Chapter 4
Genetics and Cellular Function

- DNA and RNA – the nucleic acids
- Genes and their action
- DNA to Proteins

Discovery of the Double Helix

- By 1900: components of DNA were known
  - sugar, phosphate and bases
- By 1953: x-ray diffraction determined geometry of DNA molecule
- 1962 Nobel Prize awarded to: Watson, Crick and Wilkins
  - Rosalind Franklin died of cancer at 37.

DNA Structure

- Double helix
  - Composed of Nucleotides
    1. phosphate group
    2. deoxyribose sugar
    3. nitrogenous base
Nucleotides: phosphate group, sugar, and nitrogenous base

DNA Molecular Structure

- DNA – threadlike molecule with uniform diameter, but varied length
  - How many in most human cells?
- DNA and other nucleic acids are polymers of nucleotides
- Each nucleotide consists of
  - one sugar - deoxyribose
  - one phosphate group
  - one nitrogenous base

Nitrogenous Bases of DNA

- There are only four
- Purines - double ring
  - Adenine (A)
  - Guanine (G)
- Pyrimidines - single ring
  - Cytosine (C)
  - Thymine (T)
- DNA bases - ATCG

Complementary Base Pairing

- Nitrogenous bases united by hydrogen bonds
  - a purine on one backbone with a pyrimidine on the other
  - A – T two hydrogen bonds
  - C – G three hydrogen bonds
- DNA base pairing
  - A – T
  - C – G
- Law of Complementary Base Pairing
  - one strand determines base sequence of other
DNA Function

- **Gene** – segment of DNA that codes for a specific protein
- **Genome** - all the genes of one person (or species)
  - humans have ~35,000
  - 2% of total DNA
  - other 98% is non-coding DNA
    - plays role in chromosome structure
    - regulation of gene activity
    - no function at all – “junk” DNA

Chromatin and Chromosomes

- **chromatin** – thread of DNA material with proteins
  - occurs as 46 long filaments called chromosomes
  - in nondividing cells, chromatin is so slender it cannot be seen
  - **histones** – cluster of eight proteins
  - **nucleosome** consists of:
    - Histones with DNA around them

Cells Preparing to Divide

- exact copies are made of all DNA (DNA replication)
- each chromosome consists of two parallel **sister chromatids**
  - joined at **centromere**
  - **kinetochore** – proteins
- During cell division
  - sister chromatids pull apart
  - each new cell gets a chromatid

What is a Gene?

- Previous definition - **gene** - a segment of DNA that carries the code for a particular protein???
  - Body has millions of proteins but only 35,000 genes?
  - Small % of genes produce only RNA molecules
  - Some segments of DNA belong to 2 different genes
- Amino acid sequence of a protein is determined by the nucleotide sequence in the DNA

Human Genome

- **Genome** – all the DNA in one 23-chromosome set
  - 3.1 billion nucleotide pairs in human genome
- 46 human chromosomes comes in two sets of 23 chromosomes
  - one set of 23 chromosomes came form each parent
  - each pair of chromosomes (homologous chromosomes) has same genes but different versions (alleles) exist
- **Human Genome Project** (1990-2003) identified nitrogenous base sequences of 99% of the human genome

- **Homo sapiens** has only about 35,000 genes
- genes generate millions of different proteins
  - single gene can code for many different proteins
  - genes average about 3,000 bases long
  - range up to 2.4 million bases
- all humans are at least 99.99% genetically identical
  - 0.01% variations that we can differ from one another in more than 3 million base pairs
- some chromosomes are gene-rich and some gene-poor
- known locations for >1,400 disease-producing mutations
Genetic Code

- Millions of different proteins, all made from **20 amino acids**, encoded by genes made of **4 nucleotides** (A,T,C,G)
- **Genetic code** — Arrangement of nucleotides that code for amino acid sequence of proteins
  - i.e., nucleotides arrangement determines amino acid arrangement
- **Base triplet** — a sequence of 3 DNA nucleotides that codes for 1 amino acid
  - **codon** - the 3 base sequence in mRNA

RNA: Structure and Function

- **RNA**
  - Much smaller than DNA
  - a single nucleotide chain
  - Ribose sugar (not deoxyribose)
  - No thymine nitrogenous base (replaced by Uracil)
- 3 types of RNA
  1. **messenger RNA** (mRNA) over 10,000 bases
  2. **ribosomal RNA** (rRNA) 3.
  3. **transfer RNA** (tRNA) 70 - 90 bases
- **Function**
  - interprets code in DNA
  - uses those instructions for protein synthesis

Overview of Protein Synthesis

- all body cells contain identical genes (except sex cells and some immune cells)
- different genes are activated in different cells
- **Once activated a gene**
  - Makes **messenger RNA** (mRNA) — a mirror-image copy of the gene is made
  - migrates from the nucleus to cytoplasm
  - its code is read by the ribosomes
  - **ribosomes** — ribosomal RNA (rRNA) and enzymes
  - **transfer RNA** (tRNA) — delivers amino acids to the ribosome
  - ribosomes assemble amino acids in the order directed by codons of mRNA

