Chapter 2
Genes, Chromosomes, Cells and Tissues: Their Structure and Function in Health and Disease

Learning Objectives
• Explain
  – Organization of cells
  – Types of tissues
  – Organ systems
  – Germ layers and derivatives
• Describe
  – Cell function and genetic code
  – DNA and enzyme synthesis
• Movement of materials in and out of cells
• Cell adaptation to changing conditions
• Cell injury, cell death, cell necrosis

Learning Objectives Cont.
• Chromosomes analysis and karyotype
• Mitosis versus meiosis
• Spermatogenesis versus oogenesis: implications of abnormal chromosome separations in older women
• Inheritance pattern of genes: dominant, recessive, codominant, sex-linked
• HLA system: application to organ transplantation, disease susceptibility
• Gene therapy: applications and limitations

Basic Structure and Organization of Cells
• Nucleus: contains genetic information; directs metabolic function of cells
• Cytoplasm: surrounds nucleus; structures carry out directions of the nucleus
• Cell: basic structural and functional unit of the body
• Tissues: group of similar cells performing the same functions
• Organs: groups of tissues
• Organ Systems: groups of organs functioning together
• Functioning Organisms: integrated organ systems

Organization of Cells
• Cells
• Tissues
• Organs
• Organ systems
• Functioning organism
• An abnormality at any level of organization can cause disease

The Cell
• Nucleus
• Cytoplasm
  – Mitochondria
  – Endoplasmic reticulum
  – Golgi apparatus
  – Lysosomes
  – Centrioles
  – Cytoskeleton
• Membranes of lipid and protein molecules
The Cell
© Courtesy of Leonard Crowley, M.D./University of Minnesota Medical School

Nucleus and Cytoplasm

- **Nucleus**
  - Two types of nucleic acid combined with protein
  - Nuclear membrane: double-layered; with pores; separates nucleus from cytoplasm
    - Deoxyribonucleic acid (DNA): in chromosomes in the nucleus, contains genetic information
    - Ribonucleic acid (RNA): in nucleoli; component of messenger, transfer, ribosomal RNA
- **Cytoplasm**
  - Mass of protoplasm surrounded by a selectively permeable cell membrane
  - Contains organelles

Organelles (1 of 4)

- **Mitochondria**
  - Rod-shaped structures capable of converting food material into energy to manufacture ATP (adenosine triphosphate) that fuels chemical reactions in the cell
- **Endoplasmic reticulum**
  - Interconnected network of tubular channels enclosed by membranes; communicates with nuclear and cellular membranes
  - Rough endoplasmic reticulum (RER): with ribosomes
  - Smooth endoplasmic reticulum (SER): with lipids

Organelles (2 of 4)

- **Golgi apparatus**
  - Flattened membrane-like sacs near the nucleus
  - For synthesis of large carbohydrate molecules
  - Connected with the tubules of the RER
  - Proteins from ribosomes → RER tubules → Golgi apparatus → combine with carbohydrate molecules → form secretory granules
- **Lysosomes**: "digestive system" of cell
  - Cytoplasmic vacuoles with digestive enzymes
  - Digestion occurs within phagocytic vacuole to prevent leakage of enzymes
  - Peroxisome: with enzymes that decompose hydrogen peroxide, $\text{H}_2\text{O}_2$

Organelles (3 of 4)

- **Centrioles**
  - Short cylindrical structures adjacent to nucleus
  - Move to opposite poles of the cell during cell division to form the mitotic spindle
- **Cytoskeleton**
  - Form cell’s structural framework, shape, and cell movements (e.g. phagocytosis)
  - Consists of 3 types of protein tubules
    - Microtubules: largest
    - Intermediate filaments
    - Microfilaments: smallest

Organelles (4 of 4)

- **Cytoskeleton: intermediate filaments**
  - Small, tough protein filaments
  - Reinforce cell’s interior and keep its shape by holding the organelles in proper position
  - Identification and characterization of intermediate filaments provide diagnostic and prognostic information
    - Alzheimer disease
    - Cancer diagnosis: helps determine the cell of origin
Tissues

