

Cells

All living things are made of cells. All cells come from other cells. Cells are enclosed in a cell or plasma membrane. This membrane is made of a phospholipid bilayer, i.e. two layers of phospholipids arranged so that the hydrophilic phosphate groups are situated on the inside and outside of the membrane and the hydrophobic fatty acid chains are directed toward each other in the middle of the membrane. (pp 61 – 62) Holding these layers together is the steroid cholesterol.

Imbedded within the bilayer are many proteins which serve many different functions. Some are enzymes that facilitate chemical reactions, some are involved with the transport of materials across the membrane and some are involved with binding cells together. Still others bind with chemicals outside the cell which causes other reactions inside the cell. This last process is called transduction. Glycolipids (Sugars attached to the phospholipid) and glycoproteins (sugars attached to the membrane proteins) often serve as tags or markers that identify the kind of cell it is and as receptors for various kinds of chemicals that attach to the membrane.

Transport of materials across the cell membrane

The arrangement of the bilayer, with the hydrophilic parts inside and outside the cell and the hydrophobic parts in the middle, give the cell some unusual properties. The membrane becomes semi-permeable – it allows some things to pass through it but not others. Since the cell constantly needs the raw materials for its metabolism (chemical reactions) and must also remove materials such as manufactured products and wastes, there is continuous movement of materials back and forth across the membrane. This movement is accomplished in a number of different ways.

1. Diffusion (p 65) is caused by the constant, random motion of molecules that results in a substance eventually becoming evenly distributed throughout a liquid or gaseous environment. Molecules will always move from an area of greater concentration toward an area of lower concentration along a concentration gradient. Small molecules such as O₂ and CO₂ may pass from one side of the membrane to the other by simple diffusion. For example, if the concentration of O₂ is greater outside the cell than it is inside the cell, the O₂ will diffuse into the cell.
2. Larger molecules, such as amino acids and sugars also pass into or out of the cell along a concentration gradient but have to be helped across by binding first to a protein or moving through a protein channel. This is called facilitated diffusion.
3. Sometimes materials must pass through a cell membrane *against* a concentration gradient. In this situation energy must be expended. ATP provides the energy for this by phosphorylating a protein which can then act as a pump to move materials across the membrane. This is called active transport. (p 71)
4. Vesicular transport involves the movement of very large materials across the membrane. This may be exocytosis, moving materials out of the cell, or endocytosis, moving materials into the cell. In both cases the material is wrapped in membrane (phospholipids bilayer) and taken across. (pp 72 – 73) Endocytosis may occur as phagocytosis, where the membrane reaches out with pseudopods to engulf the material, or as pinocytosis, where a pit forms in the membrane and the material is eventually engulfed. Sometimes the material attaches to receptors on the cell surface first. This triggers the membrane to invaginate, bringing the material with it. This is referred to as receptor-mediated endocytosis. (pp 71 – 75)

Osmosis

Osmosis is the movement of water across a semi-permeable membrane. (pp 67 – 68) Water is the biological solvent both inside and outside the cell. If the concentration of solute differs on either side of the membrane, then water will move across toward the greater concentration of solute. This movement will continue until the concentration on both sides is equal. This is rarely achieved in cells because a back-pressure will develop that resists further movement into a cell.

Cells can exist in an isotonic solution, in which the concentration of solute is equal on both sides of the membrane and so no net movement of water, a hypertonic solution in which there is a greater concentration of solute outside the cell resulting in the movement of H₂O out of the cell, or a hypotonic solution in which there is a greater concentration of solute inside the cell causing water to enter the cell.

