L.13 Cell cycle (Mitosis)

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A series of events describes the sequence of activities as a cell prepares for division and then divides, occurs in all tissues with cell turnover.

Why would a cell divide?

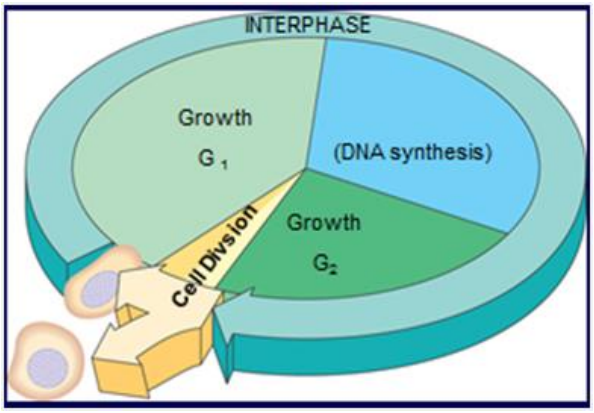
As cells absorb nutrients and get larger, the volume of the cell increases faster than the surface area. This means that a cell can no longer absorb nutrients and get rid of wastes fast enough to support its demands volume. So, what's a cell to do? Divide

Besides growth a cell would also divide for repair or replacement in multi-cellular eukaryotes and for asexual reproduction in single-celled eukaryotes

How long does the cell cycle last?

Cell cycle rate varies in different tissues at different times from minutes in embryonic cells to months or even years in some cells of adults. A cell lining the small intestine's inner wall may divide throughout life, a cell in the brain may never divide, a cell in the deepest skin layer of 90-year old may divide more if the person lives long enough. Frequent mitosis enables the embryo and fetus to grow rapidly. By birth, the mitotic rate slows. Later, mitosis must maintain the numbers and positions of specialized cells in tissues and organs.

The cell cycle consists of two phases: Interphase and mitosis.



Cell cycle

Interphase

Is often included in discussions of mitosis, but interphase is technically not part of mitosis. There are 3 phases of interphase: G1 (gap 1), S phase and G2 (gap 2).

1-Gap 1 (presynthesis):

The daughter cells formed during mitosis enter the G1 phase. In this phase, the cells synthesize RNA and proteins, including proteins that control the cell cycle such as protein

(kinases) that functions to initiate mitosis, and the cell volume, previously reduced to one –half by mitosis, is restored to its previous size. Additionally, the nucleoli reestablished during G1. Many cytoplasmic components, including organelles and membranes, are duplicate.

2-S phase (Synthesis):

Is characterized by synthesis and replication of DNA, all of the nucleo-proteins including the histones are imported and incorporates into DNA molecule forming the chromatin material, the cell now contains twice the normal complement of its DNA. The amount of DNA present in autosomal and germ cell is a diploid number (2n) and haploid number (1n) respectively before (S) phase, become 4n,2n respectively in preparation for cell division. During this phase, centrosome begins to duplicate.

3-Gap 2 (Post DNA duplication):

Is the shortest phase of the cell cycle. Many of the molecules and cell structures required for cell division are produced for example synthesis of certain proteins essential to cell division for example tubulin (a subunit of microtubules is produced in large quantities and assembled into microtubules, which will form the spindle fibers during mitosis). Also, in this phase occur the production and accumulation of energy to be utilized for mitosis.

In addition to the three phases of interphase , a cell can exit the cell cycle at G1 to enter a quiescent phase called G0. A cell in G0 maintains its specialized characteristics but does not replicate its DNA or divided either due to age or due to accumulated DNA damage, are senescence. From G0 , a cell may also proceeds to mitosis and divided, or die. Most of the cells in an animal's body are in G0 phase. Some, such as muscle and nerve cells, remaining there permanently; others, such as liver cells, can resume G1 phase in response to factors released during injury.

Mitosis (M):

Is nuclear division plus cytokinesis, to produces two identical daughter cells during the following steps :

1-Prophase

The chromatin strands condense or coil tightly to form rod-shaped or hairpin-shaped bodies called chromosomes. When first seen the chromosomes appear as long, thin and intertwined threads, this marks the beginning of prophase .

As prophase proceeds the chromosomes continue to coil and become shorter and thicker, in human cells,46 such structures can be seen; each chromosome consists of two longitudinal strands known as chromatids. The chromatids are separate structures , held together at the

centromere. Each sister chromatid contains one of the DNA molecules replicated during interphase .

