

Teacher Background

Mitosis

Note: The Teacher Background Section is meant to provide information for the teacher about the topic and is tied very closely to the PowerPoint slide show. For greater understanding, the teacher may want to play the slide show as he/she reads the background section. For the students, the slide show can be used in its entirety or can be edited as necessary for a given class.

Rudolf Virchow, a biologist and physician, (1821 – 1902) in the mid-1800s was the first to recognize leukemia (the rapid multiplication of abnormal white blood cells). He believed that diseased tissue was caused by a breakdown within the cell and not from an invasion of foreign organisms, which was also proven correct by Louis Pasteur (1822 – 1895) in the late 1800s. Virchow's understanding that cancer cells start out normal and then become abnormal is supported by years of research and continues to direct and inform the work of scientists today.(1, 2) So if cancer is the study of abnormal cell division to form tumors, let's first look at normal cell division.

What Are the Two Types of Normal Cell Division?

There are two types of normal cell division – mitosis and meiosis. Both types of cell division occur in eukaryotic organisms. Mitosis begins in the fertilized egg (or zygote) stage and continues throughout the life of the organism in one way or another. Each diploid (2n) daughter cell is genetically identical to the diploid (2n) parent cell. Meiosis occurs in the ovaries of the female and testes of the male and results in the formation of egg and sperm cells, respectively. Each diploid (2n) parent cell produces haploid (n) daughter cells. Meiosis will be discussed more fully in Chapter 5 of the Oncofertility Curriculum.

What Is Mitosis?

The term mitosis was coined by Walther Flemming in 1882 when he discovered that the chromosomes during cell division split longitudinally to distribute themselves equally between two daughter cells. (3) The end result of mitosis is growth of the eukaryotic organism and replacement of some eukaryotic cells. After fertilization, growth occurs by cell division through mitosis into the 2-cell stage, then the 4-cell stage, 8-cell stage, 16-cell stage, and so on. Each new cell formed is genetically identical to the parent cell. In addition, throughout the organism's life, some cells will be replaced through mitosis as the cells are sloughed and regenerated by basal or stem cells, such as in the skin, hair follicles, corneal cells, the lining of the alimentary canal, and the bone marrow which produces red and white blood cells. Again, each of the new cells is genetically identical to the parent cell. When minor damage occurs to these cells, the basal cells are able to replace the damaged cells which will be eventually sloughed. If basal cells are more extensively damaged, the underlying connective tissue will go through mitosis to fill in the gap by forming scar tissue which is not able to replace future damaged cells like basal cells did.



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Some cells go through mitosis as the organism grows but will eventually reach a stage where they no longer go through mitosis. This occurs in cells making up the various organs (heart, spleen, pancreas, etc.) and tissues of the central nervous system. Some select cells that are no longer able to go through mitosis can begin to go through mitosis again if some of the cells of the organ are removed, such as in the liver which can regenerate if small portions of the liver tissue are removed.

Why Do Cells Undergo Mitosis?

Mitosis is exact nuclear division. The DNA in the parent cell is copied exactly and then the cell nucleus divides exactly so each of the two daughter cells has the same kind and number of genetic base pairs arranged in chromosomes as the parent cell. Mitosis is necessary because when cells reach a surface area to volume ratio that is too small relative to the rate of diffusion of nutrients and water into the cell, the nutritional demands of the cell cannot be met. In order to address this, the cell undergoes mitosis to form two identical, but smaller cells, which increases the surface area to volume ratio, and thus the rate of diffusion can meet the nutritional demands of the entire cell.

- As the cell size increases, the surface area (length x width x number of sides) divided by the volume (length³) ratio decreases. Example: Imagine a cubic agar cell side length = 2 cm; SA/Vol = $2\text{ cm} \times 2\text{ cm} \times 6\text{ sides} / (2\text{ cm})^3 = 24\text{ cm}^2 \times \text{sides} / 8\text{ cm}^3 = 3\text{ sides/cm}$.
- When the cell divides to form two smaller cells, each cell has a larger surface area (SA) to volume (Vol) ratio. Example: Imagine a cubic agar cell side = 1cm; SA/Vol = $1\text{ cm} \times 1\text{ cm} \times 6\text{ sides} / (1\text{ cm})^3 = 6\text{ cm}^2 \times \text{sides} / 1\text{ cm}^3 = 6\text{ sides/cm}$.
- The rate of diffusion of water and most water-soluble nutrients, measured in distance diffused per time, is a fixed number at any given temperature. At room temperature, the rate of diffusion of water through agar = 0.5 cm/10 minutes.
- Given this rate of diffusion, diffusion of water and nutrients through the smaller cell would reach the center of the cell in 10 minutes while it would not reach the center of the larger cell in the same amount of time. The smaller cell could thrive, while the larger cell would experience transport issues that would result in reduced ability to function.

What Happens Prior to Mitosis?

Prior to mitosis, the two newly formed and smaller daughter cells go through interphase which consists of several stages in which the cell is growing in size, replicating the DNA, and replicating organelles in preparation for mitosis. These stages of interphase are called G₁ (first gap), S (synthesis), and G₂ (second gap) phases, respectively. In G₁ the cells grow in size. Some cells go from G₁ to G₀ and do not divide further, such as cells in the central nervous system. If a cell is destined to divide, the cell will go from G₁ to S phase in which the chromosomes replicate exactly and the resulting sister chromatids are held



together by a centromere. The chromatin material is not usually visible at this point since the chromosome must be uncondensed or uncoiled to replicate. The cell then proceeds to G₂ phase in which the cell continues to grow by replicating the cytoskeleton, including microtubules, centrosome and spindles, and organelles in preparation for mitosis to occur. Single and double membrane-bound organelles must be inherited from parent cells since they cannot be formed *de novo* (4). After G₂ has occurred, the cell begins the M stage or mitotic division.

How Does Mitosis Proceed?

After the G₂ phase has been completed, the cell begins the M stage (mitosis), which is the orderly process of nuclear division. There are 4 phases of mitosis – prophase, metaphase, anaphase, and telophase. In prophase, the nuclear membrane and nucleolus appear to disappear, the chromatid pairs become more pronounced as they condense in preparation for division, each of the two centrosomes containing a pair of centrioles migrate to opposite poles, and spindle fibers made of microtubules begin to appear and attach to each of the sister chromatid pairs at the kinetochore found on the side of the centromere of each chromatid. In metaphase, the chromatids line up along the equator by being pulled at the centromere by the spindle fibers. In anaphase, the sister chromatids are pulled apart by the spindle fibers toward opposite poles becoming distinct sister chromosomes. In telophase, at the opposite poles, the sister chromosomes begin to form into a new distinct nucleus which is genetically identical to the nucleus of the parent cell.

What Is Cytokinesis?

Toward the end of mitosis, the cytoplasm will begin to furrow or pinch in the middle from all sides in a process called cytokinesis. While the genetic material is exactly replicated and divided, the organelles, cytoplasm including the cytoskeleton, and cell membrane are roughly divided evenly between the two new daughter cells during cytokinesis. Cytokinesis is much more evident in animal cells than in plant cells which contain a rigid cell wall.

The larger cell has divided into two smaller cells. This gives the two smaller cells a larger surface area to volume ratio and, therefore, the rate of diffusion can meet the nutritional demands of each new cell. Once mitosis has occurred following G₂, the two smaller daughter cells begin interphase at G₁ and start to grow.

Bibliography

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4. http://jmicro.oxfordjournals.org/content/60/suppl_1/S117.full