Filtration

If the pressure gradient is great enough, hydrostatic pressure may force both water and solutes from one side of a membrane to the other. (p 69)

Nucleus

The nucleus within each cell contains the hereditary material DNA. (p 89 – 91) Nuclear DNA acts as the template from which proteins are constructed so ultimately it determines what kind of cell and what kind of organism a living being is. This nucleus is bound with a double membrane (two phospholipids bilayers) that is porous to allow things to move in and out. Most of the time the DNA is in an unraveled state called chromatin. If all the DNA of a cell were to be stretched out, it would be about a meter long. During cell division (which we will examine later) the chromatin becomes coiled and condenses into structures visible under a microscope that we call chromosomes. Also with the nucleus is a structure called the nucleolus which is important in the assembly of ribosomes (which we will also examine later.) Most of the cells of the body contain one nucleus but a few are multinucleate.

Cytoplasmic Organelles

Between the outer plasma membrane and the nuclear membrane is the cytoplasm where most of the cell's activities occur. Within the cytoplasm are a number of important structures. (pp 78 – 86)

- Ribosomes. These are structures made of RNA and protein and are important in the process of protein synthesis. Some ribosomes float freely in the cytoplasm and others are attached to membrane (rough ER) within the cell.
- Endoplasmic reticulum. This is a complex of tubes and sheets of membrane material that may be continuous with the outer plasma membrane and the nuclear membrane. It occurs as two types:
 1. Rough ER. This is membrane studded with ribosomes and is therefore important in protein synthesis.
 2. Smooth ER. This contains no ribosomes but is important in the synthesis of lipids and lipoproteins, the detoxification of certain chemicals and the breakdown of glycogen into individual glucose molecules.
- Mitochondria. These are double membrane-bound organelles that probably originated as symbiotic bacteria. They have their own DNA and divide independently of cell division. It is on the inner membrane of the mitochondria that most of the cell's (not all) ATP is manufactured. For this reason it has earned the nickname "powerhouse" of the cell.
- Golgi apparatus. The Golgi apparatus occurs as stacks of flattened sacs of membrane. Within these certain proteins and other complex chemicals are modified and packaged for export out of the cell by exocytosis.

- Lysosomes. These are membrane-bound organelles containing acid hydrolases, enzymes that digest many kinds of biological chemicals. They also degrade other worn out organelles. If the contents of lysosomes spill out of the membrane, it will destroy the cell. This is sometimes desirable as in the case of apoptosis, or programmed cell death.
- Peroxisomes. These are also membrane-bound organelles that contain oxidases and catalases. Oxidases render free radicals harmless by converting them to H_2O_2 (hydrogen peroxide). H_2O_2 is also toxic but is quickly converted to H_2O by the catalases. Free radicals are highly reactive chemicals that can destroy many important biological chemicals.
- Cytoskeleton. This gives internal support to the cell and provides a way for organelles to move within the cell as well as providing a way for certain structures to move on the outside of the cell. The cytoskeleton is made up of three kinds of filaments.
 1. Microfilaments. These are made up of the protein actin. It is found on the inside of plasma membranes and helps to maintain the shape of the cell. It is also important in the physiology of muscle contraction.
 2. Microtubules. These are the largest of the filaments and are generated by structures called **centrioles** that occur in pairs. They are hollow tubes made of protein subunits that can quickly be added or subtracted. In this way things attached to microtubules can be moved within the cell and can also create movement of structures on the outside of cells.
 3. Intermediate filaments. These protein filaments do not cause movement but act to resist outside stresses on the cell.
- Organelles of locomotion. There are two types of structures on the outside of the cell membrane involved in locomotion. Flagella are long, whip-like structures that propel certain cells. Although common in bacteria and other simpler organisms, the only human flagellated cells are sperm cells. Cilia are shorter and more numerous surface organelles that can work in a coordinated fashion to propel not the cell, but other objects along the surface of the cell. Cilia, in the human body, are found on cells lining the trachea and the fallopian tubes.
- Microvilli. These are small cytoplasmic extensions of the plasma membrane that serve to increase the surface area of the cell and are especially important in cells of absorption.

