Chapter 3
The Cellular Level of Organization

• Basic, living, structural and functional unit of the body
  – compartmentalization of chemical reactions within specialized structures
  – regulate inflow & outflow of materials
  – use genetic material to direct cell activities
• Cytology = study of cellular structure
• Cell physiology = study of cellular function

Generalized Cell Structures

• Plasma membrane = cell membrane
• Nucleus = genetic material of cell
• Cytoplasm = everything between the membrane and the nucleus
  – cytosol = intracellular fluid
  – organelles = subcellular structures with specific functions

The Typical Cell

• Not all cells contain all of these organelles.
Plasma Membrane

- Flexible but sturdy barrier that surrounds cytoplasm of cell
- Fluid mosaic model describes its structure
  - "sea of lipids in which proteins float like icebergs"
  - membrane is 50% lipid & 50% protein
    - held together by hydrogen bonds
  - lipid is barrier to entry or exit of polar substances
  - proteins are "gatekeepers" -- regulate traffic

Lipid Bilayer of the Cell Membrane

- Two back-to-back layers of 3 types of lipid molecules
- Cholesterol and glycolipids scattered among a double row of phospholipid molecules

Phospholipids

- Comprises 75% of lipids
- Phospholipid bilayer = 2 parallel layers of molecules
- Each molecule is amphipathic (has both a polar & nonpolar region)
  - polar parts (heads) are hydophilic and face on both surfaces a watery environment
  - nonpolar parts (tails) are hydrophobic and line up next to each other in the interior
Glycolipids within the Cell Membrane

• Comprises 5% of the lipids of the cell membrane
• Carbohydrate groups form a polar head only on the side of the membrane facing the extracellular fluid

Cholesterol within the Cell Membrane

• Comprises 20% of cell membrane lipids
• Interspersed among the other lipids in both layers
• Stiff steroid rings & hydrocarbon tail are nonpolar and hide in the middle of the cell membrane

Types of Membrane Proteins

• Integral proteins
  – extend into or completely across cell membrane
    • if extend completely across = transmembrane proteins
  – all are amphipathic with hydrophobic portions hiding among the phospholipid tails
  – glycoproteins have the sugar portion facing the extracellular fluid to form a glycocalyx
    • gives cell “uniqueness”, protects it from being digested, creates a stickiness to hold it to other cells or so it can hold a fluid layer creating a slippery surface

• Peripheral proteins
  – attached to either inner or outer surface of cell membrane and are easily removed from it
Membrane Proteins

Integral versus Peripheral Proteins

Functions of Membrane Proteins

- **Formation of Channel**
  - passageway to allow specific substance to pass through
- **Transporter Proteins**
  - bind a specific substance, change their shape & move it across membrane
- **Receptor Proteins**
  - cellular recognition site
    - bind to substance

- **Cell Identity Marker**
  - allow cell to recognize other similar cells
- **Linker**
  - anchor proteins in cell membrane or to other cells
  - allow cell movement
  - cell shape & structure
- **Act as Enzyme**
  - speed up reactions
Membrane Fluidity

• Membranes are fluid structures (oil layer)
  – self-sealing if punctured with needle
• Explanation -- a compromise of forces
  – membrane molecules can rotate & move freely
  – need to stay in one half of lipid bilayer
    • difficult for hydrophilic parts to pass through hydrophobic core of bilipid layer
  – fluidity is reduced by presence of cholesterol
    • increases stiffness of membrane it forms hydrogen bonds with neighboring phospholipid heads

Selective Permeability of Membrane

• Lipid bilayer
  – permeable to nonpolar, uncharged molecules – oxygen, CO₂, steroids
  – permeable to water which flows through gaps that form in hydrophobic core of membrane as phospholipids move about
• Transmembrane proteins act as specific channels
  – small and medium polar & charged particles
• Macromolecules unable to pass through the membrane
  – vesicular transport

Gradients Across the Plasma Membrane

• Membrane can maintain difference in concentration of a substance inside versus outside of the membrane (concentration gradient)
  – more O₂ & Na⁺ outside of cell membrane
  – more CO₂ and K⁺ inside of cell membrane
• Membrane can maintain a difference in charged ions between inside & outside of membrane (electrical gradient or membrane potential)
• Thus, substances move down their concentration gradient and towards the oppositely charged area
  – ions have electrochemical gradients
Gradients Across Membrane

