DNA Molecular Structure

- **DNA** – deoxyribonucleic acid - a long threadlike molecule with uniform diameter, but varied length
  - 46 DNA molecules in the nucleus of most human cells
    - total length of 2 meters
    - average DNA molecule 2 inches long

- DNA and other nucleic acids are polymers of nucleotides

- Each **nucleotide** consists of
  - one sugar - deoxyribose
  - one phosphate group
  - one nitrogenous base
    - Either pyrimidine (single carbon-nitrogen ring) or purine (double ring)

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*Figure 4.1a*
Nitrogenous Bases of DNA

- **Purines** - double ring
  - Adenine (A)
  - Guanine (G)

- **Pyrimidines** - single ring
  - Cytosine (C)
  - Thymine (T)

- **DNA bases** - ATCG

Figure 4.1b
DNA Structure

- Molecular shape is a double helix (resembles a spiral staircase)
  
  - each sidepiece is a backbone composed of phosphate groups alternating with the sugar deoxyribose.

  - steplike connections between the backbones are pairs of nitrogen bases

Figure 4.2
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

Figure 4.2 partial
DNA Function

- **Genes** – genetic instructions for synthesis of proteins

- **Gene** – segment of DNA that codes for a specific protein

- **Genome** - all the genes of one person
  - humans have estimated 25,000 to 35,000 genes
    - 2% of total DNA
    - other 98% is noncoding DNA
      - plays role in chromosome structure
      - regulation of gene activity
      - no function at all – “junk” DNA
Chromatin and Chromosomes

- **chromatin** – fine filamentous DNA material complexed with proteins

Figure 4.4b

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Cells Preparing to Divide

- exact copies are made of all the nuclear DNA

- each chromosome consists of two parallel filaments of identical DNA - sister chromatids

- in prophase, final coiling and condensing
  - now visible with light microscope

- final compaction enables the two sister chromatids to be pulled apart and carried to separate daughter cells without damage to the DNA
  - joined at centromere
  - kinetochore – protein plaques on either side of the centromere

Figure 4.5a
RNA: Structure and Function

• **RNA** smaller than DNA (fewer bases)
  - **messenger RNA** (mRNA) over 10,000 bases
  - **ribosomal RNA** (rRNA)
  - **transfer RNA** (tRNA) 70 - 90 bases
  - DNA averages 100 million base pairs

• **one nucleotide chain** (not a double helix as DNA)

• **ribose** replaces deoxyribose as the sugar

• **uracil** replaces thymine as a nitrogenous base

• Essential function
  - interprets code in DNA
  - uses those instructions for protein synthesis
  - leaves nucleus and functions in cytoplasm
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

• Current Definition – gene - an information-containing segment of DNA that codes for the production of a molecule of RNA that plays a role in synthesizing one or more proteins

• 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 has same genes but different versions (alleles) exist

• **Human Genome Project** (1990-2003) identified the nitrogenous base sequences of 99% of the human genome
  – **genomics** – the comprehensive study of the whole genome and how its genes and noncoding DNA interact to affect the structure and function of the whole organism.
Human Genome

• Findings of Human Genome Project
  – Homo sapiens has only about 25,000 to 35,000 genes
    • not the 100,000 formerly believed
  – genes generate millions of different proteins
    • not the old one gene one protein theory
    • 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
    • various combinations of these single-nucleotide polymorphisms account for all human variation
  – some chromosomes are gene-rich and some gene-poor
  – we now know the locations of more than 1,400 disease-producing mutations
Genetic Code

- body can make millions of different proteins, all from the same **20 amino acids**, and encoded by genes made of just **4 nucleotides** (A,T,C,G)

- **Genetic code** – a system that enables these 4 nucleotides to code for the amino acid sequence of all proteins

- minimum code to symbolize 20 amino acids is 3 nucleotides per amino acid

- **Base triplet** – a sequence of 3 DNA nucleotides that stands for one amino acid
  - **codon** - the 3 base sequence in mRNA
  - **64 possible codons** available to represent the 20 amino acids
    - 61 code for amino acids
    - **Stop Codons** – UAG, UGA, and UAA – signal the ‘end of the message’, like a period at the end of a sentence
    - **Start Codon** – AUG codes for methionine, and begins the amino acid sequence of the protein
Overview of Protein Synthesis

• all body cells, except sex cells and some immune cells, contain identical genes.