From DNA to Protein

- **Transcription:** RNA Polymerase
  - The enzyme that oversees mRNA synthesis
  - Starts at a promoter site (thanks to a transcription factor)
  - Breaks H bonds & Unwinds DNA
  - Adds complementary nucleotides on DNA template strand
    - following Law of Complimentary Base Pairing
    - Joins RNA nucleotides together to match DNA coding strand
  - Encodes a termination signal to stop transcription
Fixing pre-mRNA

- Pre-mRNA is much larger than mRNA
  - Contains non-coding regions - introns
  - Coding regions - exons
  - In nucleus, introns are removed and exons spliced together to produce final mRNA

Splicing of mRNA

- One gene can code for more than one protein
- Exons can be spliced together into a variety of different mRNAs.
Translation of mRNA

1. **Polyosome: mRNA binding to ribosome**
   - mRNA binds to the ribosome, forming a polyosome.
   - The ribosome scans the mRNA, looking for the start codon (AUG).

2. **Codon 15**
   - The ribosome moves to the first codon on the mRNA, where it encounters the start codon.
   - The ribosome binds to the start codon, initiating translation.

3. **Codon 16**
   - The ribosome moves to the next codon, where it binds to the A site.
   - The aminoacyl-tRNA binds to the A site, and the ribosome moves to the P site, releasing the tRNA.

4. **Codon 17**
   - The ribosome moves to the next codon, where it binds to the A site again.
   - The aminoacyl-tRNA binds to the A site, and the ribosome moves to the P site, releasing the tRNA.

5. **Released mRNA**
   - Once the ribosome reaches the stop codon (UAA, UAG, or UGA), it dissociates from the mRNA.
   - The released mRNA is free to leave the cytoplasm.

6. **Direction of ribosome advance**
   - The ribosome moves in the 5' to 3' direction along the mRNA, translating the message.

7. **Free amino acids**
   - Amino acids are synthesized outside the cell and transported into the cytoplasm.

8. **Template strand of DNA**
   - DNA is transcribed into mRNA in the nucleus.
   - The mRNA is transported out of the nucleus and into the cytoplasm, where it binds to ribosomes.

9. **Anticodon bearing tRNA "head"**
   - tRNA anticodons hydrogen bond with complementary mRNA codons.

10. **Energized by ATP**
    - tRNA synthetase enzymes attach amino acids to tRNA molecules, consuming 1 ATP per amino acid.

11. **Translation with the same ribosomal subunits**
    - The ribosome dissociates from the mRNA after translation, and the ribosomal subunits rejoin to repeat the process.

12. **New amino acid to the protein**
    - A new amino acid is added to the growing protein chain.
    - The preceding tRNA hands off its amino acid to the ribosome, and the ribosome links the amino acid to the growing protein.

13. **Rejoin to repeat the process**
    - The ribosome moves to the next codon, where it binds to the A site.
    - The aminoacyl-tRNA binds to the A site, and the ribosome moves to the P site, releasing the tRNA.
    - This process repeats until the ribosome reaches the stop codon.

14. **Translation mechanism**
    - The ribosome moves in the 5' to 3' direction along the mRNA, translating the message.
    - Amino acids are synthesized outside the cell and transported into the cytoplasm.
    - DNA is transcribed into mRNA in the nucleus, and the mRNA is transported into the cytoplasm, where it binds to ribosomes.
    - tRNA anticodons hydrogen bond with complementary mRNA codons, and tRNA synthetase enzymes attach amino acids to tRNA molecules, consuming 1 ATP per amino acid.
    - The ribosome dissociates from the mRNA after translation, and the ribosomal subunits rejoin to repeat the process.
    - A new amino acid is added to the growing protein chain, and the preceding tRNA hands off its amino acid to the ribosome, and the ribosome links the amino acid to the growing protein.
    - This process repeats until the ribosome reaches the stop codon.
Information Transfer from DNA to RNA

Protein Synthesis

Review of Peptide Formation

Genetic Code:
- RNA codons code for amino acids according to a genetic code
- Remember there are 20 amino acids
Protein Processing and Secretion

- Protein synthesis is not finished when the amino acid sequence (primary structure) has been assembled.
- To be functional, it must coil or fold into precise secondary and tertiary structures.
- Chaperone proteins (stress proteins or heat-shock proteins)

Proteins to be secreted are made in ribosomes of rough ER
- Contains a leader sequence of 30+ hydrophobic amino acids.
- Inside ER leader sequence is removed; protein is modified.

Protein Packaging and Secretion

![Figure 4.11](image)

Mechanism of Gene Activation

![Mechanism of Gene Activation](image)

Synthesizing Compounds Other Than Proteins

- Cells synthesize glycogen, fat, steroids, phospholipids, pigments, and other compounds
  - No genes for these
  - Synthesis under indirect genetic control
  - Produced by enzymatic reactions
  - Enzymes are proteins encoded by genes
- Example – Testosterone production
  - A steroid
  - A cell of the testes takes in cholesterol
  - Enzymatically converts it to testosterone
  - Only occurs when genes for enzyme are activated