

Chapter 2: Cytology—The Study of Cells

Chapter Overview

Cell structure and function form the basis for human anatomy and physiology. In the past 150 years, the study of cells, cytology, has transformed ideas about the body. In the 1800s, scientists formalized the central position of the cell in the cell theory. It seems obvious that all organisms are composed of cells and that cells only come from pre-existing cells but these concepts are based on painstaking observation. Our current understanding has been revolutionized by the molecular revelations of recent decades. Studies of DNA and genes and metabolism have informed our most fundamental ideas of how organisms are built and how they work. It is essential for students to understand the modern concept of the cell if they wish to understand the totality of human anatomy.

Advances in cytology depend on technology. The simple light microscope developed by Leeuwenhoek (1632-1723) enabled him to see specimens magnified by about 200 times. Modern light microscopes (such as those used by students) may magnify up to 1,200 times with good resolution. In the 20th century, images from electron microscopes revealed the tiny internal landscape of cells, including organelles and millions of large molecules such as proteins and nucleic acids. Electron microscopes rely on beams of electrons instead of light. The transmission electron microscope (TEM) magnifies objects by as much as 600,000 times. The scanning electron microscope (SEM) produces dramatic 3-dimensional images that give a sense of texture and landscape. Often, we talk about the features of a general cell but human cells come in a variety of forms. The diversity mirrors function. For example, thin flat squamous cells line the esophagus and are rapidly replaced when scraped off by passage of food. Red blood cells are discoid, or disc-shaped, which enhances the surface area for exchange of gases. Muscle cells are elongated and slender, a shape that facilitates contraction.

Cells are so tiny that we cannot see them with the naked eye (except egg cells, and they are enormous compared to other cells). Cells are measured in micrometers (millionths of meters). Most human cells are 10–15 μm in diameter. Cells depend on diffusion and transport of molecules from the extracellular fluid to sustain them. If the cell were too large, the distance that molecules would have to travel within the cytoplasm would make metabolism impossible, and the surface area would be insufficient to efficiently transport materials across the plasma membrane.

The plasma membrane is the boundary between the extracellular fluid and the intracellular fluid—it is the boundary between the non-living environment outside the cell and the living interior. The cell surface is a complex environment that regulates the passage of molecules in and out of the cell, and plays an important role in determining the function of the cell.

The fluid-mosaic model describes the structure of the plasma membrane. The vast majority (90–99%) of the molecules in the membrane are lipids, and of those, most (75%) are phospholipids. Phospholipids have a hydrophilic head that interacts with water and a hydrophobic tail composed of fatty acids. The phospholipids are arranged in two layers, creating a sandwich effect with the fatty acid tails inside. This arrangement means

that fat-soluble molecules pass easily through the membrane but water-soluble molecules are restricted.

In addition to phospholipids, cholesterol is found in all animal membranes, and is essential for maintaining the integrity, flexibility, and strength of the membrane fabric. Glycolipids in the membrane enable it to heal itself. If there is a breach, the lipids flow back together to seal the opening.

Proteins associated with the membrane have varied structures and functions. Integral proteins may span the membrane (transmembrane), while peripheral proteins adhere to one side. Glycoproteins are integral proteins that have an attached carbohydrate chain.

Membrane protein functions:

- Receptors
These proteins act as catcher's mitts that bind to specific signal molecules such as steroids or neurotransmitters. The binding triggers changes in cellular activity.
- Enzymes
Many proteins in the membrane catalyze chemical reactions. For example, enzymes associated with G-protein receptors catalyze reactions that produce 2nd messengers, leading to a physiological response to a signal molecule.
- Channel Proteins
Channel proteins allow hydrophilic molecules to enter or leave the cell and may be either gated or non-gated.
- Carriers
These proteins bind to a substance on one side of the plasma membrane and release it on the other.
- Cell-identity Markers
Some proteins act as genetic identification tags that enable the body to distinguish "self" from "non-self" and play an important role in immunity.
- Cell-adhesion Molecules (CAMs)
These proteins bind cells to each other and to extra-cellular material.

An important function of the plasma membrane is that it regulates what goes in and out of the cell. There are several means by which molecules are transported.

- Filtration
Filtration occurs when pressure forces material through a membrane, for example when blood pressure forces material through capillary walls.
- Simple Diffusion
Molecules move down their concentration gradient from areas of high concentration to low concentration does not require cellular energy.
- Osmosis
Osmosis is the diffusion of water molecules through a selectively permeable membrane. Water flows from areas of lower concentration of solutes to higher concentration of solutes, a concept that requires some thought but is important for understanding the functional importance of movement of water into and out of the cell.
- Facilitated Diffusion

Carrier proteins ferry a molecule from one side of the membrane to another down the concentration gradient. Thus, ions and water-soluble molecules can still cross the membrane. This passive process does not require cellular energy.

