Chapter 4  
Genetics and Cellular Function

- Nucleus and nucleic acids
- Protein synthesis and secretion
- DNA replication and the cell cycle
- Chromosomes and heredity

The Nucleic Acids (medical history)

Organization of the Chromatin

- Threadlike chromatin
- Chromosomes – compacted DNA
- How many human chromosomes?
  - Fruitflies?
  - Butterflies?

Chromosome loci

Y Chromosome

Nucleotide Structure
DNA Structure: Twisted Ladder

Nitrogenous Bases

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Complementary Base Pairing

DNA Function

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RNA: Structure and Function

Genetic Control of Cell Action through Protein Synthesis

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Preview of Protein Synthesis

Genetic Code

<table>
<thead>
<tr>
<th>1st base in codon</th>
<th>2nd base in codon</th>
<th>3rd base in codon</th>
<th>Amino Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>U</td>
<td>A</td>
<td>G</td>
<td>Urea</td>
</tr>
<tr>
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</tr>
<tr>
<td>G</td>
<td>G</td>
<td>U</td>
<td>Glycine</td>
</tr>
</tbody>
</table>

Transcription – making an RNA strand

Alternative Splicing of mRNA

Transfer RNA (tRNA)

- Activation by ATP binds specific amino acid and provides necessary energy to join amino acid to growing protein molecule
- Anticodon binds to complementary codon of mRNA
Translation of mRNA

Polyribosomes and Signal Peptides

Review: DNA & Peptide Formation

- DNA double helix
- DNA coding strand
- Codons of mRNA
- Anticodons of tRNA
- Amino acids
- Peptide

Chaperones and Protein Structure

- Newly forming protein molecules must coil, fold or join with another protein or nonprotein moiety
- Chaperone proteins
  - prevent premature folding of molecule
  - assists in proper folding of new protein
  - may escort protein to destination in cell
- Stress or heat-shock proteins
  - chaperones produced in response to heat or stress
  - help protein fold back into correct functional shapes

Protein Packaging & Secretion

DNA Replication

- Old DNA
- New DNA
- DNA polymerase
- Replication fork
DNA Replication: Errors and Mutations

- Error rates of DNA polymerase
  - in bacteria, 3 errors per 100,000 bases copied
  - every generation of cells would have 1,000 faulty proteins
- Proofreading and error correction
  - a small polymerase proofreads each new DNA strand and makes corrections
  - results in only 1 error per 1,000,000,000 bases copied
- Mutations - changes in DNA structure due to replication errors or environmental factors
  - some cause no effect, some kill cell, turn it cancerous or cause genetic defects in future generations

Cell Cycle

- $G_1$ phase, the first gap phase
- $S$ phase, synthesis phase
- $G_2$ phase, second gap phase
- $M$ phase, mitotic phase
- $G_0$ phase, cells that have left the cycle
- Cell cycle duration varies between cell types

Mitosis

- Chromatin supercoils into chromosomes
  - each chromosome = 2 genetically identical sister chromatids joined at the centromere
  - each chromosomes contains a DNA molecule
- Nuclear envelope disintegrates
- Centrioles sprout microtubules pushing them apart towards each pole of the cell

Mitosis: Prophase

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Prophase Chromosome
Mitosis: Metaphase
- Chromosomes line up on equator
- Spindle fibers (microtubules) from centrioles attach to centromere
- Asters (microtubules) anchor centrioles to plasma membrane

Mitosis: Anaphase
- Centromeres split in 2 and chromatids separate
- Daughter chromosomes move towards opposite poles of cells
- Centromeres move down spindle fibers by kinetochore protein (dynein)

Mitosis: Telophase
- Chromosomes uncoil forming chromatin
- Nuclear envelopes form
- Mitotic spindle breaks down

Cytokinesis
- Division of cytoplasm / overlaps telophase
- Myosin pulls on microfilaments of actin in the membrane skeleton
- Causes crease around cell equator called cleavage furrow
- Cell pinches in two
- Interphase has begun

Timing of Cell Division

- Have enough cytoplasm for 2 daughter cells
- DNA replicated
- Adequate supply of nutrients
- Growth factor stimulation
- Open space in tissue due to neighboring cell death

Chromosomes and Heredity

- Loss of growth factors or nutrients
- Contact inhibition
This is my son, Irvine

Karyotype of Normal Human Male

Genetics of Earlobes

Genetics of Earlobes

Punnett square

Multiple Alleles, Codominance, Incomplete Dominance

Polygenic Inheritance

- 2 or more genes combine their effects to produce single phenotypic trait, such as skin and eye color, alcoholism and heart disease
Pleiotropy

- Single gene causes multiple phenotypic traits (ex. sickle-cell disease)
  - sticky, fragile, abnormal shaped red blood cells at low oxygen levels cause anemia and enlarged spleen

Sex-Linked Inheritance

- Recessive allele on X, no gene locus for trait on Y, so hemophilia more common in men (mother must be carrier)

Penetrance and Environmental Effects

- Penetrance
  - % of population to express predicted phenotype given their genotypes
- Role of environment
  - brown eye color requires phenylalanine from diet to produce melanin, the eye pigment

Pedigree analysis

Genetics of sickle cell anemia

Inheritance of achondroplasia
### Alleles at the Population Level

- Dominance and recessiveness of allele do not determine frequency in a population
- Some recessive alleles, blood type O, are the most common
- Some dominant alleles, polydactyly and blood type AB, are rare

### Cancer

- Tumors (neoplasms)
  - abnormal growth, when cells multiply faster than they die
  - oncology is the study of tumors
- Benign
  - connective tissue capsule, grow slowly, stays local
  - potentially lethal by compression of vital tissues
- Malignant
  - unencapsulated, fast growing, metastatic (causes 90% of cancer deaths)

### Causes of Cancer

- Carcinogens - estimates of 60 - 70% of cancers from environmental agents
  - chemical
    - cigarette tar, food preservatives
  - radiation
    - UV radiation, α particles, γ rays, β particles
  - viruses
    - type 2 herpes simplex - uterus, hepatitis C - liver

### Mutagens

- Trigger gene mutations
  - cell may die, be destroyed by immune system or produce a tumor
- Scavenger cells
  - remove them before they cause genetic damage
- Peroxisomes
  - neutralize nitrates, free radicals and oxidizing agents
- Nuclear enzymes
  - repair DNA
- Tumor necrosis factor (TNF) from macrophages and certain WBCs destroys tumors

### Malignant Tumor (Cancer) Genes

- Oncogenes
  - mutated form of normal growth factor genes called proto-oncogenes
  - sis oncogene causes excessive production of growth factors
    - stimulate neovascularization of tumor
  - ras oncogene codes for abnormal growth factor receptors
    - sends constant divide signal to cell
- Tumor suppressor genes
  - inhibit development of cancer
  - damage to one or both removes control of cell division

### Effects of Malignancies

- Displaces normal tissue, organ function deteriorates
  - rapid cell growth of immature nonfunctional cells
  - metastatic cells have different tissue origin
- Block vital passageways
  - block air flow and compress or rupture blood vessels
- Diverts nutrients from healthy tissues
  - tumors have high metabolic rates
  - causes weakness, fatigue, emaciation, susceptibility to infection
  - cachexia is extreme wasting away of muscle and adipose tissue