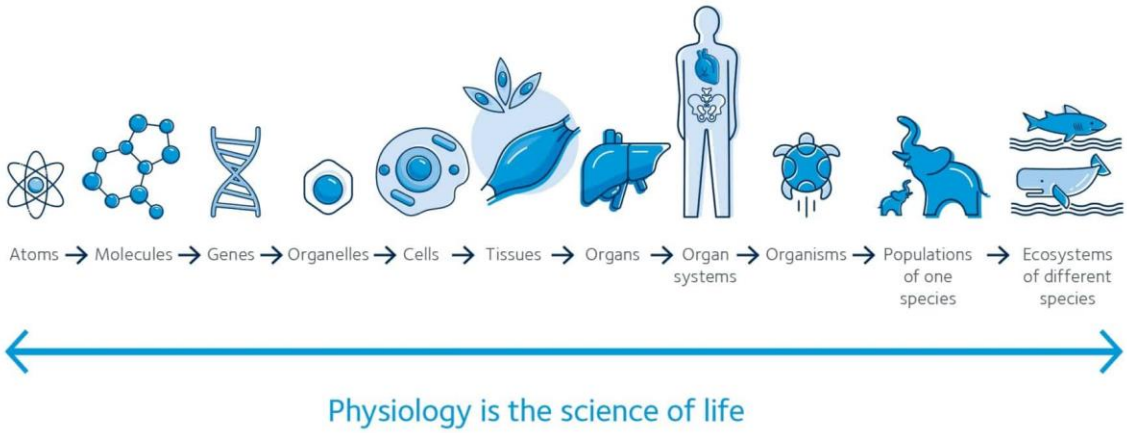
Introduction

Physiology is commonly referred to as the science of life.
It aims at explaining the mechanisms of living beings, departing from the basis of cell function at the ionic and molecular level up to the integrated behavior of the whole body and the influence of the external environment.



Function and organization of the human body

The cell is the basic and smallest structural, functional, and biological unit of all known living organisms (except viruses). These cells range in size from 1-100 µm, therefore are visible only under a microscope.
Living organisms are designated as either *unicellular* (micro-organisms) or *multicellular*.
Unicellular organisms are categorized as *prokaryotes* and multicellular organisms as *eukaryotes*.
The unicellular prokaryotes lack a nucleus and cytoplasmic organelles … as seen in bacteria.
The multicellular Eukaryotes have a *nucleus* and *cytoplasmic organelles* … as seen in human and animal cells as well as microorganisms such as fungi, protozoa, algae.
However, what's common between these two types is that both possess a *cell membrane* and contain *deoxyribonucleic acid* (DNA).
In humans and vertebrates, cells are grouped in tissues and these tissues are organized in specialized organ systems, each is designed to perform different functions. These functions are highly complex and are integrated and coordinated through different mechanisms.

Cell physiology

An adult human body contain nearly 35-75 trillion cells, among which over 200 varieties of specialized cells have so far been recognized. Additionally, there are 400 to 1000 different complex and dynamic species of microorganisms (*Microbiome* or *Microbiota*), inhabit our bodies; 70% of these microorganisms inhabit the gastrointestinal tract. These micro-organisms are estimated in trillions outnumbering human cells and have more diverse genome that exceed even human genes.

Human cellular physiology studies the specific characteristics and mechanisms of the "normal" human body functions, linking these functions to clinical medicine and providing the basis to understand and explain "abnormal" or distorted functions: *pathophysiology*.

Generally speaking, each cell of the body performs one or few more essential functions, and these functions are controlled and coordinated on different levels to keep the "constant or balanced" body state, which is referred to as *homeostasis*; (the maintenance of nearly constant conditions in the internal environment). Cells utilizes oxygen to produce energy from nutrients components in order to these maintain different functions.

