Unit 1 Lecture 2

THE CELLULAR LEVEL OF ORGANIZATION

It is within the cell where the functions of the body occur. We are going to look at structure, function and reproduction of cells in this chapter. Cytology is the study of cells. Animal cells differ from plant cells in that animal cells do not have cell walls. This allows much material to easily diffuse across the plasma membranes into the cytosol of the cell where the materials can be stored as inclusion bodies or can be utilized in the organelles of the cell.

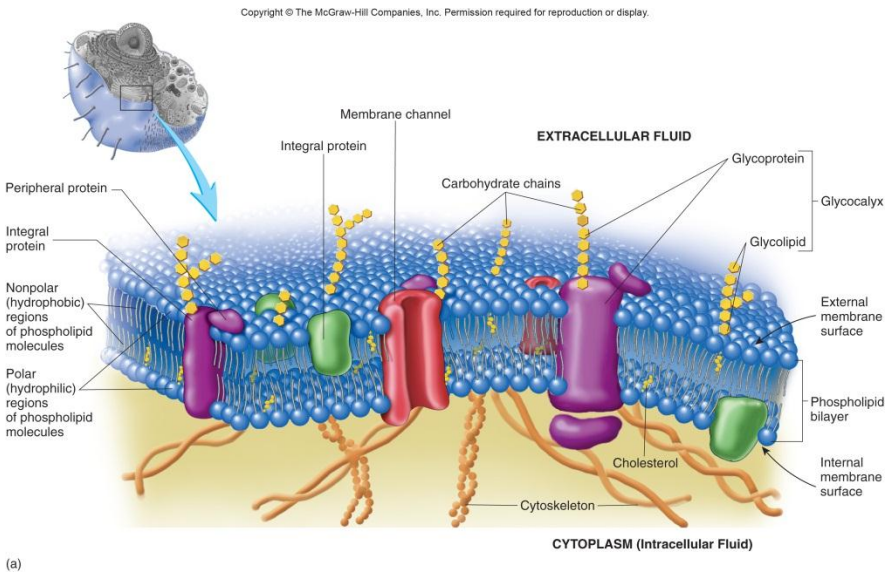
The **PLASMA MEMBRANE** is a very thin barrier that separates the internal components of a cell from the external environment. The membrane is composed of lipids (phospholipids, glycolipids, and cholesterol), proteins (mostly glycoproteins) that form channels through which materials pass. There are over forty protein channel diseases that affect us. Proteins also act as transporters and serve as receptors, enzymes, cytoskeleton anchor, and cell identity markers. The membrane functions in cellular communication, as an electrochemical gradient which is important for proper function of the cells.

In selective permeability certain substances are allowed to pass through while others are restricted. Permeability depends on size of the molecule, lipid solubility, electric charge, and the presence of transporters and channels. Proteins, nucleotides, and other large molecules needed for the structure and function of the cell cannot penetrate this membrane. Other molecules and many ions can penetrate the membrane to varying degrees. The plasma membrane provides two-way traffic for nutrients and waste needed to sustain metabolism, while it prevents the passage of other substances between the intracellular and extracellular compartments.

A phospholipid molecule is made up of a **phosphate** "head" and **fatty acid** (or **lipid**) "tails." The fatty acid tails of a phospholipid molecule are **hydrophobic** (they do not like water), while the phosphate heads are **hydrophilic** (they like water). Consequently, when many phospholipids are thrown into water, they will align themselves into a **lipid bilayer** so that the head groups all face out toward the water and the tails away from the water. Since the fatty acid tails are hydrophobic, they are the major barrier to water and water-soluble substances (anything that dissolves in water) such as ions, glucose, urea, and most of the other molecules found in living organisms. Fat-soluble substances like oxygen, carbon dioxide, and steroid hormones can penetrate this portion of the membrane with ease since they can "dissolve" through the lipid region of the membrane.