• different genes are activated in different cells

• any given cell uses 1/3 to 2/3rds of its genes
  – rest remain dormant and may be functional in other types of cells

• activated gene
  – 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 – cytoplasmic granules composed of ribosomal RNA (rRNA) and enzymes
  – transfer RNA (tRNA) – delivers amino acids to the ribosome
  – ribosomes assemble amino acids in the order directed by the codons of mRNA
Summary of Protein Synthesis

• process of protein synthesis
  – DNA → mRNA → protein

• transcription – step from DNA to mRNA
  – occurs in the nucleus where DNA is located

• translation – step from mRNA to protein
  – most occurs in cytoplasm
  – 15-20% of proteins are synthesized in the nucleus
Transcription

- **Transcription** – copying genetic instructions from DNA to RNA

- **RNA Polymerase** – enzyme that binds to the DNA and assembles the mRNA
  - The start and end of the gene are determined by codes in the DNA sequence.
Translation

• **translation** – the process that converts the language of nucleotides into the language of amino acids

• **ribosomes** - translate sequence of nucleotides into the sequence of amino acids
  
  – occur mainly in cytosol, on surface of rough ER, and nuclear envelope
  
  – consists of two granular subunits, large and small
    • each made of several rRNA and enzyme molecules
Translation of mRNA

• ribosome pulls mRNA molecule through it like a ribbon, reading the bases as it goes
  – when start **codon (AUG)** is reached, protein synthesis begins
  – all proteins begin with **methionine** when first synthesized
1. mRNA leaves the nucleus.
2. Ribosome binds mRNA.
3. tRNA binds an amino acid; binding consumes 1 ATP.
4. tRNA anticodon binds to complementary mRNA codon.
5. The preceding tRNA hands off the growing protein to the new tRNA, and the ribosome links the new amino acid to the protein.
6. tRNA is released from the ribosome and is available to pick up a new amino acid and repeat the process.
7. After translating the entire mRNA, the ribosome dissociates into its two subunits.
8. Ribosomal subunits rejoin to repeat the process with the same or another mRNA.
Translation

- requires the participation of transfer RNA (tRNA)
  - one end of the tRNA includes three nucleotides called an anticodon
  - other end has binding site specific for one amino acid
  - ribosome binds and holds tRNA with its specific amino acid
  - ribosome contains an enzyme that forms peptide bond that links amino acids together
Transfer RNA (tRNA)

(a) Anticodon

(b) Anticodon

Figure 4.8
Review of Peptide Formation

1. DNA double helix
2. Seven base triplets on the template strand of DNA
3. The corresponding codons of mRNA transcribed from the DNA triplets
4. The anticodons of tRNA that bind to the mRNA codons
5. The amino acids carried by those six tRNA molecules
6. The amino acids linked into a peptide chain

Figure 4.10
Gene Regulation

- genes are turned on and off from day to day
- their products are need or not
- many genes are permanently turned off in any given cell
DNA Replication and Cell Cycle

• before cells divide, it must **duplicate its DNA** so it can give a complete copy of all its genes to each daughter cell.

• since DNA controls all cellular function, this replication process must be very exact

• **Law of Complementary Base Pairing** – we can predict the base sequence of one DNA strand if we know the sequence of the other
  – enables a cell to reproduce one strand based on the information in another
DNA Replication

Figure 4.14

Key
A  T
C  G

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Steps of DNA Replication

- Double helix unwinds from histones

- enzyme DNA helicase opens one short segment of helix at a time
  - exposing its nitrogen bases

- replication fork – the point where the DNA is opened up (like two separated halves of a zipper)

- DNA polymerase molecules move along each strand
  - read the exposed bases
  - matches complementary free nucleotides

- the two separated strands of DNA are copied by separate polymerase molecules proceeding in opposite directions
  - the polymerase molecule moving toward the replication fork makes a long, continuous, new strand of DNA
  - the polymerase molecule moving away from the replication fork makes short segments of DNA at a time… DNA ligase joins them together
Steps of DNA Replication

- from the old *parental DNA* molecule, two new *daughter* DNA molecules are made

- **semiconservative replication** - each daughter DNA consists of one new helix synthesized from free nucleotides and one old helix conserved from the parental DNA

- new histones are synthesized in cytoplasm
  - millions of histones are transported into the nucleus within a few minutes after DNA replication
  - each new DNA helix wraps around them to make a new nucleosome

- each DNA polymerase works at a rate of 100 base pairs per second
  - would take weeks for one polymerase to replicate one chromosome
  - thousands of polymerase molecules work simultaneously on each DNA molecule

10. all 46 chromosomes are replicated in 6 - 8 hours
Errors and Mutations

• DNA polymerase does make mistakes
  – multiple modes for correction of replication errors
  – double checks the new base pair and tend to replace incorrect, biochemically unstable pairs with more stable correct pairs
  – result is only 1 error per 1 billion bases replicated

• mutations - changes in DNA structure due to replication errors or environmental factors (radiation, viruses, chemicals)
  – some mutations cause no ill effects. others kill the cell, turn it cancerous or cause genetic defects in future generations.