• Group of cells that perform a similar function
• Four types:
  – Epithelium
  – Connective and supporting
    • Fibrous Cartilage
    • Elastic Bone
    • Reticular Hematopoietic
    • Adipose Lymphatic
  – Muscle
  – Nerve

Epithelium (1 of 2)

• Covers exterior of the body
• Lines interior of body surfaces communicating with the outside: GIT, urinary tract, and vagina
• Forms glands and parenchymal (functional) cells of excretory or secretory organs (liver and kidneys)
• Contains no blood vessels but nourished by diffusion
• Functions
  – All types of epithelium protect
  – Absorb
  – Secrete: mucus, sweat, oil, enzymes, hormones

Epithelium (2 of 2)

• Exocrine glands: discharge secretions through a duct
  – Pancreas: both an exocrine and endocrine gland
• Endocrine glands: discharge secretions directly into the bloodstream
  – Example: thyroid and adrenals
• Endothelium: layer of simple squamous epithelium
• Mesothelium: layer of simple squamous epithelium lining pleural, pericardial, and peritoneal cavities

Types of Epithelium

– A. Simple squamous
– B. Cuboidal
– C. Columnar
– D. Pseudostratified columnar
– E. Transitional
– F. Stratified squamous

Connective and Supportive Tissues (1 of 3)

• Types of connective tissue fibers
  – Collagen fibers
    • Connect and support tissues
    • Contain collagen; long and flexible, strong but do not stretch
  – Elastic fibers
    • Responsible for distensibility of arteries
    • Contain elastin, not as strong but stretches
  – Reticulin fibers
    • Form supporting framework of organs
    • Similar to collagen but thin and delicate

Connective and Supportive Tissues (2 of 3)

• Examples
  – Hematopoietic (blood-forming)
  – Lymphatic (lymphocyte-forming)
  – Loose and dense fibrous tissues
  – Elastic tissue
  – Reticular tissue
  – Adipose tissue
  – Cartilage: hyaline, elastic, fibrocartilage
  – Bone
  – Subcutaneous tissue
Connective and Supportive Tissues (3 of 3)

- Ligaments
- Tendons
- Blood vessel wall membranes
- Bronchi walls
- Trachea
- Supporting framework of organs
  - Liver, spleen and lymph nodes

Muscle

- Smooth muscle
  - Located in walls of hollow internal organs
    - Gastrointestinal, biliary, and reproductive tracts
    - Blood vessels
  - Functions automatically, not under conscious control
- Striated muscle
  - Moves skeleton
  - Under conscious control
- Cardiac muscle
  - Found only in the heart
  - Resembles striated but with features common to both smooth and striated muscle

Nerve

- Neurons: nerve cells, transmit nerve impulses
- Neuroglia: supporting cells
  - More numerous than neurons
  - Astrocytes: long, star-shaped cells, numerous highly branched process
  - Oligodendroglia: small cells, scanty cytoplasm, surround nerve cells
  - Microglia: phagocytic cells

Organ

- Groups of different tissues integrated to perform a specific function
  - One tissue performs primary function
  - Other tissues perform supporting function
- Parenchymal cells: primary functional cells of an organ
- Parenchyma: functional cells of an organ
- Stroma: tissue that forms the supporting framework of an organ

Cell Function, DNA, Genetic Code

- Genetic coding
  - DNA in nucleus “tells the cell what to do”
  - Directs synthesis of enzymes and other proteins by the ribosomes in the cytoplasm
  - Messenger RNA (mRNA) carries out the “instructions” encoded in the DNA to the ribosomes in the cytoplasm

Movement of Materials In and Out of Cells (1 of 2)