Membrane Proteins are another important component of the cell's membrane. Membrane proteins have many different functions, including the following:

Receptors for the attachment of chemical hormones and neurotransmitters
Enzymes that help with chemical reactions or breakdown molecules
Ion channels or pores that allows water-soluble substances, into the cell



Membrane-transport carriers that transport molecules across the membrane (this may include gated channels). This is probably the most important function of the proteins.

Cell-identity markers like antigens or glycoproteins. Antigens are foreign particles that can stimulate the immune system

Movement of Materials Across Cell Membranes

Passive processes don't use energy. In simple diffusion (particles move from an area of high concentration to a lower concentration to reach a point of equilibrium). This is seen in gas exchange in tissues and lung. A second type is osmosis or the movement of a solvent through a selectively permeable membrane. Here osmotic pressure, or the pressure needed to stop the flow of water across the membrane, depends on the permeability of the membrane and the tonicity of the solutions involved (hypotonic, isotonic, or hypertonic). Filtration occurs when water and some dissolved substances move across a membrane due to gravity or hydrostatic water pressure. It always moves from higher levels of pressure to lower levels. In facilitated diffusion certain molecules are helped across a membrane by a transporter that moves the molecules from a higher concentration gradient to a lower concentration. Facilitated diffusion depends on difference in concentrations, number of transporters available (once the system becomes saturated, it cannot operate any faster), and how quickly the transporter and the substance combine. Facilitated diffusion shows chemical specificity (a given carrier protein will interact only with a specifically shaped molecule) and may be competitively inhibited by molecules that are very similar in shape.

Lipolytic molecules can diffuse through the phospholipid bilayer easily whereas water soluble molecules either diffuse slowly or not at all. Lipid-soluble (or fat-soluble) substances include oxygen, carbon dioxide, fatty acids, and some steroid hormones. These molecules can diffuse right through the membrane's lipid bilayer and are not stopped by the hydrophobic fatty acid chains. The rate of diffusion:

1. depends on the ability of the molecule to dissolve in the lipid layer of the membrane,
2. is directly proportional to the surface area of the membrane,
3. is inversely proportional to the thickness of the membrane (the thicker the membrane, the slower diffusion will occur).

Active Processes use energy from splitting ATP. Active transport can be either primary active transport in which ATP directly moves a substance across the membrane or secondary active transport in which energy stored in ion differences drives the substance across the membrane. Another active process is Bulk transport. Examples of this mechanism include endocytosis (brining substances into a cell), phagocytosis (engulf a substance and bringing that substance into the cell), pinocytosis (engulf tiny droplet of extracellular fluid), receptor-mediated endocytosis (takes in specific substances), and exocytosis (discharges substances from cell).

Osmosis

By far the most abundant substance to diffuse through the cell membrane is water. It requires special pores since it cannot diffuse through the hydrophobic portion of the lipid membrane. Normally the amount of water that diffuses into cells is exactly equal to the amount of water that diffuses out; therefore, the volume of the cell remains constant. Under certain conditions, however, it is possible for a concentration difference for water to develop across a membrane. When this happens, there is a net movement of water down its concentration gradient, which is called **osmosis**. The body is in a state of osmotic equilibrium.

- A **solute** is the substance that is being dissolved in a liquid.
- A **solvent** is the liquid that is doing the dissolving; in most cases, it will be water.
- A **solution** is what you get when you dissolve a solute in a solvent.

A solution that has a high concentration of a solute (such as glucose) will consequently have a low water concentration. Pure water, on the other hand, will have a high water concentration. Therefore, if a cell with a high intracellular concentration of glucose (low water concentration) were placed in a pure water solution (high water concentration), water would move down its concentration gradient, from high to low, into the cell, causing it to swell. Osmosis always involves water moving down its concentration gradient (higher concentration to lower concentration) and is always a passive process (one that does not require energy).