The centrosome divides into 2 regions each half containing a pair of centrioles moves to each side, or pole of the cell. Microtubules assemble from tubulin building blocks in the cytoplasm to form the spindles near the centrioles and project in all directions, some of them end blindly and are called aster , others known as spindle fibers project toward an invisible line called equator. At the end of prophase, the nucleoli are no longer visible.

2-Prometaphase:

Is the transition period between prophase and metaphase. At the beginning, the nuclear lamins are phosphorylated, resulting in the breakdown and disappearance of the nuclear envelope (the nuclear envelope and its components reabsorbed in ER). Proteins attach to the centromeres creating the kinetochores .

In this phase the chromosomes are arranged randomly throughout the cytoplasm and microtubules that become attached to the electron dense protein complexes called kinetochores which are located at a constricted region of each chromatid called centromere, which is known as mitotic spindle microtubules, these spindles assist in migration of the chromosomes, so that they become oriented into an alignment with mitotic spindle.

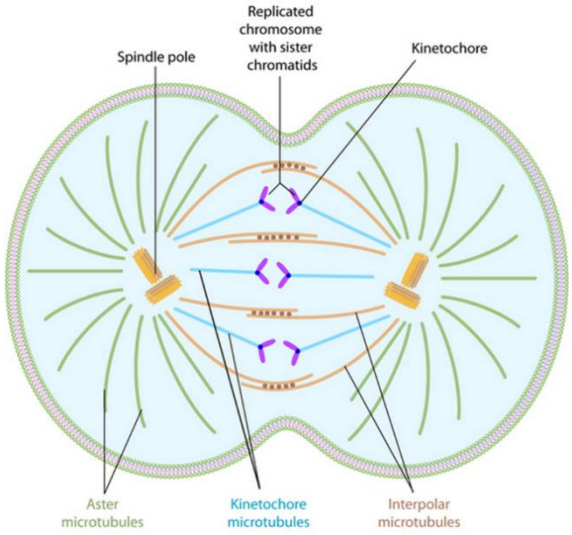
3- Metaphase:

The two chromatids are still attached to a single centromere, giving chromosomes an X – shaped appearance. The chromosomes become aligned along the equatorial plane of the cell by the assist of mitotic spindle microtubules. At this stage, there are 46 centromeres, each attached to two sister chromatids.

4- Anaphase:

The sister chromatids separate from each other and migrate toward the opposite poles of the cell following the direction of spindle microtubules and form V –shape or J -shape. The separation of chromatids signals the beginning of anaphase, and by the time anaphase has ended; the chromosomes have reached to poles of the cell. Sometimes, cytokinesis began during this phase .

The kinetochore microtubules shorten and draw the chromosomes toward the spindle poles. Then, the astral microtubules that are anchored to the cell membrane pull the poles further apart and the microtubules slide past each other, exerting additional pull on the chromosomes by assist of two proteins make up the microtubule motors that allow motion: kinesin and dynein.



5-Telophase

The migration of each set of chromosomes is complete, the nuclear lamins are dephosphorylated and the nuclear envelope is reformed around each set of sister chromatids which can now be called chromosomes since each has its own centromere. The chromosomes soon begin to uncoil and become less distinct chromatin threads and organized into heterochromatin and euchromatin of interphase cell.

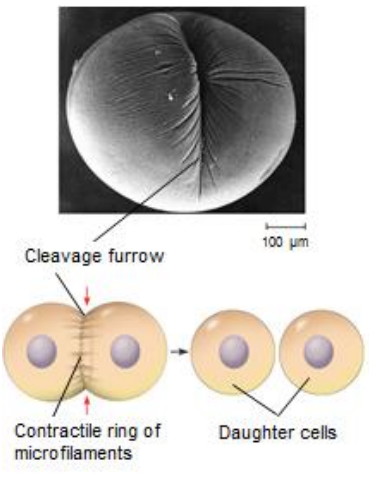
The nucleoli of two daughter cells assume the appearance of interphase nuclei from nucleolus organizing regions. During the later portion of telophase, the spindle apparatus is disassembled as the microtubules are broken down into tubulin monomers that can be used to construct the cytoskeletons of the daughter cells. Cytokinesis will start at early telophase and proceeds until to form 2 daughter cells **.**