- Active Transport

Active transport requires ATP and moves molecules against their concentration gradient. An important example of active transport is the Na⁺-K⁺ (sodium-potassium) pump that maintains an appropriate ion balance for nerve conduction and muscle excitation.

- Vesicular Transport

Larger particles or droplets of water are moved in and out of the cell through the energy-requiring processes of endocytosis and exocytosis. Phagocytosis (literally, cell “eating”) occurs when a cell surrounds a substance and engulfs it. Pinocytosis (cell “drinking”) enables cells to engulf droplets of extracellular fluid. Receptor-mediated endocytosis allows a cell to take in specific molecules from the ECF such as insulin. Exocytosis is the process of expelling material from the cell by enclosing a cell product in a secretory vesicle and fusing the bubble with the plasma membrane.

Some of the proteins and lipids associated with the plasma membrane have carbohydrate molecules attached that form a sugary coating called the glycocalyx. The glycocalyx protects the cell from physical and chemical injury, plays a role in cell identification, and includes cell-adhesion molecules (CAMs) that give integrity to tissues.

Various extensions may protrude from the cell surface, depending on the function of the cell. Microvilli are small outcroppings that increase surface area for absorption. Cilia are longer hairlike processes. Some are motile and beat in waves across the surface of epithelial sheets. Flagella are similar in structure to cilia but are longer and are single. In humans, only sperm cells have whip-like flagella.

No cell is an island. Specialized proteins associated with the plasma membrane link cells to the ECF or bind cells to one another at points called intercellular junctions. Intercellular junctions allow cells to communicate with one another and maintain the integrity of tissue fabric. Tight junctions bind epithelial cells together towards the apical surface and seal the intercellular space. Desmosomes are patches that resist mechanical stress and hold cells together in cohesive sheets. Gap junctions are formed by connexons, tiny tunnel-like structures that allow ions and small molecules to diffuse from one cell to the next. Cardiac muscle fibers rely on gap junctions to pass the electrical signals underlie a coordinated heart beat.

The plasma membrane surrounds a complex world inside the cytoplasm. The cytoskeleton forms a structural link between the extracellular and intracellular environments. Extracellular mechanical forces transmitted through cytoskeletal components may alter gene expression. The cytoskeleton determines and supports cell shape, helps organize and move contents inside the cytoplasm, and facilitates cell movement. The cytoskeleton is composed of microfilaments, intermediate filaments, and microtubules. These components are made of various proteins; for example, microfilaments are mostly made of the protein actin. Microfilaments support the plasma membrane and play a role in cell movement. Intermediate filaments are thicker and give strength to cells and tissues. Microtubules are small strands that hold organelles in place,

guide organelles and macromolecules to destinations within the cell, and are involved in cell division.

Organelles are marvelously complex “little organs” that carry out the detailed work of the cell.

Nucleus

The genetic material, DNA, is located in chromosomes in the nucleus and, therefore, it is “command central” because DNA directs cellular activity. Most cells have a single nucleus but some are multinucleate. Ribosomes, structures important in the process of protein synthesis, are produced in the nucleus, and are among the many substances that pass through nuclear pores. Nuclear pores are openings in the nuclear envelope that regulate traffic into and out of the nucleus.

Endoplasmic Reticulum

The endoplasmic reticulum (ER) consists of interconnected channels called cisternae. Rough ER is studded with ribosomes, while the membrane of smooth ER lacks the ribosomes. Endoplasmic reticulum synthesizes steroids and lipids, detoxifies alcohol and drugs, and manufactures membranes. Cells that synthesize proteins for export have abundant rough ER, whereas cells that produce steroids or engage in detoxification have higher proportions of smooth ER.

Ribosomes

Ribosomes are found in the cytoplasm, and are where the genetic code is translated into amino acid chains, the fundamental building blocks of proteins.

Golgi Complex

Like the endoplasmic reticulum, the Golgi complex consists of cisternae. It synthesizes carbohydrates and puts the finishing touches on proteins, sometimes attaching carbohydrate bits so that they become glycoproteins. The Golgi complex sorts proteins and packages them into Golgi vesicles that may be exported in the process of exocytosis. Some of the vesicles become lysosomes.

Lysosomes

Lysosomes are membrane-enclosed packets of enzymes that break down large molecules and play a role in apoptosis (programmed cell death). The lysosomal enzymes in phagocytic white blood cells digest bacteria.