Osmosis across the cell membrane is affected by the following:

- The permeability of the membrane to the solutes in the intracellular and interstitial fluids
- The concentration gradients of the solutes in the intracellular and interstitial fluids
- The pressure gradient across the cell membrane

There are two units used to describe the **concentration** of a solution:

- Osmolality is equal to the number of osmoles per kilogram (kg) of water.
- Osmolarity is equal to the number of osmoles per liter of solution.

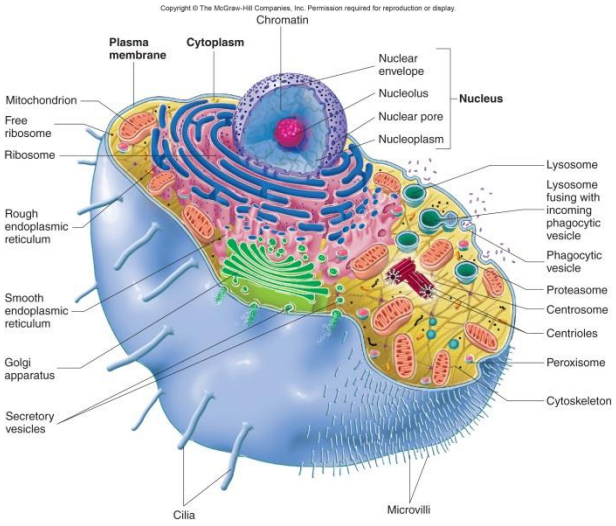
These terms are used interchangeably by physiologists. Osmolality is used in clinical situations.

Tonicity

Tonicity is a term used to describe the ability of a solution to cause osmosis across a biological cell membrane. The fluid inside a typical human cell has a concentration of roughly **300 mOsm/kg water**. An **isotonic solution** has the same concentration as body fluids. If a typical human cell, like a red blood cell, were placed in such a solution, no osmosis would take place since the concentrations of the solution and the inside of the cell are the same. A **hypotonic solution** has a lower concentration compared to cellular fluids and would cause osmosis into the cell—the cell would swell. A **hypertonic solution** has a higher concentration compared to the cell and would cause osmosis out of the cell—the cell would shrink.

Cell Organelles

All cells in the body share similar features and organelles. The Cell can be divided into two parts, the **CYTOSOL** or Intracellular Fluid and the **ORGANELLES**. The cytosol is a semi-fluid portion of the cytoplasm in which organelles and inclusions are suspended. The function of the cytosol is to provide a place where metabolic reactions occur.



The organelles are specialized structures in the found in the cytosol. Organelles can be distinguished on the presence or absence of a membrane. Non-membranous organelles are in direct contact with the cytosol and are further divided into those made from protein and RNA and those made from insoluble protein fibers. **Ribosomes** are small dense granules of RNA that participate in protein synthesis. They are either free floating or attached to the endoplasmic reticulum. The protein fibers are of various sizes and compose the cytoskeleton. Functions of the cytoskeleton include determining the cell shape, stabilize the positions of organelles within the cell, help with intracellular transport of materials, help in the assembly of cells into tissues, and movement of the cell.

The centrosome and centrioles are microtubules associated with DNA replication. **Cilia** and **flagella** are moveable hair-like structures that either aids the cell in

moving (sperm) or the passage of materials across a cell surface (ciliated epithelial cells).

Membranous organelles create compartments for specialized functions. **Mitochondria** generate ATP (energy source of the cell). The **Endoplasmic Reticulum** is a network of membrane-enclosed channels continuous with the nuclear membrane. Its function is to transport substances, store newly synthesized molecules, detoxify chemicals, and release calcium ions involved in muscle contractions. Rough endoplasmic reticulum is the site of protein synthesis, whereas smooth ER is the site of fatty acid, steroid and lipid synthesis. Another structure is the **Golgi Complex** which processes, sorts, and delivers proteins and lipids to the plasma membrane, lysosomes and secretory vesicles. Lysosomes contain digestive enzymes that dissolve cellular contents and extracellular materials.