- Concentration gradient
- Electrical gradient

Transport Across the Plasma Membrane

- Substances cross membranes by a variety of processes:
  - mediated transport moves materials with the help of a transporter protein
  - nonmediated transport does not use a transporter protein
  - active transport uses ATP to drive substances against their concentration gradients
  - passive transport moves substances down their concentration gradient with only their kinetic energy
  - vesicular transport move materials across membranes in small vesicles – either by exocytosis or endocytosis

Principles of Diffusion

- Random mixing of particles in a solution as a result of the particle’s kinetic energy
  - more molecules move away from an area of high concentration to an area of low concentration
    - the greater the difference in concentration between the 2 sides of the membrane, the faster the rate of diffusion
    - the higher the temperature, the faster the rate of diffusion
    - the larger the size of the diffusing substance, the slower the rate of diffusion
    - an increase in surface area, increases the rate of diffusion
    - increasing diffusion distance, slows rate of diffusion
- When the molecules are evenly distributed, equilibrium has been reached
**Diffusion**

- Crystal of dye placed in a cylinder of water
- Net diffusion from the higher dye concentration to the region of lower dye
- Equilibrium has been reached in the far right cylinder

**Osmosis**

- Net movement of water through a selectively permeable membrane from an area of high water concentration to an area of lower water concentration
  - Diffusion through lipid bilayer
  - Aquaporins (transmembrane proteins) that function as water channels
- Only occurs if membrane is permeable to water but not to certain solutes

**Osmosis of Water Through a Membrane**

- Pure water on the left side & a membrane impermeable to the solute found on the right side
- Net movement of water is from left to right, until hydrostatic pressure (osmotic pressure) starts to push water back to the left
Affects of Tonicity on RBCs in Lab

- Normally the osmotic pressure of the inside of the cell is equal to the fluid outside the cell – cell volume remains constant (solution is isotonic)

- Effects of fluids on RBCs in lab
  - water enters the cell faster than it leaves
  - water enters & leaves the cell in equal amounts
  - water leaves the cell

Effects of Tonicity on Cell Membranes

- Isotonic solution
  - water concentration the same inside & outside of cell results in no net movement of water across cell membrane

- Hypotonic solution
  - higher concentration of water outside of cell results in hemolysis

- Hypertonic solution
  - lower concentration of water outside of cell causes crenation

Diffusion Through the Lipid Bilayer

- Important for absorption of nutrients -- excretion of wastes

- Nonpolar, hydrophobic molecules
  - oxygen, carbon dioxide, nitrogen, fatty acids, steroids, small alcohols, ammonia and fat-soluble vitamins (A, E, D and K)
Diffusion Through Membrane Channels

- Each membrane channel specific for particular ion (K+, Cl-, Na+ or Ca+2)
- Slower than diffusion through membrane but still 1 million K+ through a channel in one second
- Channels may be open all the time or gated (closed randomly or as ordered)

Facilitated Diffusion

- Substance binds to specific transporter protein
- Transporter protein conformational change moves substance across cell membrane
- Facilitated diffusion occurs down concentration gradient only
  - if no concentration difference exists, no net movement across membrane occurs
- Rate of movement depends upon
  - steepness of concentration gradient
  - number of transporter proteins (transport maximum)

Facilitated Diffusion of Glucose

- Glucose binds to transport protein
- Transport protein changes shape
- Glucose moves across cell membrane (but only down the concentration gradient)
- Kinase enzyme reduces glucose concentration inside the cell by transforming glucose into glucose-6-phosphate
- Transporter proteins always bring glucose into cell
Active Transport

- Movement of polar or charged substances against their concentration gradient
  - energy-requiring process
    - energy from hydrolysis of ATP (primary active transport)
    - energy stored in an ionic concentration gradient (secondary active transport)
- Exhibits transport maximums and saturation
- Na\(^+\), K\(^+\), H\(^+\), Ca\(^{2+}\), I\(^-\), amino acids, and monosaccharides

Primary Active Transport

- Transporter protein called a pump
  - works against concentration gradient
  - requires 40% of cellular ATP
- Na\(^+\)/K\(^+\) ATPase pump
  - most common example
  - all cells have 1000s of them
  - maintains low concentration of Na\(^+\) and a high concentration of K\(^+\) in the cytosol
  - operates continually
- Maintenance of osmotic pressure across membrane
  - cells neither shrink nor swell due to osmosis & osmotic pressure
  - sodium continually pumped out as if sodium could not enter the cell (factor in osmotic pressure of extracellular fluid)
  - K\(^+\) inside the cell contributes to osmotic pressure of cytosol

