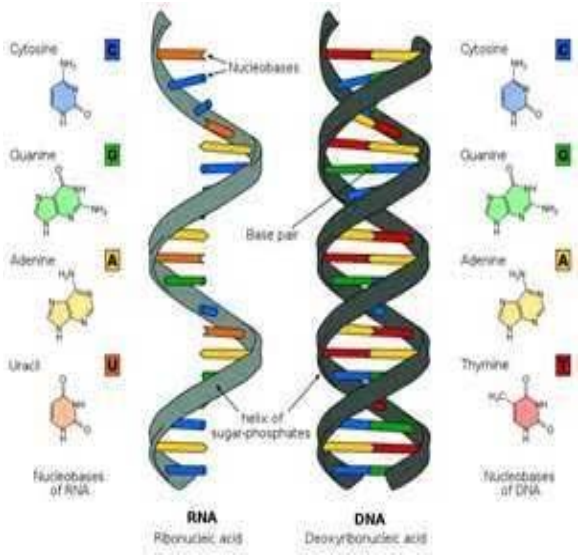
Jane Ades. Source: National Human Genome Research Institute



Modified from Strachan and Read . Source: http://geneticssuite.net/node/33

General Structure of Nucleic Acid

DNA and **RNA** are long chain polymers of small chemical compound called nucleotides.



Nucleotides

Nucleotides; ring shaped structures composed of:

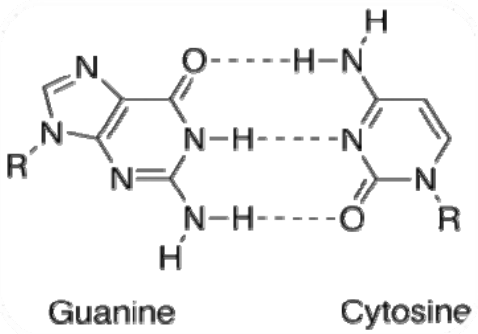
- Nitrogenous base; these bases are classified based on their chemical structures into two groups:
  - Purine; double ringed structure (Adenine and Guanine).
  - Pyrimidine; single ring structures (cytosine and thymine).
- Sugar
- Phosphate group

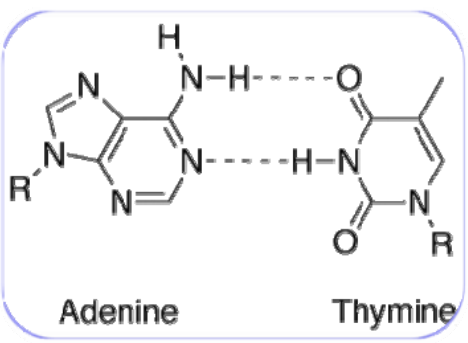
Nucleotides

- DNA: Four different types of nucleotides differ in nitrogenous base:
  - A is for adenine;
  - G is for guanine;
  - C is for cytosine and
  - T is for thymine.

- RNA: thymine base replaced by uracil base.

Nucleotides





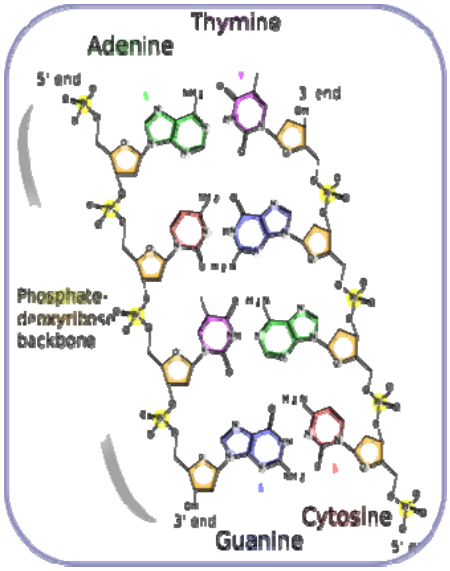
The DNA

- **Deoxyribonucleic Acid (DNA);** the genetic material of all cellular organisms and most viruses.
- **DNA**; the gigantic molecule which is used to encode genetic information for all life on Earth.
- A human cell contains about 2 meters of **DNA**. **DNA** in the body could stretch to the sun and back almost 100 times. So it is tightly packed.
- **DNA** responsible for preserving, copying and transmitting information within cells and from generation to generation.

DNA Double Helix

- Linked as a twisted ladder.
- The curving sides of the ladder represent the sugar-phosphate backbone of the two DNA strands; the rungs are the base pairs.
- Possess antiparallel polarity.
- Stabilized by hydrogen bonds between the bases.

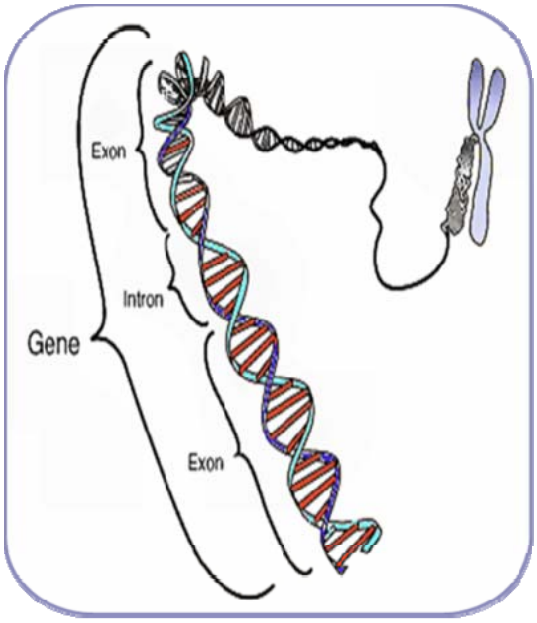
DNA Double Helix



The Gene

- **The gene;** it is a segment within a very long strand of DNA.
- **Genes** are the basic units of hereditary.
- **Genes** located on chromosome on its place or locus.
- **Allele;** a variant of the DNA sequence at a given locus. Each allele inherited from a different parent.