- Oxygen and nutrients must enter the cell and waste products must be eliminated by crossing through a selectively permeable membrane
- Diffusion: solutes move from concentrated \( \rightarrow \) dilute solution
- Osmosis: water molecules move from dilute \( \rightarrow \) concentrated solution
- Active transport: movement from ↓ concentration \( \rightarrow \) ↑ concentration; requires cell to expend energy due to concentration gradient
- Phagocytosis; pinocytosis
Movement of Materials In and Out of Cells (2 of 2)

• Phagocytosis: ingestion of particles too large to pass across cell membrane
  – Cytoplasm flows around the particle and cytoplasmic processes fuse to engulf particle within a vacuole into the cytoplasm
• Pinocytosis: ingestion of fluid rather than solid material

Adaptation of Cells to Changing Conditions (1 of 3)

• Atrophy: reduction in cell size in response to
  – Diminished function
  – Inadequate hormonal stimulation
  – Reduced blood supply
• Examples
  – Reduction of skeletal muscle size when extremity is immobilized in a cast for a prolonged period
  – Shrinkage of breasts and genitals following menopause due to diminished estrogen secretion

Adaptation of Cells to Changing Conditions (2 of 3)

• Hypertrophy: increase in cell size without increase in cell number
  – Muscles of a weight lifter
  – Heart of a person with high blood pressure
• Hyperplasia: increase in both cell size and number in response to increased demand
  – Glandular tissue of breasts during pregnancy in preparation for lactation
  – Enlargement of thyroid gland to increase output of hormones

Adaptation of Cells to Changing Conditions (3 of 3)

• Metaplasia: change from one type of cell to another
  – Example: lining of a chronically inflamed bladder
• Dysplasia: cell development and maturation are disturbed and abnormal
  – Individual cells vary in size and shape
  – Example: chronic inflammation of epithelial cells of uterine cervix may progress to cervical epithelial dysplasia and neoplasia
• Increased enzyme synthesis
  – Adaptive response as in inactivating/detoxifying drugs or chemicals through SER enzymes

Cell Injury, Cell Death, Cell Necrosis (1 of 2)

• Normal conditions: potassium actively transported into cell, sodium is moved out
• Changes resulting from cell injury
  – Cell swelling: sodium diffuses into cell together with water molecules
  – Fatty change: accumulation of fat droplets within the cytoplasm due to impairment of enzyme systems that metabolize fat
• Cell necrosis: cell damage + cell death
  – All necrotic cells are dead, but not all dead cells are necrotic.
Cell Injury, Cell Death, Cell Necrosis (2 of 2)

- **Cell aging**
  - Genetic and environmental factors play a role in cell longevity.
  - Aging of cells may be caused by damage to cellular DNA, RNA, and cytoplasmic organelles.
  - The more efficient the cell’s repair process, the greater the likelihood of survival.
  - As cell ages, its enzyme systems gradually decline, and cell is less able to protect itself from injury.

Genes

- Segments of DNA chains that determine cell properties (structure and functions)
- Basic units of inheritance
- Exist in pairs or alleles one in each chromosome; occupy a specific site on a chromosome (locus)
- Paired in same way as chromosomes except in sperm and ova
- Homozygous: both alleles are the same
- Heterozygous: alleles are different

Genes and Inheritance

- **Expression of genes**
  - 1. Dominant gene: expressed in either homozygous or heterozygous state
  - 2. Recessive gene: expressed only in homozygous state
  - 3. Codominant gene: both alleles of a pair are expressed
  - 4. Sex-linked gene: genes carried on sex chromosomes producing sex-linked traits
- Female carrier of recessive X-linked trait is normal, effect of defective allele offset by normal allele on other X chromosome
- Male carrier of recessive X-linked trait, defective X chromosome functions like a dominant gene

Chromosomes (1 of 2)

- Double coils of DNA combined with protein
- Present in the nucleus and control cell activities
- Exist in pairs, one derived from the male parent and one from the female parent
- Autosomes: 22 pairs in humans; similar in size, shape, appearance

Chromosomes (2 of 2)