The most important organelle is the **Nucleus**. The nucleus has two functions: protein synthesis and controlling cellular reproduction. It controls cellular activities, contains the genetic material of the cell, which is seen as chromosomes during cellular division, and is separated from the cytoplasm by a nuclear membrane. Within the nucleus are nucleoli which are the site of assembly of ribosomes.

The total amount of DNA in a cell is called its genome. DNA is the blueprint that tells the cell through RNA what proteins to make. DNA is composed of two strands of nucleotides which contain nitrogenous bases [purines (adenine & guanine) and pyrimidines (cytosine & thymine)]. Base pairing rules dictate that they always, always pair up as A-T or C-G only. Also included in DNA is a sugar, deoxyribose and a phosphate, HPO_4. The structure forms a double alpha helix (a twisted ladder formation). Sections of DNA are the genes (a certain segment of DNA that contains the necessary code to make a protein or RNA molecule). These sections maintain the genetic code during reproduction, yet provide variability due to crossing over during meiosis. DNA replication is the production of identical strands of DNA. This must occur prior to cell reproduction. Semi-conservative replication means that each "old strand" of DNA serves as a template upon which the "new strand" is synthesized. The double strands separate to form two templates.

Proteins are the key to cell function. We are what we are because of the proteins our cells make and do. Therefore, protein synthesis is necessary for cell function. The function of cell is to make proteins and the instructions on how to make the proteins is found on the genes. The process is pretty simple. In transcription genetic information (the sequence of the nucleotides) encoded in a region of the DNA helix is copied (transcribed) onto messenger RNA (mRNA). The next step is translation, a process by which the mRNA specifies the amino acid sequence of a protein in the ribosome. The result is an amino acid. Combinations of amino acids make different proteins. In summary, **DNA ---> RNA ---> protein**. Proteins may be modified in the rough endoplasmic reticulum or the Golgi apparatus.

Review of Steps in Protein Synthesis Sequence

1. DNA unzips Transcription produces mRNA using the DNA code by complimentary base pairing
2. mRNA attaches to ribosome
3. tRNA anticodons attach to complimentary codons of mRNA amino acids join to produce protein
4. Translation: production of a protein from a mRNA strand
5. All elements needed to synthesize a protein are brought together on the ribosome.

RNA Code

RNA is composed of single strands of nucleotides which contain nitrogenous bases [purines (adenine & guanine) and pyrimidines (cytosine and uracil)]. RNA also contains a sugar, ribose, a HPO_4. There are three types of RNA, messenger RNA (mRNA) which is produced from DNA patterns in transcription. The master DNA code is first copied onto mRNA through transcription. Transfer RNA (tRNA) is also produced from DNA patterns. Sixty-four varieties of codons are determined by anti-codons (nucleotide triplets) and amino acid binding sites. 61/64 types represent some type of amino acid, other types are either start or stop codons. Each variety of tRNA converts the master code on mRNA into a specific amino acid. Ribosomal RNA (rRNA) forms the major part of the ribosome and participates in protein synthesis.

The process of NORMAL CELL DIVISION is a means by which cells replicate themselves. It consists of a nuclear division (mitosis) and a cytoplasmic division (cytokinesis). Somatic Cell Division results in an increase of body cells. Parent cells and daughter cells both contain the diploid (2n) number of chromosomes. Interphase is the time period between cell divisions during which replication of DNA occurs and the original DNA molecule becomes two DNA molecules. Some terms of mitotic cell division you should become familiar with are:

- prophase: chromatin material shortens and condenses
- metaphase: centromeres of the chromatid spindles line up at the exact center of the mitotic spindle
- anaphase: centromeres divide and chromosomes move to opposite ends of the cell
- teleophase: nuclear envelope reappears and encloses chromosomes which resume chromatin form, nucleoli reappear, and mitotic spindle disappears
- cytokinesis: division of the parent cell's cytoplasm and organelles, cleavage appears to separate cytoplasm into usually two equal portions

Meiosis or Reproductive Cell Division is a process that produces a haploid number of chromosomes and consists of two nuclear divisions called reduction division and equatorial division. In meiosis the homologous chromosomes undergo synapsis (chromosomes become arranged in homologous pairs) and crossing-over to result in two diploid daughter cells. Then the two haploid daughter cells undergo mitosis (equatorial division). The entire process results in four haploid daughter cells. More about meiosis will be presented in the unit on reproduction.