The Gene

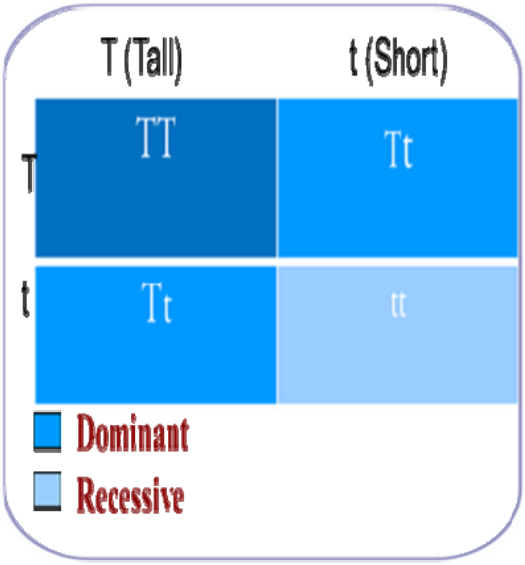


Source: National Human Genome Research Institute.

Dominant and Recessive

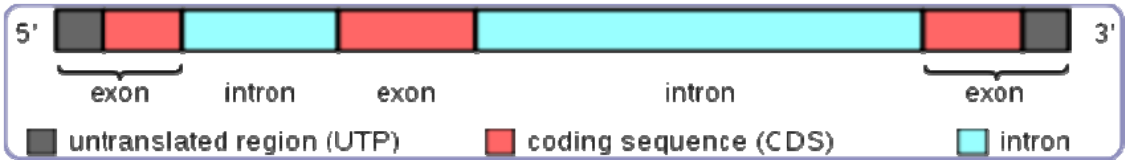
- **Dominant**
  - The one pair of allele that masks the effect of the other when present in the same cell.
- **Recessive**
  - The one pair of allele that is masked by the other when present in the same cell and capable of producing its characteristics phenotype in the organism only when two alleles is present and identical.

Dominant and Recessive



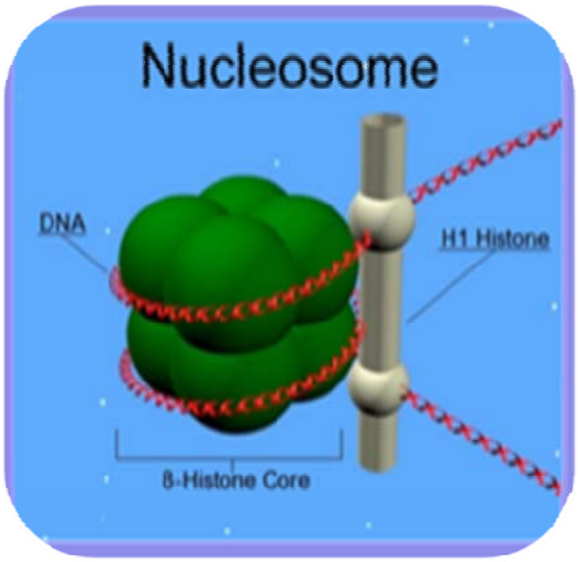
Gene Structure

- Most of the genes consist of; short coding sequences or exons are interrupted by a longer intervening noncoding sequence or introns; although a few genes in the human genome have no introns.

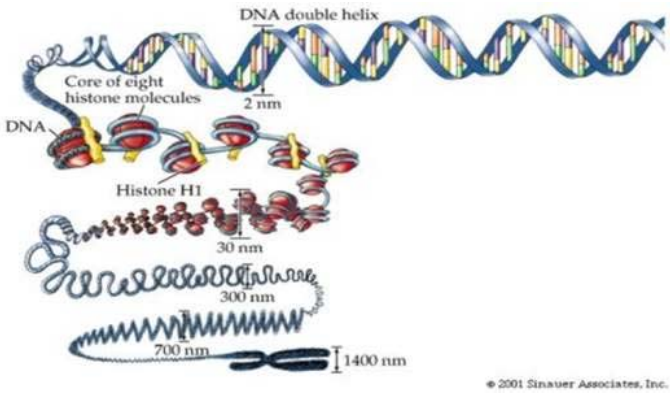


DNA Organization

DNA molecules complexed with other proteins, especially basic proteins called histones to form a substance known as chromatin.



DNA Organization

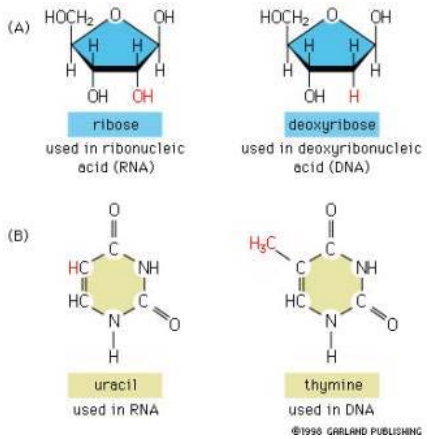


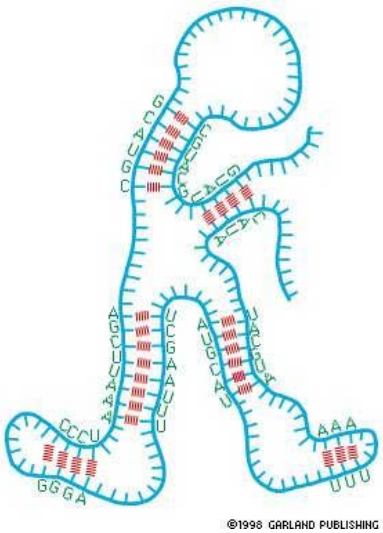
The RNA

- Three major classes of RNA: messenger (mRNA), transfer (tRNA) and ribosomal (rRNA). Minor classes of RNA include small nuclear RNA; small nucleolar RNA;…….

- RNA is a single stranded; the pyrimidine base **uracil** (U) replaces thymine and ribose sugar replaces deoxyribose.