Cell Junctions

Some cells occur individually in the body but many are bound together. There are three basic types of cell junctions: (pp 63 – 64)

1. Gap junctions. These connect two adjacent cell membranes by proteins that form pores or channels between the cells so that materials can diffuse more quickly from cell to cell.
2. Tight junctions. Protein molecules on the surface of adjacent cells form tight junctions that are impermeable to most substances and prevent molecules from passing in the space between the cells.
3. Desmosomes. These are long protein filaments that extend between adjacent membranes anchoring them together. From these proteins other proteins extend within the cell (sometimes across the entire width) to anchor them in place. They help resist mechanical stress such as that found within the heart.

The Cell Cycle

No cells last forever and so they must be replenished from time to time and so go through a reproductive cycle. Usually the longest phase in the cell cycle is called **Interphase**. This is when the cell is carrying out its functions of growing, metabolizing, absorbing, synthesizing – all the various workings of the cell. This is the G₁ subphase of interphase. When it comes time to divide (a number of things can initiate cell division e.g. the surface to volume ratio which in turn triggers certain proteins that begin the process) the cell first must duplicate its DNA in what is called the Synthesis (S) subphase. Every cell carries in its nucleus the complete blueprint for an entire organism. The different kinds of cells occur because some of the DNA is expressed in some cells while not in others. A complex set of mechanisms can turn the DNA “on” and “off”. To copy itself the double helix splits apart, each strand acting as a template for a complimentary new strand. This process is aided by several enzymes one of which is called DNA polymerase. As the bonds between the A’s & T’s and the C’s & G’s break, new nucleotides (nitrogenous base + sugar + phosphate) will take their place. (p 94) Two new, identical strands are now present. Mistakes in copying the DNA only occur about once in a billion times.

A second, G₂, subphase occurs after the S subphase during which the final preparations are made for division. The division of a cell into two genetically identical daughter cells is called Mitosis and there are four stages: (pp 96 – 97)

1. Prophase. The events of prophase include the disappearance of the nuclear membrane and the condensing of the chromatin into chromosomes. Human cells have 23 pairs of chromosomes (= 46). Because the DNA has now replicated, each of the 46 chromosomes is attached to an identical chromosome called the sister chromatid. Also at this time the centrioles divide, migrate to opposite ends of the cell, and form long strands of microtubules between them. This is referred to as the mitotic spindle. Each of the chromosomes and their sister chromatids are attached to a microtubule at a constriction in the chromosome called the centomere that also attaches the two sister chromatids together.
2. Metaphase. The chromosomes with their chromatids line up along the equator (or metaphase plate) of the cell.
3. Anaphase. The microtubules of the spindle shorten toward the centrioles at opposite ends of the cell. As it shortens, it drags one chromosome toward one end and the sister chromatid toward the other. The cell now has 46 chromosomes at each end of the cell.
4. Telophase. The chromosomes now start to uncoil back into chromatin and so become invisible under a light microscope. The nuclear membrane reappears around the chromatin at each end of the cell. The mitotic spindle disappears.

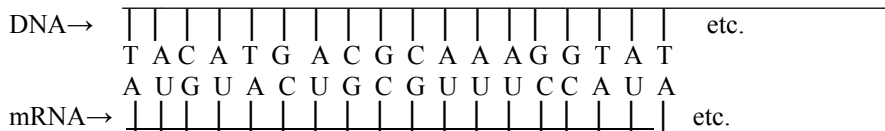
Cytokinesis. As the events of telophase proceed, the plasma membrane pinches inward at about the middle of the cell. This inward constriction is called a cleavage furrow. When the membranes meet in the middle they are now two distinct daughter cells. The whole process of cytoplasmic division is called cytokinesis.

The rate of cell division varies among the various kinds of cells. Skin cells divide rapidly so that the outer layer of skin is replenished about once a month. Nerve cells, on the other hand, do not divide once we become adults.

Protein Synthesis

The sequence of base pairs in DNA determines the sequence of amino acids in protein. The process of constructing a protein occurs in two basic steps: transcription and translation. (pp98 – 103) A sequence of base pairs in DNA that codes for a particular polypeptide is called a gene.