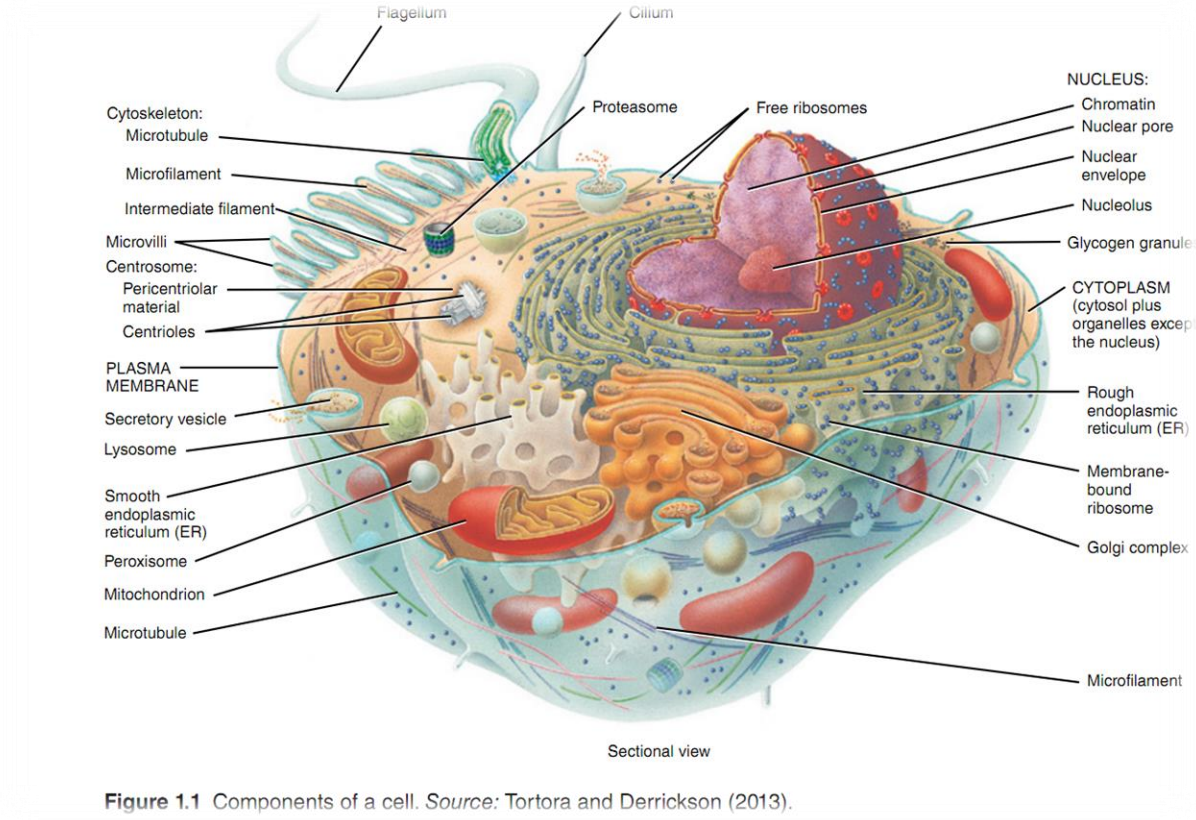


Figure 1.1 Components of a cell. *Source:* Tortora and Derrickson (2013).

Figure 1: the cell structure

Components of the Human Cell and their functions

The typical cell has two major parts: 1) the nucleus and 2) the cytoplasm. The nucleus is separated from the cytoplasm by a nuclear membrane, and the cytoplasm is separated from the surrounding fluids by a cell membrane, also called the plasma membrane.
The different substances that make up the cell are collectively called *protoplasm*, which is composed mainly of five basic substances: water (70%-85%), proteins (10%-20%; structural or functional), electrolytes (ions), lipids (2%), and carbohydrates (1%).

I. CELL MEMBRANE

- The cell membrane (s.t. called plasmalemma) forms the exterior boundary of the cell.
- The membrane is composed of a combination of **lipids** (phospholipids 25%; cholesterol 13%; and sphingolipids), **proteins** (~ 55%) and a small amount of **carbohydrates** (~ 3%).