Peroxisomes

Peroxisomes contain enzymes that detoxify substances such as alcohol and other drugs and neutralize free radicals. They also break fatty acids into 2-carbon molecules that may enter metabolic pathways that ultimately produce ATP. They produce hydrogen peroxide as a by-product.

Mitochondria

Mitochondria are sometimes called the “power-houses” of the cell because they are the primary source of ATP. A double membrane encloses them. The inner membrane has folds called cristae, surface area for enzymes associated with production of ATP. Mitochondria are fascinating partly because they have their own DNA, probably because they were once (billions of years ago) an independent organism that was “hijacked” by larger cells. The mitochondrial DNA has been utilized in recent decades to explore genetic relationships among closely related species and populations. For example, studies of mtDNA suggest that all modern humans descended from a population in Sub Saharan Africa some 150–200 thousand years ago.

Centrioles

Centrioles consist of an assembly of microtubules. Centrioles found in the centrosome, an area near the nucleus, play a role in cell division. The centrosome is a center for organization of microtubules, components of the cytoskeleton. Centrioles may also form cilia and flagella, structures which are made up of bundles of microtubules.

Inclusions

Inclusions may be either stored products of the cell such as pigments or may be foreign bodies such as dust particles.

Normal cells are mortal—they have a life cycle. Most body cells divide and produce two daughter cells. The G₁ (first gap) phase is the interval when the cell carries out its normal functions including protein synthesis. The S (synthesis) phase is when DNA replicates. During the brief G₂ (second gap) phase the cell continues to ready itself for division. The M (mitotic) phase is the time when the cell replicates the nucleus and the two identical sets of DNA are pulled apart. G₁, S, and G₂ are collectively called interphase.

Cell cycles vary in different cell types. For example, most neurons never reproduce themselves, whereas cells that line the stomach or cover the surface of the skin divide rapidly and pass relatively quickly through the phases of the cell cycle.

Human reproductive cells (eggs and sperm) divide through the process of meiosis. The rest of the cells of the body undergo mitosis. Mitosis is the means by which we grow from a one-celled fertilized egg to an adult, and the way that we replace the millions of cells that die each day for as long as we are alive.

Mitosis is divided into four phases.

Prophase

The chromosomes (each consisting of two identical strands of DNA, chromatids) condense and become visible under the microscope, and the centrioles form spindle fibers, which pull the chromosomes so that they line up on the equator of the cell.

Metaphase

The centrioles move to opposite sides of the cell and their spindle fibers attach to the chromosomes.

Anaphase

The chromatids pull apart at the centromere of the chromosome. The distinct chromatids are now regarded as daughter chromosomes and they are pulled to opposite poles of the cell.

Telophase

The chromatids begin to return to the chromatin form. The rough Endoplasmic reticulum produces a new nuclear envelope. This is the end of nuclear division. It overlaps with cytokinesis, the division of the cytoplasm. The result is the formation of two complete new cells.

Stem cells are immature cells that have the potential to divide and become more specialized adult cells. Early cells in the developing embryo are pluripotent--that is they have the ability to develop into any type of cell. Adult stem cells exist in most organs, and may be either unipotent, able to develop into only one type of cell, or multipotent, able to differentiate into multiple cell types. Stem cell research, offers hope to repair tissue damage that results from heart attacks or degenerative diseases such as Parkinson's

disease. Adult stem cells are more limited in clinical application than embryonic stem cells, which are easier to obtain and have more developmental potential. However, ethical considerations surrounding embryonic stem cell use are the subject of ongoing political debate.

Key Concepts

- **Cytology**
The study of cellular structure and function.
- **Microscopy**
The use of microscopes to explore the invisible world of the cell. Light microscopes magnify up to 1,200 times while electron microscopes may magnify up to 600,000 times.
- **The Cell Theory**
The concept developed in the 19th century that all organisms are composed of cells and that all cells come from other cells. Additional tenets are that all life traces its ancestry to the same cells, and all cells have similar chemical composition and metabolic processes.
- **Micrometer**
A useful measurement for designating cell size. Each micrometer is one-millionth (10^{-6}) of a meter.
- **Plasma Membrane**
The boundary of the cell that separates the external non-living environment from the interior world of the cell.
- **Cytoplasm**
Material between the plasma membrane and the nucleus.
- **Phospholipid**
Molecules with hydrophobic fatty acid tails and hydrophilic heads that provide the basic lipid bilayer structure of the plasma membrane.
- **Hydrophilic**
Literally “water-loving”; a substance that dissolves easily in water is hydrophilic.
- **Hydrophobic**
Substances that do not dissolve in water are hydrophobic (“water-hating”).
- **Membrane Proteins**
Integral proteins pass through the plasma membrane, glycoproteins have carbohydrate chains attached, and peripheral proteins adhere to either face of the membrane.
- **Receptors**
Bind to specific signal molecules such as hormones.
- **Membrane Transport**
Movement of molecules differentiates the interior of the cell from the extracellular environment. Processes include filtration, simple diffusion, osmosis, etc.
- **Glycocalyx**
Carbohydrate coating of the cell.
- **Surface Extensions**
Microvilli, cilia, and flagella extend from the plasma membrane and serve to increase surface area, sensation, and mobility.
- **Intercellular Junctions**

Bind cells to one another and to the extracellular fluid.