- Sex chromosomes: one pair in humans
  - Determine genetic sex by composition of X and Y chromosomes
  - Normal female: XX; one X inactivated and appears attached to nuclear membrane
  - Normal male: XY chromosomes; Y chromosome appears as bright fluorescent spot in intact cell

Chromosome Analysis

- Study composition and abnormalities in chromosomes in terms of number and structure
- Methods
  - Use human blood as source of cells and then cultured
  - Lymphocytes induced to undergo mitotic division
  - Division of cells stopped in metaphase and cells caused to swell. Cell has 46 chromosomes. Each chromosome consists of 2 chromatids joined at centromere
  - Prepare stained smears of chromosomes
  - Chromosomes arranged in standard pattern (karyotype)
X Chromosome Inactivation: Lyon Hypothesis

- X-inactivation or lyonization: only one of the two X chromosomes in females is genetically active; one is inactivated very early in embryonic development; theorized by Mary Frances Lyon
- Barr body or sex chromatin body: inactive X chromosome
- X-inactivation occurs so female with two X chromosomes does not have twice as many X chromosome gene products as the male
- Choice of which X chromosome will be inactivated is random; once inactivated, remains inactive throughout the lifetime of the cell

Mitosis (1 of 2)

- Characteristic of somatic cells
- Each somatic cell contains 46 chromosomes
  - Not all mature cells able to divide (cardiac, skeletal muscle, nerve cells)
  - Connective tissue and liver cells divide as much as needed
  - Cells lining testicular tubules that produce sperm cells divide continually
  - Blood-forming cells in bone marrow divide continually to replace circulating cells in bloodstream

Mitosis (2 of 2)

- No reduction in chromosomes
- Each of two new daughter cells receives same number of chromosomes as in the parent cell
  - Each chromosome and its newly duplicated counterpart lie side by side; called chromatids
  - Each chromosome duplicates itself before beginning cell division

Mitosis: Sequence

- Sequence of mitosis
  - Prophase
  - Metaphase
  - Anaphase
  - Telophase

Mitosis: Prophase

- Each chromosome shortens and thickens
- Centrioles move to opposite poles of the cell and form mitotic spindle consisting of small fibers radiating in all directions
- Some fibers attach to the chromatids
- Nuclear membrane breaks down
Mitosis: Metaphase and Anaphase

- **Metaphase**
  - Chromosomes line up at center of the cell
  - Chromatids partially separated but remain joined at centromere, a constricted area where the spindle fibers are attached

- **Anaphase**
  - Chromatids separate to form individual chromosomes, which are pulled to opposite poles of the cell by spindle fibers

Mitosis: Telophase

- Nuclear membranes of two daughter cells reform
- Cytoplasm divides
- Two daughter cells are formed, each an exact duplicate of the parent cell

Meiosis

- Characteristic of germ cells
- Intermixing of genetic material between homologous chromosomes; chromosomes reduced by half
- Entails two separate divisions
  - First meiotic division: reduces number of chromosomes by half
    - Daughter cells receive only half of number of chromosomes by the parent cell
    - Chromosomes are not exact duplicates of those in parent cell
  - Second meiotic division: similar to mitosis, but each cell contains only 23 chromosomes

Gametogenesis

- Process of forming gametes (mature germ cells)
  - Gonads (testes and ovaries): contain precursor cells called germ cells capable of developing into mature sperm or ova
  - Spermatogenesis: development of sperm
    - Spermatogonia: precursor cells in the testicular tubes
  - Oogenesis: development of ova
    - Oogonia: precursor cells
  - Both processes have similarities and differences
Gametogenesis

Spermatogenesis
- Spermatogonia form primary spermatocytes by mitosis (46 chromosomes)
- Primary spermatocytes form secondary spermatocytes by meiosis (23 chromosomes)
- Secondary spermatocytes form spermatids (23 chromosomes)
- Spermatids
- Sperm