- The membrane is formed by a dual (bilayer) **phospholipid**. The *hydrophilic (phosphate)* head region faces both 1) the *external*: extracellular fluid (ECF) or interstitial or tissue fluid and 2) the *internal* cytoplasm or intracellular fluid (ICF) of the cell, while the *hydrophobic (fatty acid portion)* tails face each other and remain isolated (Figure 2).
- The Phospholipid bilayer allows only the fat-soluble substances like O_2, CO_2 and steroid hormones (because they can dissolve because they can dissolve in the hydrophobic lipid bilayer) but NOT water-soluble substances such as glucose, Na^+, Cl^-, water and urea (these cross through water-filled channels, or pores, or may be transported by carriers).
- The **cholesterol** serves to keep the membrane at normal body temperature (37°C). It is especially important for the maintaining accurate permeability and fluidity of membrane.
- **Sphingolipids**, present in smaller amounts especially nerve cells also have hydrophobic and hydrophilic groups. Complex sphingolipids serve in signal transmission, cellular protection from harmful environmental factors, and as adhesion sites for extracellular proteins.

- Different **proteins** are found in the phospholipid layer: some are attached to the surface of the membrane, others cross it partly or completely and perform diverse functions:

  Integral proteins: maintain the membranes structural integrity
  Channel (or pores) proteins: facilitate *passive* transport across the cell membrane;
  Protein Pumps or Carrier proteins**:** for *active* transport: pass substances in a direction that is opposite to their electrochemical gradients.
  Receptor proteins for hormones and other endogenous and exogenous chemicals.
  Enzymes: control certain chemical reactions within the cell membrane
  Antigens: inducing antibody production process.

- **Carbohydrates** are either combined with proteins (glycoproteins) or with lipids (glycolipids). They are found on the surface of the cell membrane and function as *recognition markers*, allowing the immune system to recognize 'self' from foreign cells. Sometimes act as receptors for binding hormones, such as insulin.

Functions of the cell membrane

- ✓ Protection: protects the cytoplasm and its organelles.
- ✓ Structural maintenance: maintaining the shape and size of the cell.
- ✓ Selective permeability (semipermeable): allows certain substances to pass between the ECF and ICF, while serves as a barrier against others.
- ✓ Absorption: absorbed nutrients into the cell.
- ✓ Excretion: excrete metabolites and waste products outside the cell.
- ✓ Gases exchange: allows oxygen into the cell from the blood and CO_2 out to the blood.