RNA vs DNA



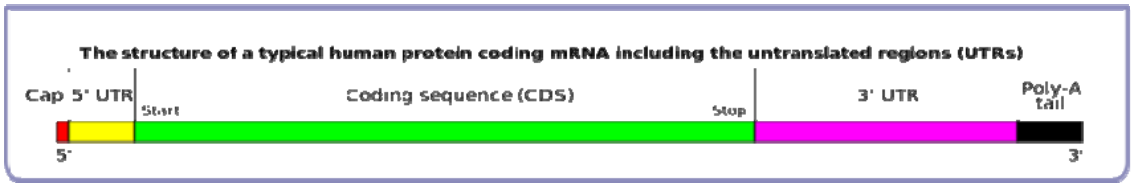


mRNAs	**codes for proteins**
rRNAs	**forms part of the structure of the ribosome and participates in protein synthesis**
tRNAs	**used in protein synthesis as an adaptor between mRNA and amino acids**
Small RNAs	**used in pre-mRNA splicing, transport of proteins to ER, and other cellular processes**

Messenger RNA/ mRNA

- Transcripts of structural genes.
- Encode all the information necessary for the synthesis of a polypeptide of protein.
- The 5' terminus is capped by 7 methyguanosine triphosphate.
- Synthesis of the poly (A) tail involves cleavage of its 3' end and then the addition of about 200 adenine residues.
- Intermediate carrier of genetic information; deliver genetic information to the cytoplasm.

mRNA

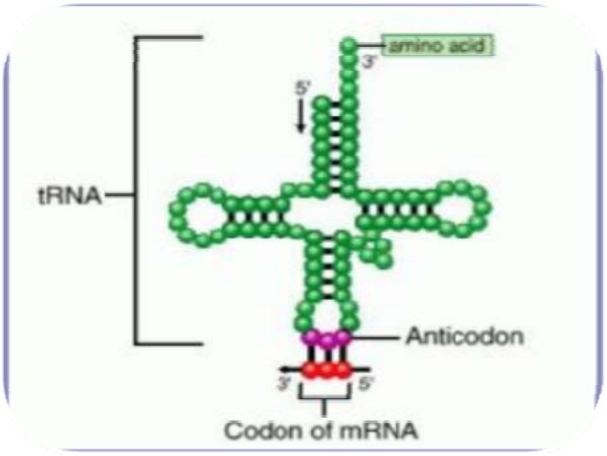


Transfer RNA/ tRNA

- All the tRNAs share a common secondary structure resembles a cloverleaf: They have four base- paired stems defining three stem-loops (the D loop, anticodon loop, and T loop) and the acceptor stem.

- tRNA carry correct amino acids to their position along the mRNA template to be added to the growing polypeptide chain.

tRNA



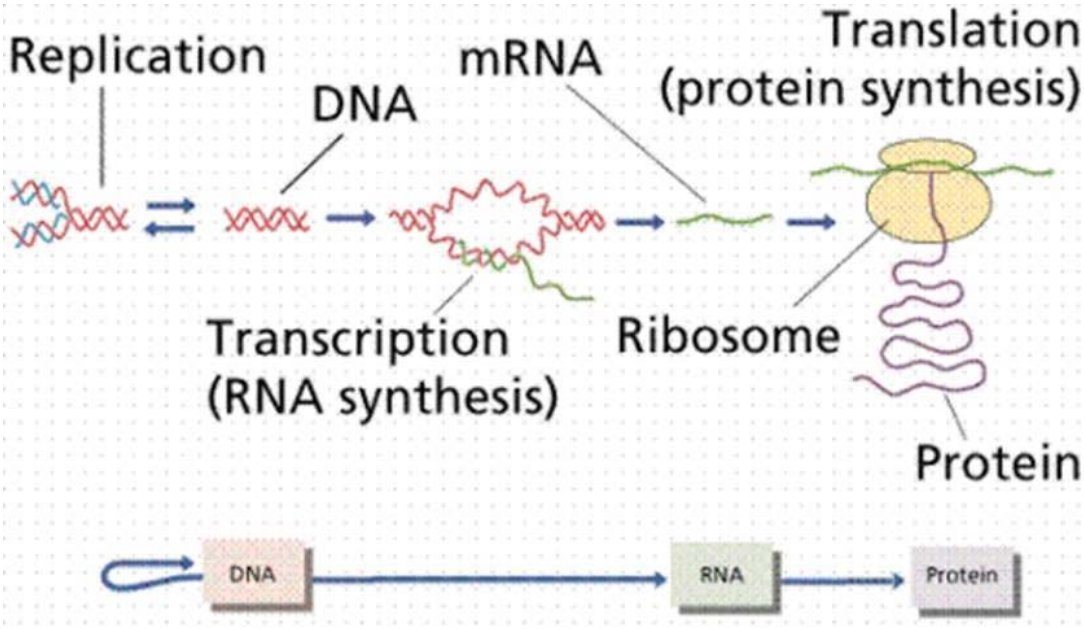
Ribosomal RNA/ rRNA

- The central component of the ribosome.
- Ribosome; factory for protein synthesis; composed of ribosomal RNA and ribosomal proteins (known as a Ribonucleoproteinor RNP).
- rRNA provides a mechanism for decoding mRNA into amino acids.

The Central Dogma of Molecular Biology

- DNA molecules serve as templates for either complementary DNA strands during the process of replication or complementary RNA during the process of transcription.
- RNA molecules serve as a template for ordering amino acids by ribosomes during protein synthesis.