- **Cytoskeleton**

Protein filaments and tubules that support cellular shape, move substances through the cell, and are involved with movement of entire cell.

- **Organelles**

Structures that play specific physiological roles in the cell, including the nucleus, endoplasmic reticulum, mitochondria, etc.

- **Cell Cycle**

The life cycle of cells includes periods of growth and normal function such as protein synthesis, replication of DNA, and cell division (G₁, S, G₂, and M).

- **Mitosis**

Cell division of all body cells except eggs and sperm. Produces daughter cells that are a replica of the original cell.

- **Stem Cells**

Immature cells that have the ability to develop into one or more types of mature, specialized cells. **Adult stem cells** are unipotent or multipotent, are found in most organs, and give rise to cells that replace cells that have died. **Embryonic stem cells** are pluripotent (in embryos up to 150 cells), and may develop into any type of cell.

Learning Strategies/Teaching Tips

- In lab and/or lecture, show students relevant portions of Anatomy & Physiology Revealed, the interactive cadaver dissection experience.
- Have students look at a structure (Red Blood Cell, for example) through a light microscope then show photomicrographs of the same structures viewed through electron microscopes to help them grasp the concept of how technology has changed our perception and understanding.
- To assist students with the challenge of visualizing the size of cells and the size of the structures inside, use the analogy of a city. If one increased the scale of a cell by 100 million times, the cell would be approximately 2 kilometers across—a metropolis. On this scale, the human body would be ten times the size of earth, while an atom would be 1cm, about the size of a pea. The tunnels of the endoplasmic reticulum would be like small roads, bounded by walls about 1/2 meter thick. The ribosomes attached to the walls would be 3 meters across, about the size of a car. Mitochondria would be 100 meters across, the size of a power station, and there would be about 1,000 per cell. The nucleus would be a vast spherical structure about 1 kilometer across. One scientist, Guy Brown, imagines the cell to be a metropolis peopled by billions of small robots doing thousands of tasks. (Source: The Energy of Life by Guy Brown, The Free Press, New York, 1999)
- Simple demonstrations in either lecture or lab help students visualize the process of osmosis. For example, make bags of colored glucose solution by tying string around two ends of dialysis tubing. Weigh the bags before lecture or at the beginning of lab and place them in beakers of deionized water. Weigh the bags at the end of the class period. Ask the students to explain the weight change.
- A laundry list of organelles may be fascinating to specialists but is rarely interesting to students unless the structures are related to function. One way to do this is to discuss diseases associated with malfunction, for example, discussion of lysosomal

storage diseases such as Tay-Sachs highlights the life or death importance of lysosomal enzymes.

- Continue the theme of “form follows function” from Chapter 1 by asking students to choose features of cells that demonstrate how structure relates to function. For example, they might discuss how cell shape (squamous, columnar, ciliated, etc.) exemplifies the concept, or they might focus on specific organelles such as mitochondria and discuss how their structure facilitates function.
- Use web resources such as animations to visualize cell structures and processes. An excellent production is “Inner Life of the Cell” produced by Harvard’s BioVisions. <multimedia.mcb.Harvard.edu/innerlife.html>.

Additional Reading

Brown, Guy. 1999. The Energy of Life: The Science of What Makes our Minds and Bodies Work. Free Press, New York.

The October, 1985 issue of *Scientific American* has several classic articles about cellular structure and function by researchers who provided a basis for our current understanding of the cell. A few examples of articles in the issue follow:

Bretscher, Mark. "The molecules of the cell membrane." 1985. *Scientific American* 253 (4): 100–109.

Weber, Klaus and Osborn, Mary. "The molecules of the cell matrix." 1985. *Scientific American* 253 (4): 110–121.

Snyder, Solomon. "The molecular basis of communication between cells." 1985. *Scientific American* 253 (4):132–141.

Web Resource

Science magazine is a premier outlet for research articles but subscriptions are relatively expensive. Free access to full text papers, Science Now stories that summarize current research, and email alerts that provide weekly table of contents is available at www.sciencemag.org.