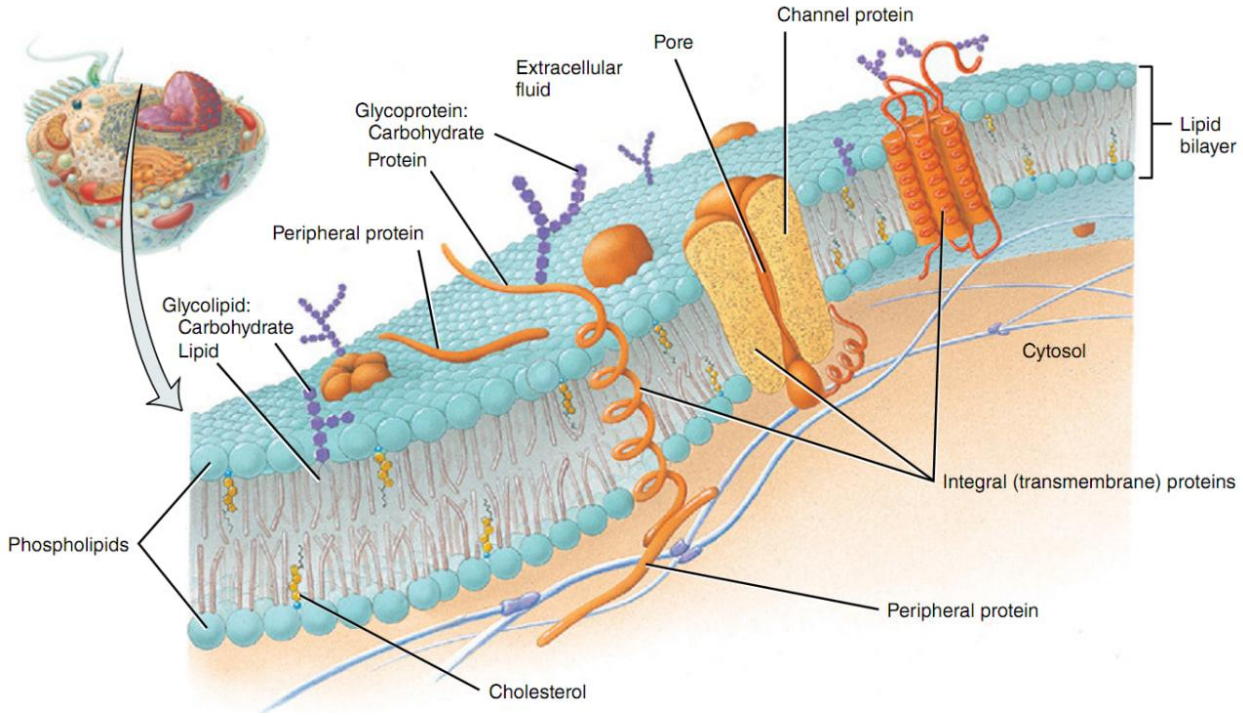


Figure 2: Fluid mosaic model of plasma membrane (Plasmalemma). From: Tortora and Derrickson.

II. The Nucleus

A double membrane-bound structure, measures approximately 3–14 µm. The nucleus contains the DNA and associated proteins (= chromatin) in the form of chromosomes.
The nuclear membrane (nucleolemma) separates the DNA from the cytoplasm and is continuous with the endoplasmic reticulum. It contains pores to allow passage of messenger RNA (mRNA).
The nucleus has a gel-like part known as nucleoplasm. Inside which, a non-membrane structure is located: the nucleolus. Around the nucleolus proteins, DNA, and RNA are concentrated in dense chromosomal regions.
The nucleus is present in all cells of the body, (except RBCs and platelets) and the function of each cell is encoded in the genetic code or nucleotide sequence of DNA inside the GENES.
The process of encoding: GENE EXPRESSION, directs protein synthesis. This is achieved through:

Transcription-Translation process:

1st: the DNA is used as a template to link nucleotides, forming a strand of an mRNA molecule using the RNA polymerase enzyme (this step is called: **Transcription**)
2nd: mRNA is then transferred across the nuclear membrane into the cytoplasm and is used as a template by ribosomes to synthesize proteins (this step is called: **Translation**)
3rd: Proteins are further processed by for ex. phosphorylation or glycosylation, through a process known as **post-translation modification**

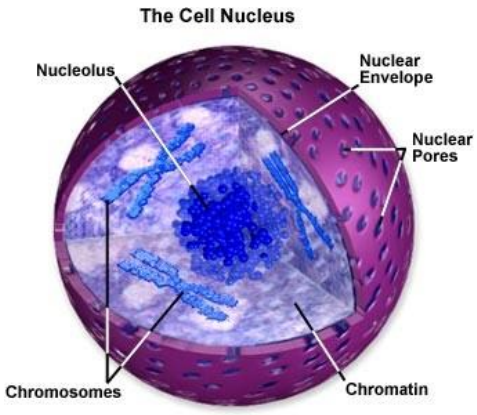


Figure 3: The nucleus

III. CYTOPLASM AND ITS ORGANELLES

The cytoplasm contains jelly-like fluid called *cytosol* that is formed of water (70–85%), dissolved proteins (10–20%), lipids (2%), carbohydrates (glucose) (1%), and electrolytes. It contains Inclusions, which are non-membrane-bound particles that do not have specific metabolic function, but may serve as energy supply when needed.
However, **FIVE** cytoplasmic organelles are **membrane-bound structures** with a specific metabolic functions and has special importance, these are:

- Endoplasmic reticulum (ER)

The ER is a complex and multi-folded system of parallel membranes, tubules and microsomal vesicles, which is connecting the nuclear membrane and Golgi apparatus.
The *rough* endoplasmic reticulum (rER) is contains and works with ribosomes to synthesize proteins which are collected in spaces called *cisternae* within the rER. Examples of the products are Insulin from β-cells of islets of Langerhans in the pancreas and antibodies from leukocytes (WBCs).
The rER functions also in the recycling damaged organelles such as mitochondria, using auto-phagosomes, which are vacuoles containing digestive lysosomal enzymes.

The *smooth* endoplasmic reticulum (sER) contributes to lipid metabolism, including synthesis of steroid hormones, the lipid portion of lipoprotein in the liver, and lipid absorption and re-synthesis of triglycerides in the intestinal mucosa.

Therefore, the major functions of ER:

- ✓ Inactivation and detoxification of harmful by-products of metabolism and drugs in the liver.
- ✓ Synthesis of cholesterol and steroids
- ✓ Possess enzymatic functions that are important in different metabolic processes
- ✓ Storage and metabolism of calcium

➢ Golgi apparatus

The Golgi apparatus (GA), like the ER, is also a has series of folded membranous sacs that are located near the nucleus. It includes two ends: a **CIS** face that is located near the ER, through which the reticular vesicles enter the GA. The **TRANS** face, which is located near the plasma membrane, serves as the exit of the substances that are processed make their exit from GA.

The main functions of the GA are:

- ✓ Processing, packaging and delivery of proteins and non-proteins ex. lipids to different parts of the cell.
- ✓ Packs cellular products to secretory granules, secretory vesicles, and lysosomes, which then bud off from main Golgi membranes and migrate to and merge with the cell membrane, releasing their contents outside the cell by a process known as **exocytosis**.
- ✓ Produces lysosomes: the digestion organelles.