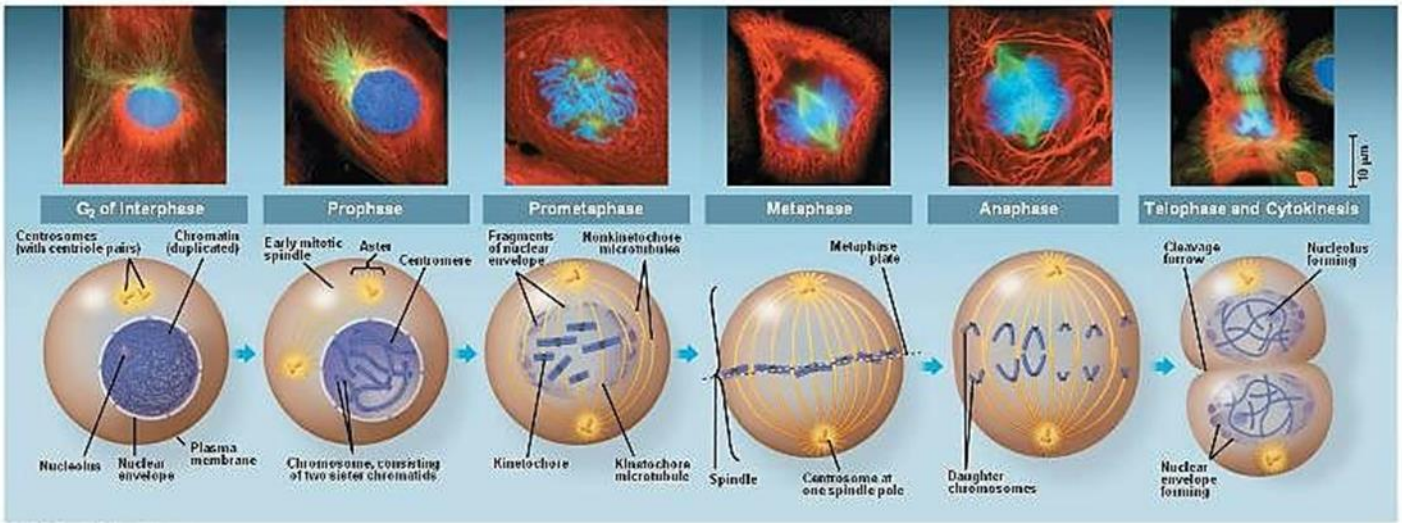
Cytokinesis:

Cytokinesis begins in anaphase, continues through telophase, and ends in the following interphase. The first mark of cytokinesis is the formation of cleavage furrow or invagination of cell membranes which forms mid-way between the centrioles which is gradually deepening until the daughter cells are completely separated.

Cleavage furrow, is a result of a contractile ring, this ring composed of primarily of actin and myosin filaments accumulate in a belt-like shape beneath the plasma membrane, pulls the plasma membrane inward dividing the cell into 2 halves. Cytokinesis is complete when the 2 halves separate to form 2 new cells.

Cytokinesis





Regulation of Cell cycle in eukaryotes:

The cell cycle in eukaryotes is regulated at certain checkpoints as well as external and internal controls.

Checkpoints:

a critical control points in the cell cycle where stop and go-ahead signals can regulate the cell cycle. The cell cycle is controlled by three principal checkpoints:

1- Cell growth checkpoint (G1)

1- Occurs toward the end of growth phase1(G1)
2- Checks whether the cell is big enough and has made the proper proteins for the synthesis phase.
3- If not, the cell goes through a resting period(G0) until is ready to divided

2- DNA synthesis checkpoint(S)

1- Which occurs during the synthesis phase(S)
2- Checks whether DNA has been replicated correctly.

If so, the cell continues on to mitosis (M)

3-M (Mitosis) checkpoint

1- Occurs during the mitosis at metaphase
2- Checks, whether all the chromosomes are attached and under bipolar tension
3- Checks whether mitosis is complete

4- If so, the cell divides, and the cycle repeats

Internal and external factors regulate cell division:

External factors: factors or signals that come from the outside of the cell that help to control the division process. For example

1- **Cell to Cell contac**t: Once a cell touches other cells it stops dividing.

2- **Growth Factors:** For example: Platelets, Erythropoietin and Hormones

Internal Factors: such as **Enzymes:** ex. **Kinases and Cyclins**

Failures of cell cycle regulation can lead to uncontrolled cell division of cells

that have lost ability to regulate cell cycle and reproduce more rapidly than normal cells. Masses formed called ‘tumors’