Mutation Mechanisms or Nucleic acids gone bad....sometimes

A Mutation is a permanent change in the DNA that may be passed along from generation to generation. The wild type (strain) of the organism exhibits, non-mutated characteristics. A mutant strain can show variance in morphology, nutritional characteristics, genetic control mechanisms, and resistance to chemicals, temperature preference, and any type of enzymatic function.

Causes of mutation can be spontaneous where there is a random change in DNA. This arises from mistakes in DNA replication. Mutations can be induced due to chemical or physical factors. Many chemical mutations are also carcinogenic and can result in cell death. The categories of mutations are as follows:

1. Point mutations change the nature of one gene. These can be either frameshift (deletion or insertion of a base pair) or substitution in which the wrong base pair is put in place of correct bp producing error in base pairing, thus a change in the codon.
2. Inversion is the change in one or two codons (adjacent base pairs change position). These can be silent (no change in amino acid) if the same bp are exchanged or missense which can have consequences of none to severe. This is due to a faulty, nonfunctional protein, a different, but functional protein, or there can be no significant alteration in protein function.
3. Some mutation result in nonsense or STOP codon. The protein stops being produced. If large mutations in which whole chromosomes are lost or large genetic sequences are inserted, the cell or organism often will not survive. Thus major mutations alter the number of genes present.

Cell death occurs by necrosis, which adversely affects neighboring cells, or by apoptosis, a programmed cell death that does not which disturb the surrounding tissue. Apoptosis is an extremely complex process regulated by a number of chemical signals that removes unwanted cells and should be considered a normal event in the life of a cell.

ABNORMAL CELL DIVISION: CANCER

Cancer is uncontrolled cell growth resulting in a tumor or neoplasm. A growth than spreads (metastasis) is a malignant tumor. Non-spreading growth is called a benign tumor. Cancer cells compete for nutrients and space. They crowd out normal tissue until that normal tissue dies. Some causes of cancer are carcinogens, which are found in the environment (such as chemicals or radiation) and viruses. The treatment of cancer employs a variety of methods depending on type of cancer. Some methods include surgical removal, chemotherapy, radiation, immunotherapy to get rid of the cancer. Bone marrow transplants may be used in certain types of cancer to regenerate blood cells.

Homeostatic Control Pathways

The simplest homeostatic control takes place at the tissue or cellular level and is known as local control. Below are examples of simple or complex reflexes.

1. Simple Endocrine reflex: The body senses an internal or external change. A message is sent to the endocrine system sensor-integrating center which responds by sending out an efferent signal (a hormone) which goes to a target cell (effectors) and yields a response. Usually is a slow process.
2. Simple nervous reflex: The body senses an internal or external change at a receptor. Via the afferent pathway, a message is sent to the nervous system integrating center. By way of an efferent neuron a response is sent to effectors which produce a response. Usually is a very rapid process.
3. Complex neuro-endocrine reflex: The body senses an internal or external change at a receptor. Via the afferent pathway, a message is sent to the nervous system integrating center. By way of an efferent neuron or a neuro-hormone is sent to the endocrine integrating center and an efferent signal (a second hormone) is sent to effectors which produce a response. Usually is slow process.

Why is this chapter important?

Everything that happens in the body happens at the cellular level. The cell is the smallest living unit capable of self-replication. It is important that we understand the structure and function of each of the cell's organelles. A wide variety of chemical reactions occur within the cell. We need to comprehend the mechanisms on how materials cross the plasma membrane and why some materials cannot cross the membrane. Finally, we need to understand the differences between mitosis and meiosis and when they occur.