Oogenesis (1 of 2)
- Oogonia form primary oocytes by mitosis in fetal ovaries (46 chromosomes)
- Primary oocyte forms primary follicle and begins prophase of meiosis
- Primary follicle matures under influence of FSH-LH; one mature follicle is ovulated each month

Oogenesis (2 of 2)
- Primary oocyte forms secondary oocyte by first meiotic division
- Secondary oocyte begins second meiotic division to form mature ovum
- Meiotic division completed when mature ovum is fertilized

Spermatogenesis and Oogenesis
(1 of 2)
- Spermatogenesis
  - 1. Four spermatozoa formed from each precursor cell
  - 2. Spermatogenesis occurs continually, carried to completion in two months, seminal fluid always containing "fresh" sperm
- Oogenesis
  - One ovum formed from each precursor cell, other three cells discarded as polar bodies
  - Oocytes not produced continually
  - Oocytes in ovary are formed before birth and remain in prolonged prophase of first meiotic division in fetal life until ovulated

Spermatogenesis and Oogenesis
(2 of 2)
- Congenital abnormalities from abnormal separation of chromosomes more frequent in older women
- Ova released late in woman’s reproductive life have been held in prophase for a long time before assuming meiosis at time of ovulation (about 45 years)
- Ova have been exposed for years to potentially harmful radiation, chemicals, and injurious agents
- Predisposes to abnormal chromosome separation when cell division resumes at ovulation = excess or deficient number of chromosomes
Histocompatibility Complex Genes (1 of 3)

- Antigens present in organ donor cells must closely resemble those of the recipient for successful organ transplantation
- Human leukocyte antigens (HLA antigens)
  - Genetically determined antigens on cell surface that make individuals distinct from one another
  - Determined by a group of genes or major histocompatibility complex, MHC, on chromosome 6
  - Also referred to as HLA complex, MHC complex, and MHC antigens

Histocompatibility Complex Genes (2 of 3)

- Involved in generating immune responses to foreign antigens
- Antigenicity depends on whether they are
  - Self antigens or HLA proteins on person’s own cells and recognized as self by the immune system or
  - Proteins from another (non-self antigens) that are recognized as foreign, triggering an immune response
- HLA complex consists of 4 separate, closely-linked gene loci: HLA-A; HLA-B; HLA-C; HLA-D (with additional subdivisions)

Histocompatibility Complex Genes (3 of 3)

- Designated by specific letter (for locus) and number (for allele) such as HLA-B27
- Haplotype: set of HLA genes on one chromosome that is transmitted as a set
- Surface proteins within the HLA system
  - MHC Class I proteins: determined by HLA-A, HLA-B, HLA-C genes; found in all nucleated cells and platelets; not in mature red blood cells as they are unucleated
  - MHC Class II proteins: determined by HLA-D genes; found only on a few cells such as macrophages

Recombinant DNA Technology (1 of 2)

- Recombinant DNA: bacteria-foreign gene combination that can produce the desired biologic product
- Areas of practical application
  - Increase understanding of the molecular basis of genetic disease by studying normal gene structure and function
  - Prenatal diagnosis of genetic disease
    - Identifying abnormal genes and gene products in fetal cells
    - Identifying mutations of the gene in the fetal cell from the amniotic fluid cells

Recombinant DNA Technology (2 of 2)

- Process requires insertion of a gene that directs the synthesis of a biologic product, such as insulin, into bacterium (through a plasmid) or yeast
- Methods
  - 1. Recombinant DNA technology: genes from two different sources recombined in a single organism
  - 2. Genetic engineering: manipulations of genes
  - 3. Gene splicing: a piece of genetic material is cut open and another piece of genetic material is introduced

Discussion

- How does the nucleus direct the activities of the cell? What is the genetic code, and what is its role in directing the functions of the cell?
- What is the difference between atrophy and hypertrophy, between metaplasia and dysplasia, and between cell death and cell necrosis?
- What are the differences between spermatogenesis and oogenesis?