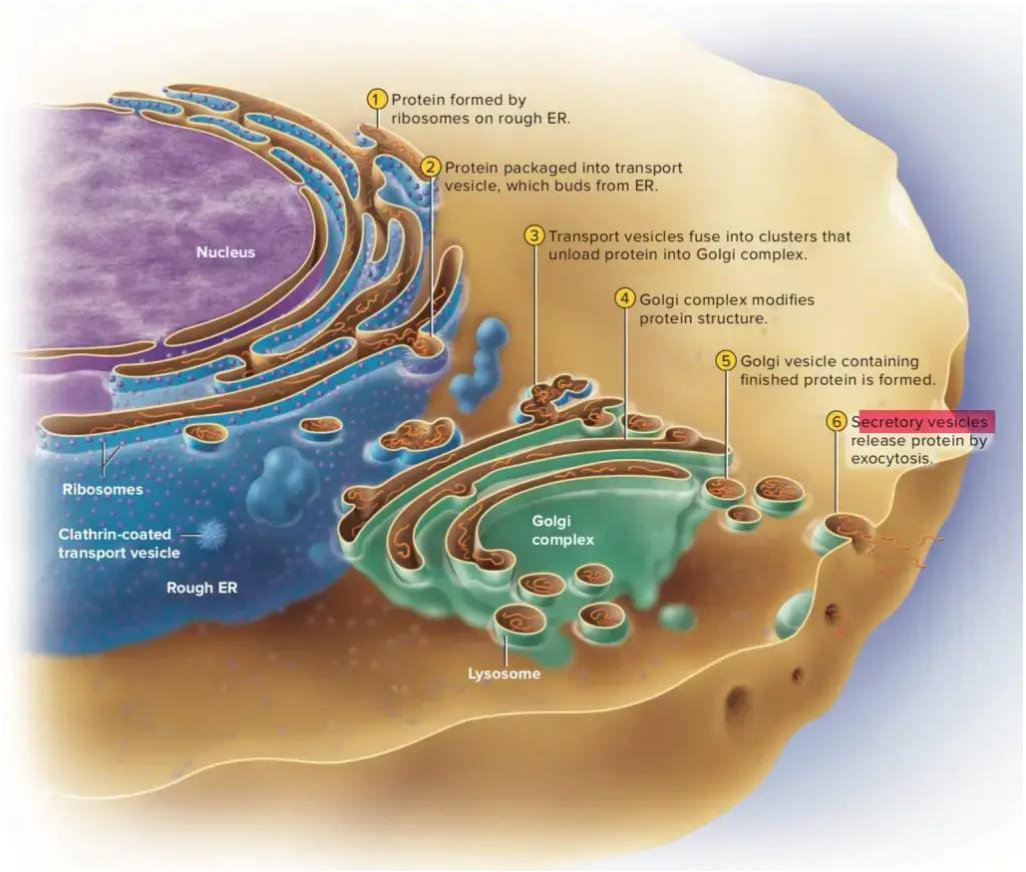


Figure 4: Protein synthesis: role of ER & GA.

➢ Mitochondria

Mitochondria are 0.75–3 µm in diameter and its main function is producing energy required by the cell (powerhouse of the cell).
They consist of a double-layered membrane, the inner membrane contains oxidative enzymes and is highly folded into *cristae*, to increase its surface area. They are filled with enzyme-rich proteins responsible for production of energy molecules: the adenosine triphosphate (ATP).
Mitochondria use oxygen (cellular respiration) to liberate energy stored in the sugars through a process known as *oxidative phosphorylation*. The energy is stored in the ATP molecules and is used for various cell functions such as protein synthesis and transport.
Mitochondria have their own DNA, which allows them to independent replicate and synthesize enzymes and proteins involved in cellular respiration.
Mitochondria are most numerous in cells with high energy requirements such as the cells in muscle and liver. Additionally, they store intracellular Ca++ and function in cellular apoptosis.

➢ Lysosomes

Lysosomes are small membranous compartments (25–50 nm in diameter), which arise from the GA. These structures contain degradative enzymes and assist in the degradation of toxic and waste products, including cell debris as well as microbial organisms (e.g. bacteria).
They are found in all cells (except RBCs), but are particularly prominent in macrophages and neutrophils. Lysosomes also play a key role in programmed cell death: apoptosis.

Functions of Lysosomes

- ✓ Degrade and detoxify toxic substances like hydrogen peroxide (H_2O_2) and other metabolic products.
- ✓ Serve as the utilization units of oxygen in the cells.
- ✓ Accelerate glucose production from fat through the process of gluconeogenesis.
- ✓ Excess fatty acids degradation
- ✓ Degrade purine to uric acid
- ✓ Play a role in the formation of myelin and bile acids.

➢ Peroxisomes

Peroxisomes are membrane-bound structures, somewhat larger than lysosomes 0.3–1.5 µm, and arise from ER. They contain specific enzymes (oxidases and catalases) that assist in the breakdown of long-chain lipids and are involved in the detoxification of certain chemicals (e.g. converting hydrogen peroxide to water).
Apart from macrophages, peroxisomes are prominent in liver cells where they are involved in the degradation of alcohol.

Other non-membrane-bound cytoplasmic organelles include:

- Ribosomes

Ribosomes are small spherical structures (15 nm in diameter) which may be found as free-floating particles or found in clusters lining the outer membrane of the rough endoplasmic reticulum (rER). Ribosomes are the factories where protein synthesis takes place through translation of the transcribed information from the DNA.

- Secretory Vesicles

The secretory vesicles are globular structures that originate from the GA have have storage and transport role. They are processed and packed in Golgi apparatus. When needed, those secretory vesicles rupture and release their contents or secretory substances into the cytoplasm.

- Centrosome and centrioles

The centrosome is found near the center of the cell in close relation to the nucleus. It consists of two cylindrical structures called *centrioles* which are responsible for the movement of chromosomes during cell division.