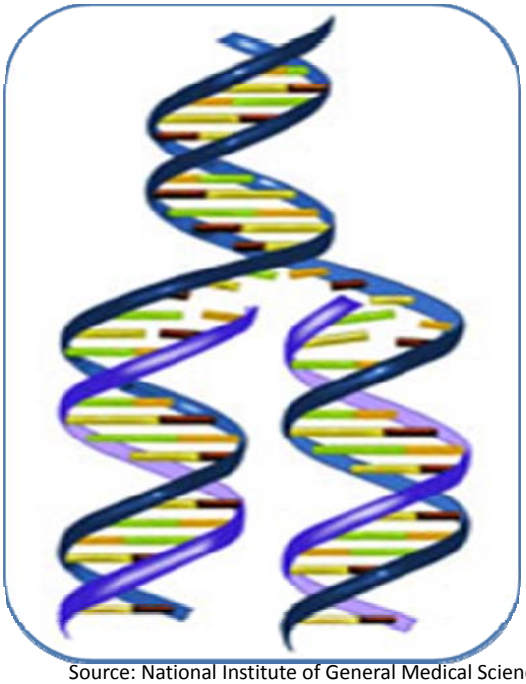
The Central Dogma of Molecular Biology



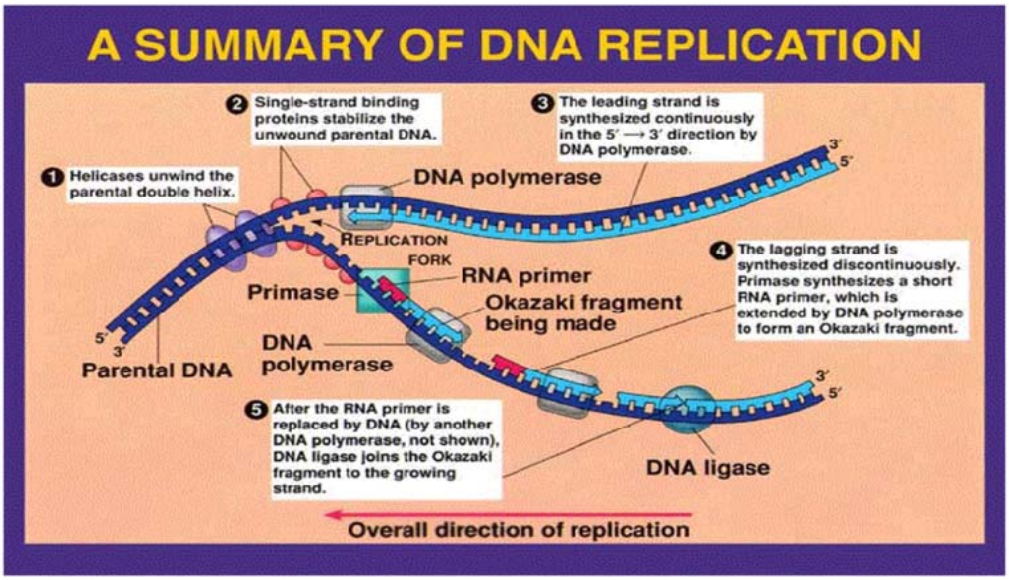
DNA Replication

- The DNA duplication.
- The transfer the genetic information from a parent to a daughter cell.
- The DNA base sequences are precisely copied.

DNA Replication



Source: National Institute of General Medical Sciences.



George Rice. Montana State University.
Source: http://serc.carleton.edu/microbelife/research_methods/genomics/replication.html

Post-Replicative Modification of DNA

- Methylation; one of the major post- replicative reactions.
- Site of methylation of eukaryotic DNA is always on cytosine residues in CG dinucleotide.
- DNA methylation plays an important role for epigenetic gene regulation in development and disease.

Gene Expression

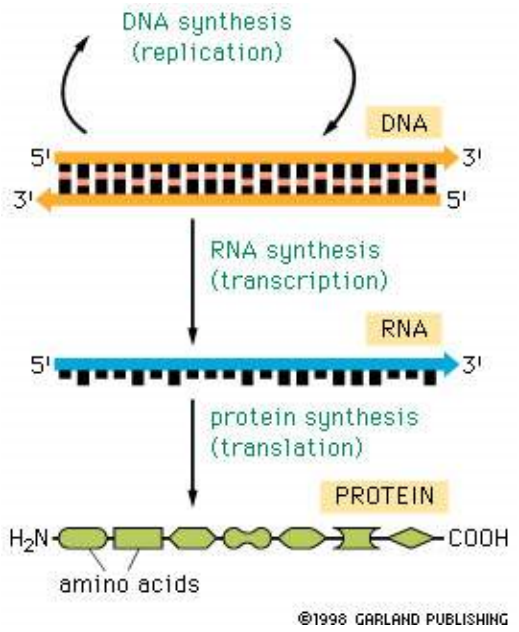
Transcription

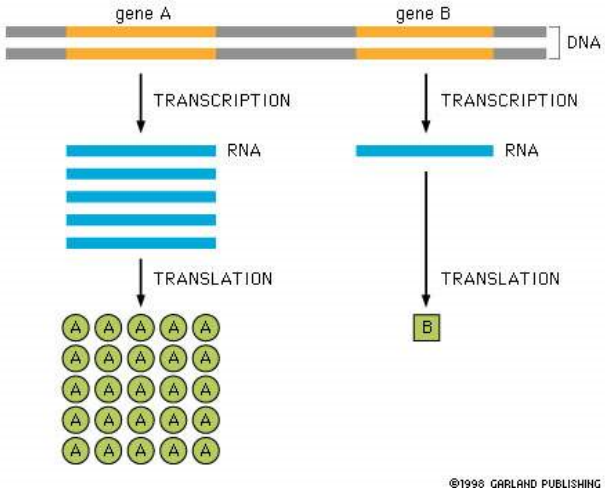
RNA polymerase makes a copy of information in the gene (complementary RNA) complementary to one strands of DNA.

Translation

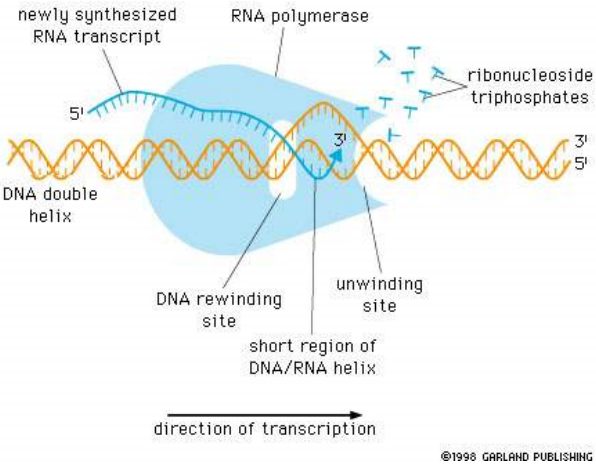
Occurs on **ribosomes,** messenger RNA decoded or translated to determine the sequence of amino acid in the protein being synthesized.