Transcription occurs in the nucleus. The two strands of DNA separate and one of the strands, the template strand, will form a complimentary strand of RNA with the help of the enzyme RNA polymerase. A specific sequence of bases is recognized by the enzyme as the starting point.



The newly transcribed piece of messenger RNA (mRNA) will be edited before leaving the nucleus, that is, certain unnecessary parts will be removed. The mRNA then moves out of the nucleus and attaches to a ribosome such as one on the rough ER. Now begins the process of translation. Each triplet of bases on the mRNA is called a codon. In this example, the first codon (AUG) is the start codon and initiates the process of translation but does not code for an amino acid. The second codon, UAA, will code for an amino acid but to translate we must bring in another player – transfer RNA (tRNA). Each tRNA has a triplet of bases on one end (called the anticodon) and one of the 20 amino acids attached to the other end. The kind of amino acid will depend on the anticodon. Only a tRNA with the anticodon of AUG will bind with the codon UAC. There is space on the ribosome for two codons so the next codon, UGC will bind with a tRNA with the anticodon ACG.

The first tRNA (AUG) will have the amino acid Tyr attached to it and the second tRNA (ACG) will have the amino acid Cys attached to it. While the two tRNA's are positioned next to each other on the ribosome, dehydration synthesis occurs and a peptide bond forms between the two amino acids. Once the peptide bond forms, the tRNA (AUG) will leave the ribosome, the next tRNA (ACG) moves into the first position and the next tRNA (CAA) moves into the second position. It codes for the amino acid Val. While these two tRNA's are together, the Ile-Thr will form a peptide bond with Val. Again, when the bond is formed the tRNA in the first position moves out, the tRNA in the second position moves to the first leaving the second position open for yet another tRNA with its amino acid.

The mRNA with the codons AUG-UAC-UGC-GUU-UCC-AUA will translate into the amino acid sequence Start-Tyr-Cys-Val-Ser-Ile-etc. A polypeptide of hundreds of amino acids long may be formed. The chain continues until one of the Stop codons is encountered and the process of translation is complete. Remember that the polypeptide must then be folded into its particular shape before it becomes a functioning protein.

Notice (on p101) that 2 or 3 or 4 codons may code for the same amino acid. GGU, GGC, GGA, and GGG all code for the amino acid Gly. There are 64 (4^3) possible codons but only 20 amino acids so there is some redundancy in the system.

Suppose a mistake were made copying the last three bases in the DNA, TAT, and suppose TGT was there instead. TGT in DNA would cause the codon ACA in the mRNA. ACA codes for a different amino acid than does AUA and that one amino acid difference may cause a very different configuration in the resulting protein. The difference between normal β hemoglobin (a protein found in blood) and sickle-cell β hemoglobin is only one amino acid.

Cancer

Cancer can be thought of as a disease of cell division. It is unrestricted mitosis. A mass caused by an abnormal proliferation of cells is called a neoplasm or tumor. The neoplasm may be benign, in which remain compacted, grow slowly and are often encapsulated. These are rarely lethal. Cancers are malignant neoplasms and grow without restriction and are often lethal if untreated. Malignant cells may break away from the main neoplasm and travel to other parts of the body and establish secondary cancer masses, a process called metastasis.

What makes a normal cell become cancerous is under genetic control. Proto-oncogenes are segments of DNA that code for protein that controls the initiation of cell division. These are normal, necessary genes as most cells need to divide. However, if these genes mutate (a mistake happens in copying the DNA) they may cause unrestricted cell division. This gene is now called an oncogene. We don't know what causes most mutations but we do know that certain physical factors (e.g. radiation), chemical factors (e.g. some chlorinated hydrocarbons) and biological factors (e.g. oncogenic viruses) may cause these mutations converting proto-oncogenes to oncogenes. These factors are called carcinogens.

There are also genes that switch off cell division. These are called cancer suppressor genes and half of all cancers involve the loss or malfunction of just two cancer suppressor genes – *p53* and *p16*. Usually a number of mutations must occur before a cell becomes cancerous.