- Cytoskeletal Components

The cytoskeletal component functions in supporting cells through a complex network of extensive *microtubules* and *microfilaments* and *intermediate filaments*, which enhance cell integrity and shape. They permit the cell to change its shape and move and also serve as an additional means of transport of substances.

a. Dynamic Microtubules

These are hollow cylindrical structures (25 nm in diameter) that are made up of mainly α-tubulin and β-tubulin proteins. They play a role in the cellular transport of organelles such as mitochondria and vesicles. They also participate in cellular appendages like: cilia (respiratory tract, fallopian tubes), flagella (sperms) and also in centrioles-mitotic spindle which help in cell division.

b. Dynamic Microfilaments

These are narrow (7 nm) filamentous structures made of the globular protein that is called: actin, which are critical components of the contractile apparatus of muscles. They are located near to the inner surface of the cell membrane and help the cell to maintain cellular shape, assist in cell junctions and are also involved in muscle contraction and movement (WBCs).

c. Static Intermediate Filaments

Intermediate filaments are made of fibrous proteins (8–10 nm) and contribute to the structural integrity and shape of the cell and also in cell adhesions. Examples of these filaments include: cytokeratin (epithelia, hair, nails); vimentin (connective tissue, blood cells); desmin and synemin (muscle); and neurofilaments (neurons).

IV. CELL JUNCTION

Cellular junctions are connecting links between the cells or between one cell and the EC compartment. They can be:

1. Occluding Junctions that fasten the cells to one another and to surrounding tissues

   Tight Junction or Zonula occludens

Found surrounding the apical margins of epithelial cells in intestinal mucosa, renal tubule, and capillary wall and allow the passage of some ions and solute between adjacent cells (para-cellular pathway). They hold the adjacent cells of the same tissues together tightly and work as a fence that inhibits lateral movement. Tight junctions also serve as barriers that prevent passage of water, ions, large molecules as in blood-brain barrier (BBB) in brain capillaries where it prevents the entry of dangerous substances into the brain. Three main transmembrane protein families contribute to these junctions: occludin, junctional adhesion molecules (JAMs), and claudins.

2. Anchoring Junction

These include junctions that provide firm structural attachment between two cells or between a cell and the extracellular matrix

Adherens Junction or Zonula adherens: (cell to cell)

Found at the basal side of the tight junction, serving as a major site of attachment for intracellular microfilaments.

Desmosome (cell to cell)

Help hold cells together

Hemidesmosome (cell to matrix) and ***Focal adhesion*** (cell to matrix)

These junctions attach cells to their basal laminas.

3. Communicating Junctions permit transfer of ions and molecules from one cell to another.

   a) Gap junction (also called NEXUS).

Forms a cytoplasmic "tunnel" for diffusion of small molecules between two neighboring cells.

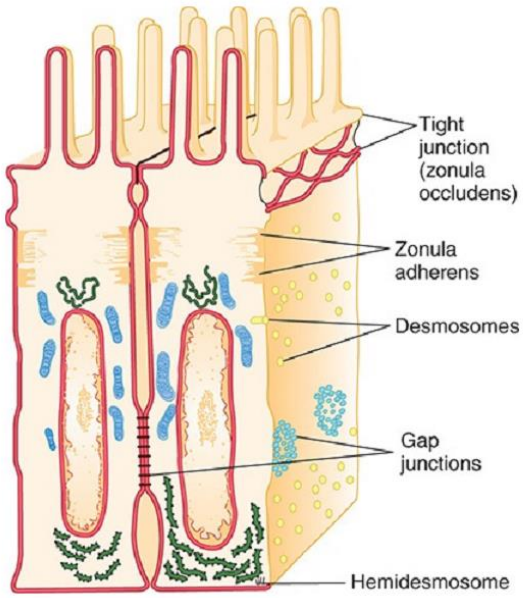


Figure 5: Intercellular junctions in the mucosa of the small intestine