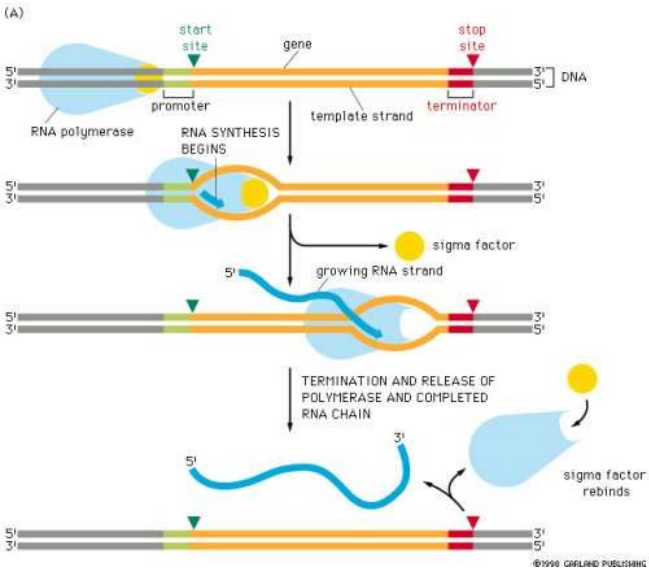
From DNA to protein

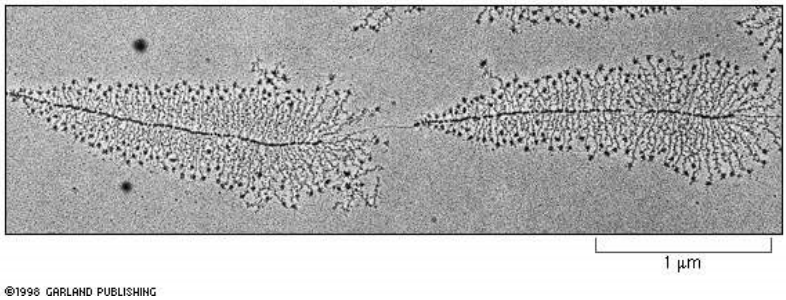




Transcription by RNA polymerase

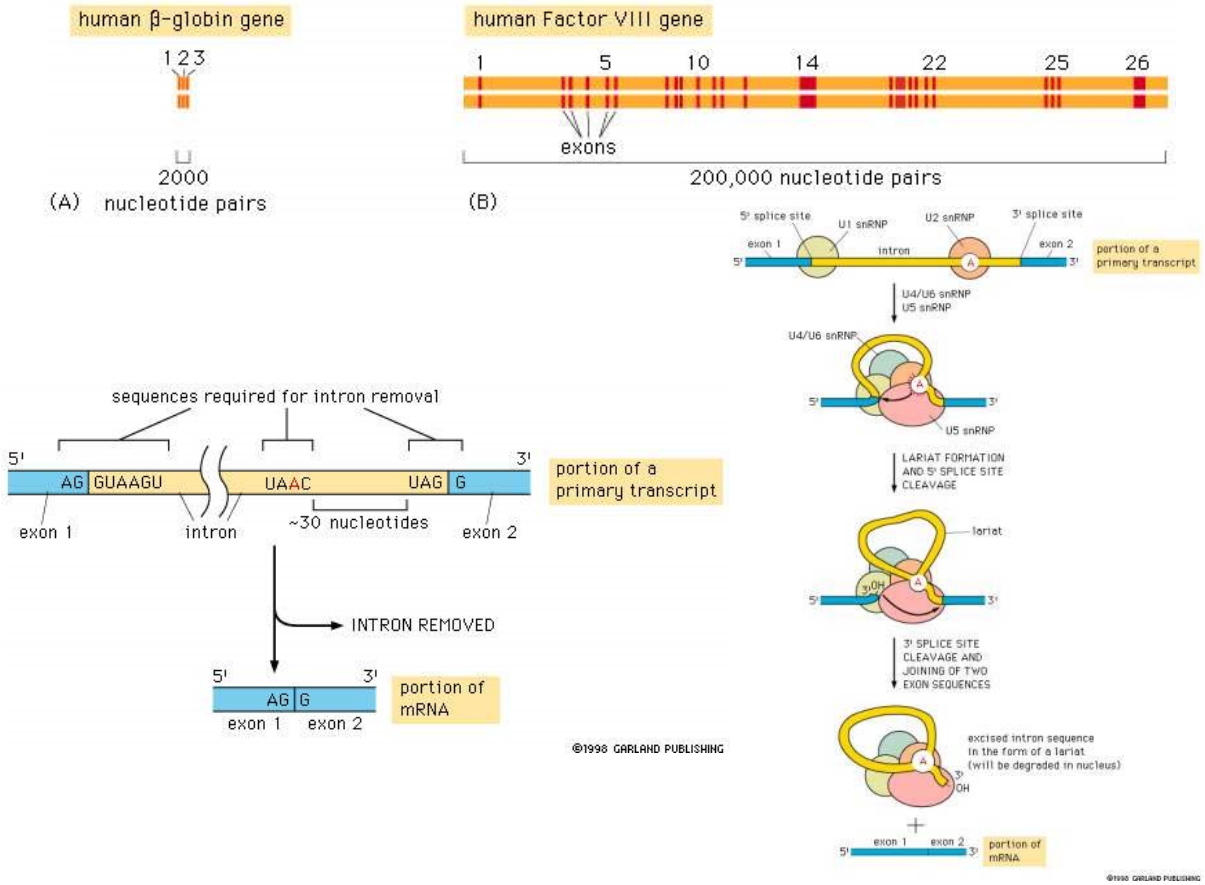






©1998 GARLAND PUBLISHING

Genes contain introns and exons



Ribosomes

- Factory for protein synthesis.
- Composed of ribosomal RNA and ribosomal proteins (known as a Ribonucleoprotein or RNP).
- Translate (mRNA) to build polypeptide chains using amino acids delivered by (tRNA).