Na\(^+\)/K\(^+\) Pump & ATP As Its Energy Source

1. Na\(^+\) binding
2. ATP split
3. Na\(^+\) pushed out
4. K\(^+\) binding
5. Phosphate release
6. K\(^+\) is pushed in

3 Na\(^+\) ions removed from cell as 2 K\(^+\) brought into cell.
Secondary Active Transport

- Uses energy stored in an ion concentration gradient to move other substances against their own concentration gradient
- Na+/K+ pump maintains low concentration of Na+ inside of cells
  - provide route for Na+ to leak back in and use energy of motion to transport other substances
  - Na+ symporter proteins
    - glucose or amino acids rush inward with Na+ ions
  - Na+ antiporters protein
    - as Na+ ions rush inward, Ca+2 or H+ pushed out

Antiporters and Symporters

One in & one out. Both going in

Digitalis

- Slows the sodium pump, which lets more Na+ accumulate heart muscle cells.
- Less Na+ concentration gradient across the membrane
- Na+/Ca+2 antiporters slow down so more Ca+2 remains inside the cardiac cells
- Strengthening the force of contraction
- Balance between concentration of Na+ and Ca+2 in cytosol & extracellular fluid is important
Vesicular Transport of Particles

- **Endocytosis** = bringing something into cell
  - phagocytosis = cell eating by macrophages & WBCs
    - particle binds to receptor protein
    - whole bacteria or viruses are engulfed & later digested
  - pinocytosis = cell drinking
    - no receptor proteins
  - receptor-mediated endocytosis = selective input
    - mechanism by which HIV virus enters cells
- **Exocytosis** = release something from cell
  - Vesicles form inside cell, fuse to cell membrane
  - Release their contents
    - digestive enzymes, hormones, neurotransmitters or waste products
  - replace cell membrane lost by endocytosis

Receptor-Mediated Endocytosis

- Mechanism for uptake of specific substances = ligands
- Desired substance binds to receptor protein in clathrin-coated pit region of cell membrane causing membrane to fold inward
- Vesicles become uncoated & combine with endosome
- Receptor proteins separate from ligands and return to surface
- Ligands are digested by lysosomal enzymes or transported across cell -- epithelial cell crossing accomplished

Pinocytosis and Phagocytosis

- No pseudopods form
- Nonselective drinking of extracellular fluid
- Pseudopods extend to form phagosome
- Lysosome joins it
Cytosol = Intracellular fluid

- 55% of cell volume
- 75-90% water with other components
  - large organic molecules (proteins, carbo & lipids)
    - suspended by electrical charges
  - small organic molecules (simple sugars) & ions
    - dissolved
  - inclusions (large aggregates of one material)
    - lipid droplets
    - glycogen granules
- Site of many important chemical reactions
  - production of ATP, synthesis of building blocks

Cell Organelles

- Nonmembranous organelles lack membranes & are indirect contact with cytoplasm
- Membranous organelles surrounded by one or two lipid bilayer membranes

Cytoskeleton

- Network of protein filaments throughout the cytosol
- Functions
  - cell support and shape
  - organization of chemical reactions
  - cell & organelle movement
- Continually reorganized
The Cytoskeletal Filaments

- **Microfilaments**
  - thinnest filaments (actin)
  - locomotion & division
  - support microvilli
- **Intermediate filaments**
  - several different proteins
  - anchor organelles
- **Microtubules**
  - large cylindrical structure (composed of tubulin)
  - flagella, cilia & centrosomes

Centrosome

- Found near nucleus
- Pericentriolar area
  - formation site for mitotic spindle and microtubules
- Centrosome
  - 2 centrioles (90 degrees to each other)
  - 9 clusters of 3 microtubules (9+0 array)
  - role in formation of cilia & flagella

Cilia and Flagella

- **Structure**
  - pairs of microtubules (9+2 array)
  - covered by cell membrane
  - basal body is centriole responsible for initiating its assembly
- **Differences**
  - cilia
    - short and multiple
  - flagella
    - longer and single
Movement of Cilia and Flagella

- Cilia
  - stiff during power stroke but flexible during recovery
  - many coordinated together
  - airways & uterine tube

- Flagella
  - single flagella wiggles in a wavelike pattern
  - propels sperm forward

Ribosomes

- Packages of Ribosomal RNA & protein
- Free ribosomes are loose in cytosol
  - synthesize proteins found inside the cell
- Membrane-bound ribosomes
  - attached to endoplasmic reticulum or nuclear membrane
  - synthesize proteins needed for plasma membrane or for export
  - 10 to 20 together form a polyribosome
- Inside mitochondria, synthesize mitochondrial proteins

Ribosomal Subunits

- Large + small subunits
  - made in the nucleolus
  - assembled in the cytoplasm
Endoplasmic Reticulum
- Network of membranes forming flattened sacs or tubules called cisterns
  - half of membranous surfaces within cytoplasm
- Rough ER
  - continuous with nuclear envelope & covered with attached ribosomes
  - synthesizes, processes & packages proteins for export
  - free ribosomes synthesize proteins for local use
- Smooth ER -- no attached ribosomes
  - synthesizes phospholipids, steroids and fats
  - detoxifies harmful substances (alcohol)

Smooth & Rough Endoplasmic Reticulum
- Rough ER is covered with fixed ribosomes.