The Protein

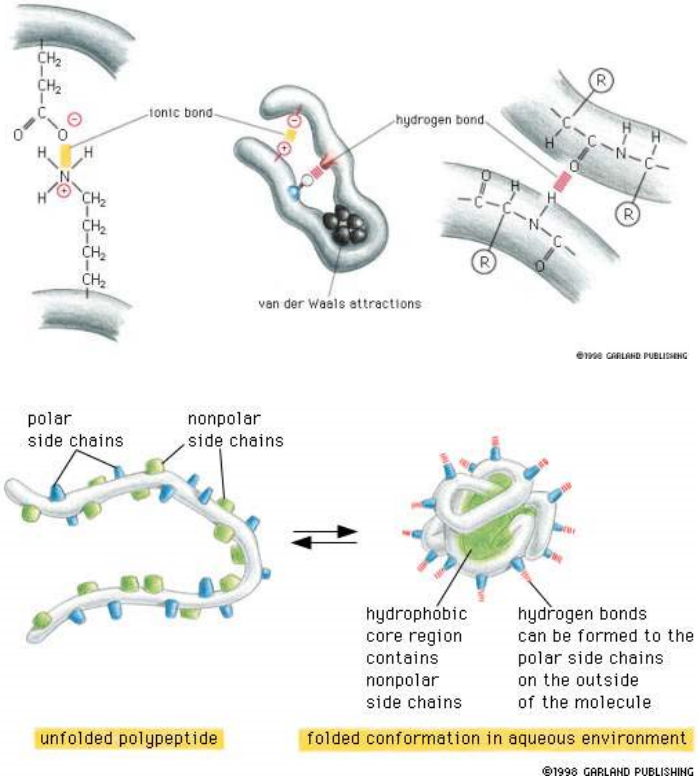
- **Proteins** are chain like polymers of a few or many thousands of amino acids.

- **Amino acids:** (3-nucleotide RNA sequences) (codon).

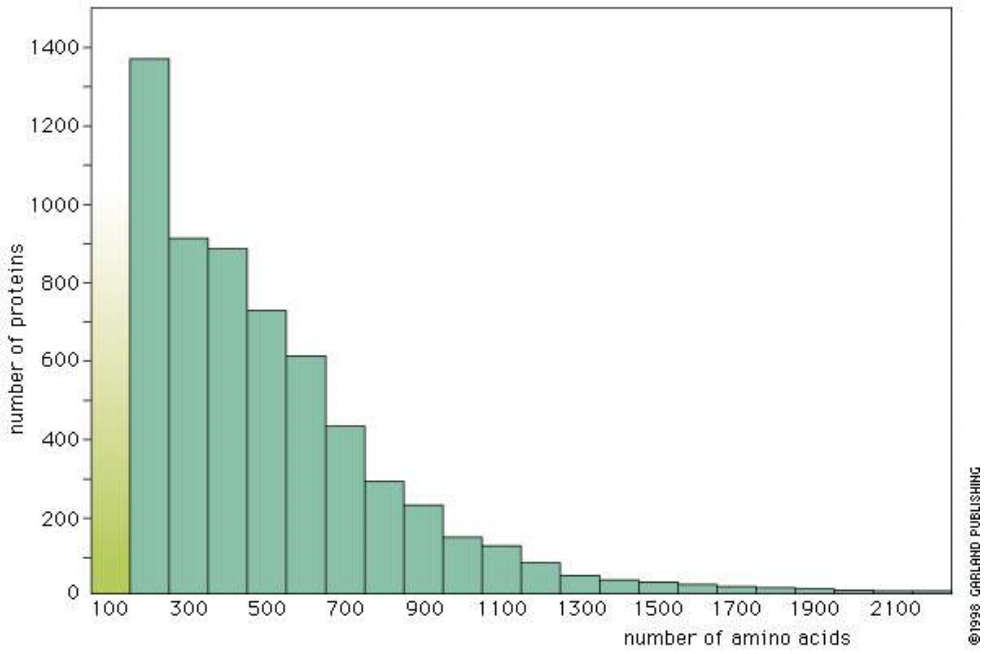
Four levels of Protein Structure

- **Primary protein structure:** Sequence of a chain of amino acid.
- **Secondary protein structure:** A chain of amino acids linked by hydrogen bonds.
- **Tertiary protein structure:** It occurs when certain attraction occurs between alpha helices and pleated sheets.
- **Quaternary protein structure:** Protein containing more than one amino acid chains.

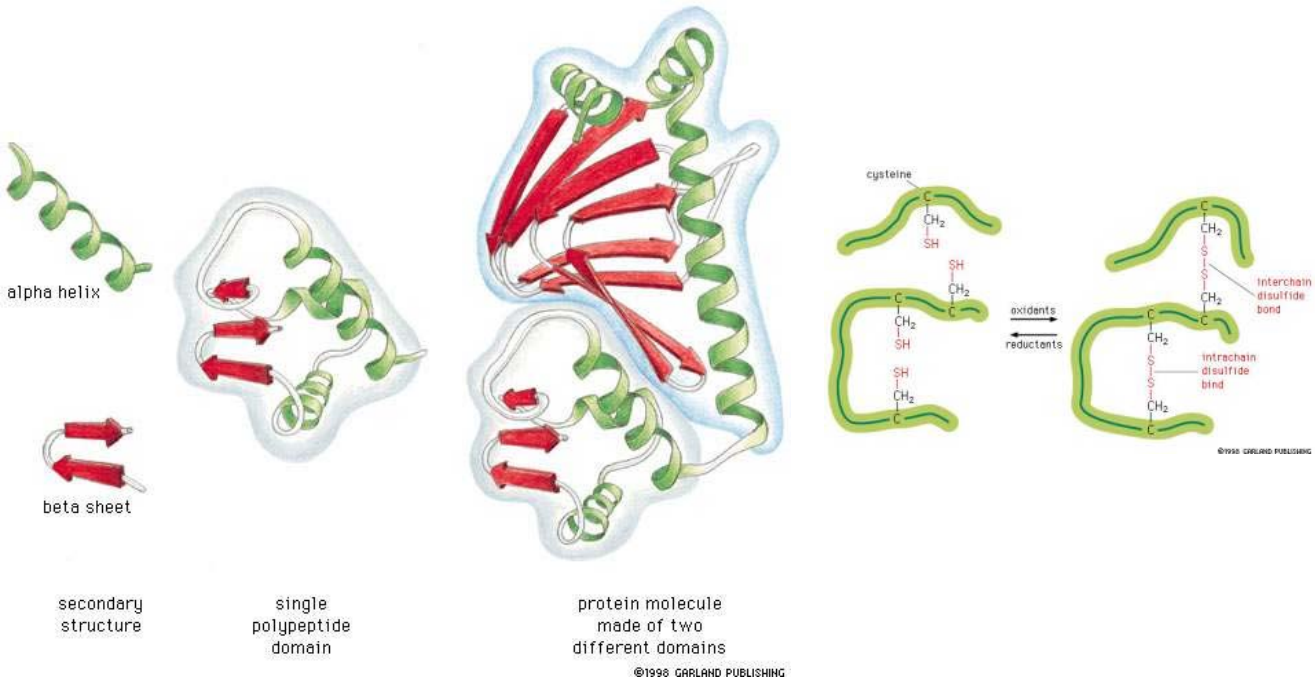
Three types of noncovalent bonds that help proteins fold



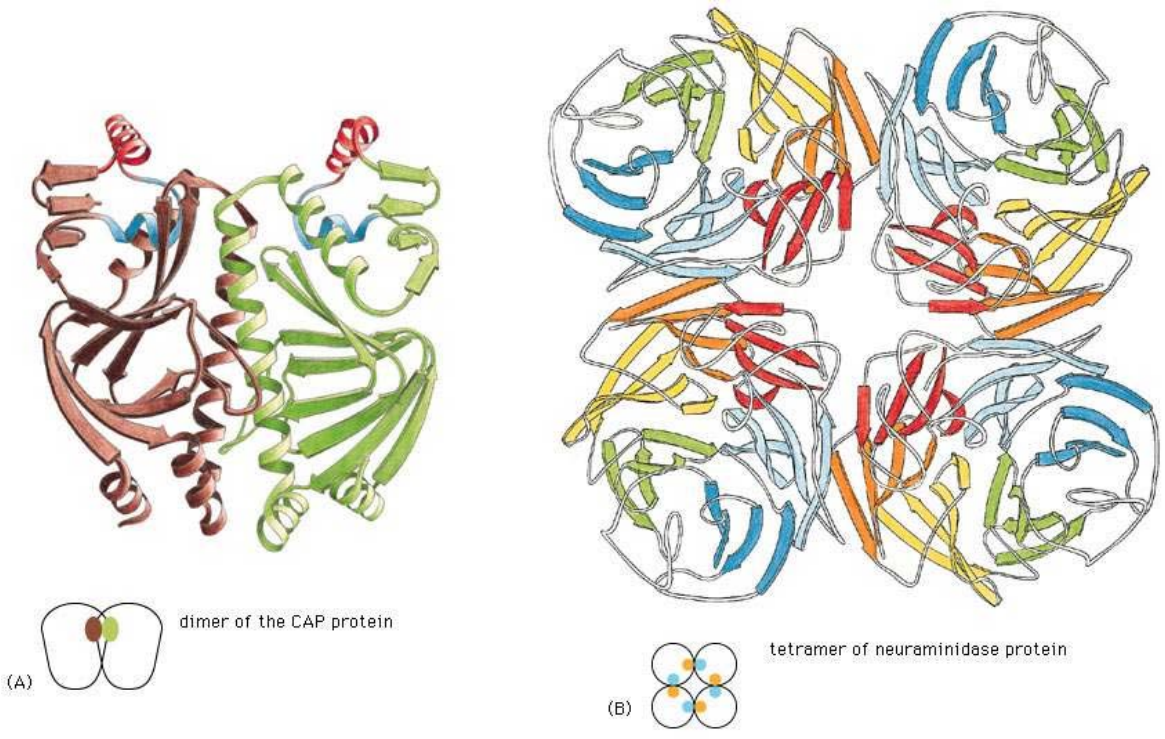
The size of proteins



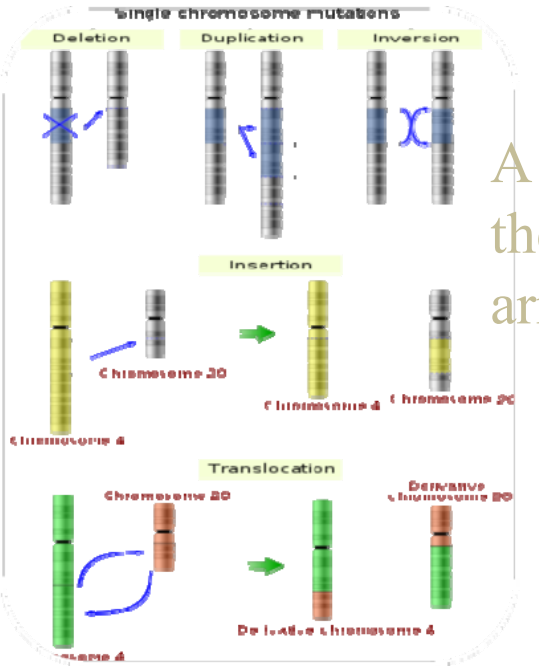
Several levels of protein organization



Many protein molecules contain multiple copies of a single protein subunit

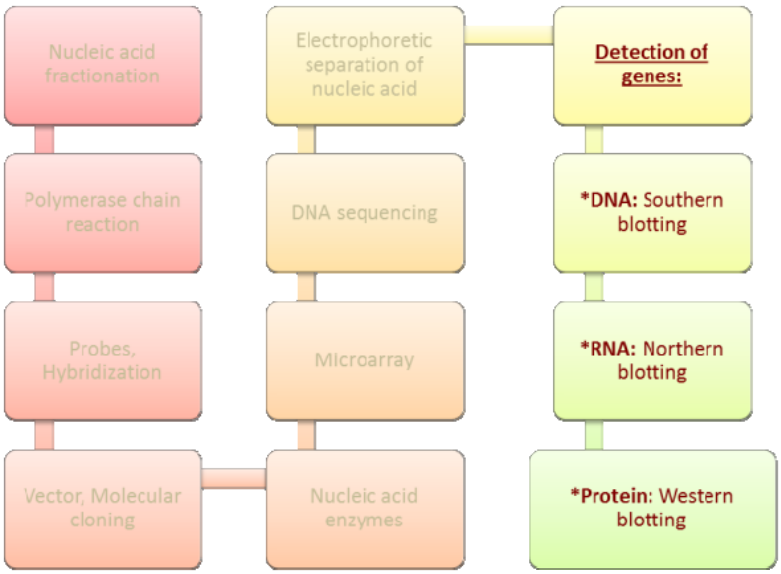


Genetic Mutation



A mutation is a change in the DNA sequence or arrangement of DNA.