Golgi Complex
- 3-20 flattened, curved membranous sacs called cisterns
- Convex side faces ER & concave side faces cell membrane
- Processes & packages proteins produced by rough ER
Packaging by Golgi Complex

- Proteins pass from rough ER to golgi complex in transport vesicles
- Processed proteins pass from entry cistern to medial cistern to exit cistern in transfer vesicle
- Finished proteins exit golgi as secretory, membrane or storage vesicle (lysosome)

Cystic Fibrosis

- Deadly inherited disorder
- Chloride ion pump protein is not properly secreted from the golgi or rough ER
- Result is an imbalance in the transport of fluid and ions across the plasma membrane
  - buildup of thick mucus outside of certain cells
    - respiratory and digestive problems

Lysosomes

- Membranous vesicles
  - formed in Golgi complex
  - filled with digestive enzymes
  - pumps in H+ ions until internal pH reaches 5.0
- Functions
  - digest foreign substances
  - autophagy (autophagosome forms)
    - recycles own organelles
    - autolysis
      - lysosomal damage after death
Tay-Sachs Disorder

• Affects children of eastern European-Ashkenazi descent
  – seizures, muscle rigidity, blind, demented and dead before the age of 5
• Genetic disorder caused by absence of single lysosomal enzyme
  – enzyme normally breaks down glycolipid commonly found in nerve cells
  – as glycolipid accumulates, nerve cells lose functionality
  – chromosome testing now available

Peroxisomes

• Membranous vesicles
  – smaller than lysosomes
  – form by division of preexisting peroxisomes
  – contain enzymes that oxidize organic material
• Function
  – part of normal metabolic breakdown of amino acids and fatty acids
  – oxidizes toxic substances such as alcohol and formaldehyde
  – contains catalase which decomposes H2O2

Mitochondria

• Double membrane organelle
  – central cavity known as matrix
  – inner membrane folds known as cristae
  – surface area for chemical reactions of cellular respiration
• Function
  – generation of ATP
  – powerhouse of cell
• Mitochondria self-replicate
  – increases with need for ATP
  – circular DNA with 37 genes
  – only inherited from mother
Nucleus

- Large organelle with double membrane nuclear envelope
  - outer membrane continuous with rough ER
  - perforated by water-filled nuclear pores (10X channel pore size)
- Nucleolus
  - spherical, dark bodies within the nucleus (no membrane)
  - site of ribosome assembly

Function of Nucleus

- 46 human DNA molecules or chromosomes
  - genes found on chromosomes
  - gene is directions for a specific protein
- Non-dividing cells contain nuclear chromatin
  - loosely packed DNA
- Dividing cells contain chromosomes
  - tightly packed DNA
  - it doubled (copied itself) before condensing

An Unraveled Chromosome

- Helical DNA wraps twice around eight histone proteins to form a “bead.”
- Linker DNA holds beads together
- Chromatin fiber folds again & again to form sister chromatids if cell is dividing
Protein Synthesis

- Instructions for making specific proteins is found in the DNA (your genes)
  - transcribe that information onto a messenger RNA molecule
    - each sequence of 3 nucleotides in DNA is called base triplet
    - each base triplet is transcribed as 3 RNA nucleotides (codon)
  - translate the “message” into a sequence of amino acids in order to build a protein molecule
    - each codon must be matched by an anticodon found on the tRNA carrying a specific amino acid

Transcription

- DNA sense strand is template for the creation of messenger RNA strand
- Transcription begins at promoter sequence where RNA polymerase attaches
- When RNA polymerase reaches the terminator sequence it detaches and transcription stops
- Pre-mRNA contains intron region that are cut out by enzymes
- Exon regions of mRNA will code for segments of the protein

Translation

- Process where mRNA, rRNA & tRNA are used to form a specific protein
  - sequence of nucleotides on mRNA is “read” by tRNA to construct a protein (with its specific sequence of amino acid)
    - 3 nucleotide sequences on mRNA are called codons
    - specific tRNA molecule carry specific amino acids
  - anticodons on tRNA are matched to specific codons on mRNA so proper amino acids can be strung together to create a protein molecule
Ribosomal RNA

• 2 Subunits in each ribosome
  – large has P site and A site for tRNA molecules
  – small hold mRNA

Translation

• Initiator tRNA
• Start codon on mRNA
• Functional ribosome is formed
  – initiator tRNA fits into P site on rRNA
• Anticodon of tRNA match codons of mRNA
• Stop codon on mRNA

Normal Cell Division

• Mitosis (somatic cell division)
  – one parent cell gives rise to 2 identical daughter cells
    • mitosis is nuclear division
    • cytokinesis is cytoplasmic division
  – occurs in billions of cells each day
  – needed for tissue repair and growth
• Meiosis (reproductive cell division)
  – egg and sperm cell production
  – in testes and ovary only
The Cell Cycle in Somatic Cells

• Process where cell duplicates its contents & divides in two
  – 23 homologous pairs of chromosomes must be duplicated
  – genes must be passed on correctly to the next generation of cells
• Nuclear division = mitosis
  – continuous process divided into 4 stages
  – prophase, metaphase, anaphase & telophase
• Cytoplasmic division = cytokinesis

Interphase Stage of Cell Cycle

• Doubling of DNA and centrosome
• Phases of interphase stage -- G₁, S, and G₂
  – G₁ = cytoplasmic increase (G₀ if never divides again)
  – S = replication of chromosomes
  – G₂ = cytoplasmic growth

Replication of Chromosomes

• Doubling of genetic material during interphase. (S phase)
• DNA molecules unzip
• Mirror copy is formed along each old strand.
• Nitrogenous bases pick up complementary base
• 2 complete identical DNA molecules formed
Stages of Nuclear Division: Mitosis

- Prophase
- Metaphase
- Anaphase
- Telophase

Prophase
- Chromatin condenses into visible chromosomes
  - pair of identical chromatids held together by a centromere
- Nucleolus & nuclear envelope disappear
- Each centrosome moves to opposite ends of cell
  - forms a mitotic spindle with 3 types of microtubules
    - those that bind to kinetochore protein on centromere
    - those that radiate outward
    - those that extend between the 2 centrosomes
  - spindle is responsible for the separation of chromatids to each new daughter cell

Metaphase
- Chromatid pairs line up across the middle of cell at the metaphase plate
Anaphase

- Chromatids (daughter chromosomes) move toward opposite poles of cell
  - movement is due to shortening of microtubules
- Chromosomes appear V-shaped as they are dragged towards the poles of the cell
  - pull is at centromere region

Telophase

- Chromosomes stop moving & appear as dark, condensed bundle
- Chromosomes uncoil & revert to chromatin
- Nucleoli and nuclear membrane reappear
- Mitotic spindle breaks up

Cytokinesis

- Division of cytoplasm and organelles
- Begins in late anaphase with formation of cleavage furrow
  - indentation of cell membrane by actin microfilaments just inside plasma membrane
  - furrow always perpendicular to the mitotic spindle so chromosomes will be separated properly
- Ends with 2 daughter cells in interphase
Control of Cell Destiny

- Cell destiny is either to remain alive & functioning, to grow & divide or to die
- Homeostasis must maintain balance between cell multiplication & cell death
- The protein cyclin builds up during interphase and triggers mitosis
- Programmed cell death (apoptosis) occurs if a triggering agent turns on suicide enzymes that kills the cell
- Necrosis is cell death caused by injury or infection

Aging

- Age alters the body’s ability to adapt to changes in the environment
- Theories to explain aging
  - cells have a limited number of divisions
  - glucose bonds irreversibly with proteins
  - free radical theory---electrically charged molecules with an unpaired electron cause cell damage
  - autoimmune responses due to changes in cell identity markers
- Evidence of aging
  - damaged skin, hardened arteries, stiff joints

Cellular Diversity

- 100 trillion cells in the body -- 200 different types
- Vary in size and shape related to their function
Cancer = out of control cell division

- Hyperplasia = increased number of cell divisions
  - benign tumor does not metastasize or spread
  - malignant --- spreads due to cells that detach from tumor and enter blood or lymph

- Causes -- carcinogens, x-rays, viruses
  - every cell has genes that regulate growth & development
  - mutation in those genes due to radiation or chemical agents causes excess production of growth factors

- Carcinogenesis
  - multistep process that takes years and many different mutations that need to occur