Common Tools of Molecular Biology

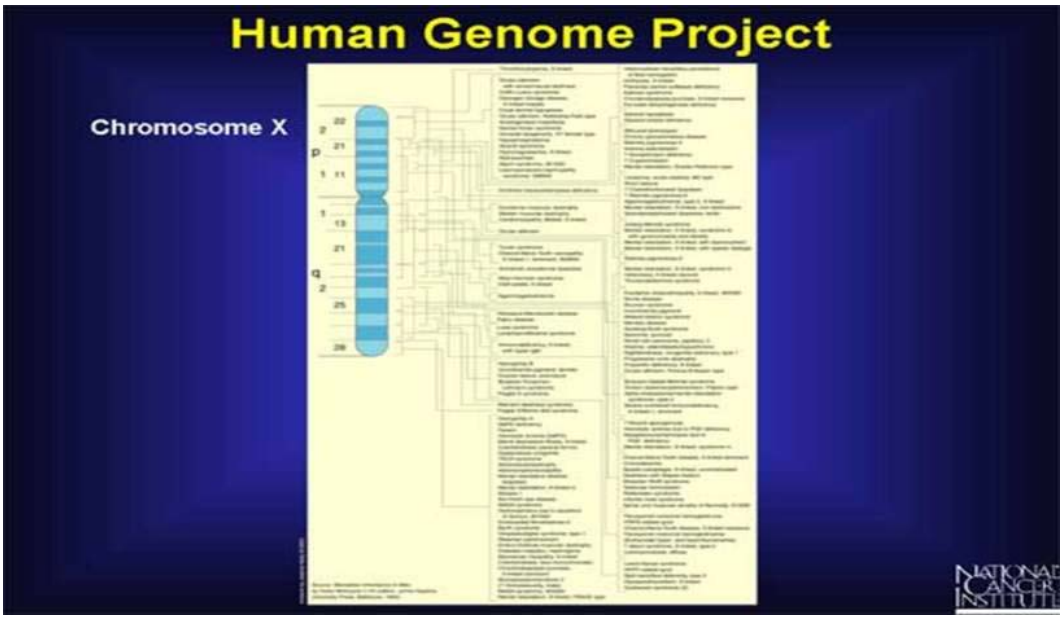


Human Genome Project

- HGP is an international project aiming for:
  - Sequencing and localization of the base sequence that makes up human DNA.
  - Store this information in databases.
  - Mapping of human genome requires a set of landmarks; some of this landmarkers are genes but many more are nameless stretches of DNA such as RFLPs, VNTRs, STSs.

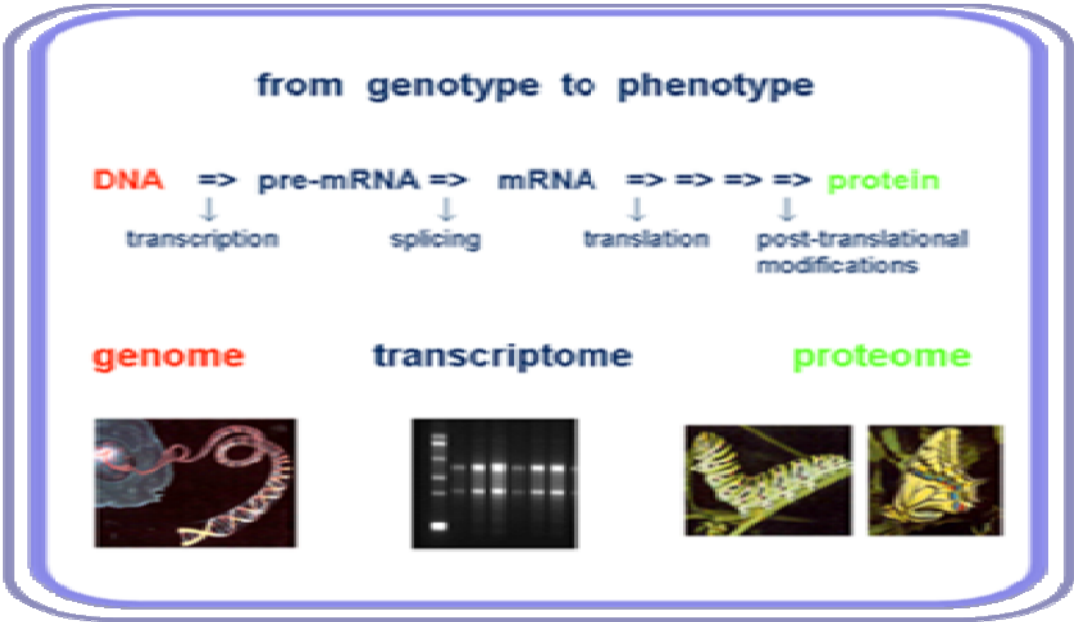
Human Genome Project

- 1990, American geneticists started an ambitious quest to map and sequence the entire human genome.
- 1999, the final draft of human chromosome 22.
- 2000, the final draft of human chromosome 21.
- 2001, working draft of the whole human genome.
- 2004, the finished sequence of the euchromatic part of human genome.



Functional Genomics / Transcriptomics/ Proteomics

- **Functional Genomics**
  - The study of expression of large number of genes.
- **Transcriptomics**
  - The study of transcriptomes (all the transcripts an organism makes at any given time).
- **Proteomics**
  - The study of proteomes (the set of expressed proteins in a given type of cells or an organism at a given time under defined conditions).



Source: European Bioinformatics Institute. http://www.ebi.ac.uk/microarray/biology_intro.html

Application of Molecular Biology

- **Research**
- **Diagnosis**
- **Transplantation**
- **Paternity**
- **Forensic analysis**
- **Gene therapy**
- **Drug Design**
- **……**