University of Al Maarif
College of Health and Medical Technology
Department of Medical Laboratories Techniques

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Human Genetics/ Third Stage
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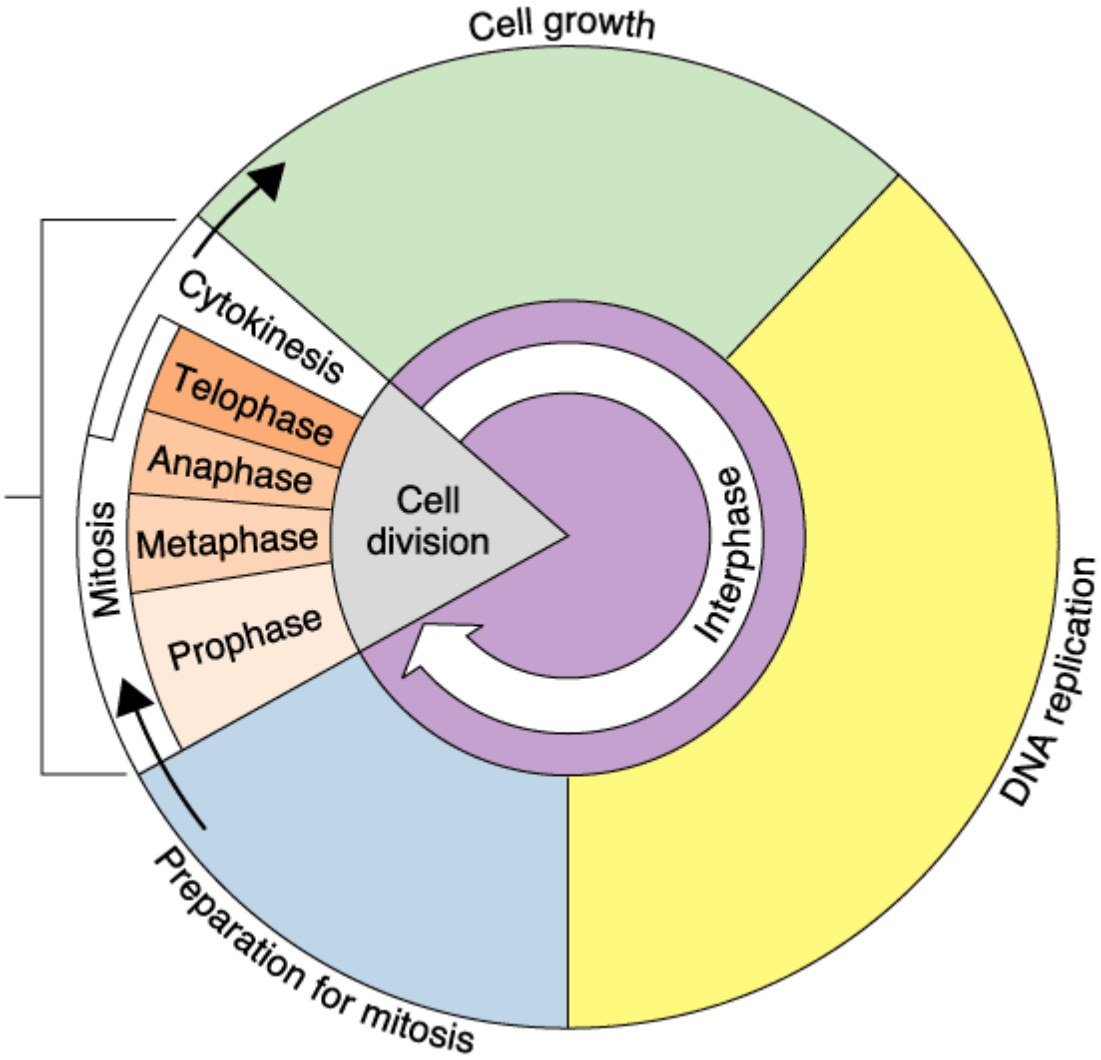
Lecture 2 - : Cell cycle and cell division

The cell cycle is an organized series of events that take place during a eukaryotic cell's existence, starting with the division of its parent cell and ending with the division of the cell itself



Chromosome sets are distributed identically throughout cell division.

A cell's genome is the collection of DNA that makes up its genetic material. Eukaryotic genomes often consist of a number of DNA molecules, but the prokaryotic genome is frequently one lengthy DNA molecule. To ensure that each daughter cell has a complete genome, all of this DNA must

first be copied, and then the two copies must be split apart before the cell may divide

.

M phase
G1 phase
S phase

The fact that the DNA molecules are condensed into chromosomes makes it possible for such large amounts of DNA to be replicated and distributed. Chromatin, a DNA-protein complex, is arranged into a long, thin fiber. The chromatin condenses after a cell replicates its DNA in order to prepare for division, revealing the chromosomes under a light microscope.

Each cell nucleus of a eukaryotic species contains a specific number of chromosomes. For instance, each human somatic cell (all body cells aside from reproductive cells) has 46 chromosomes in its nucleus. In comparison to somatic cells, which in humans have 23 chromosomes, reproductive cells, or gametes, such as sperm and egg cells, contain half as many chromosomes. In somatic cells, the chromosomal makeup is diploid (2n). In sex cells, the chromosomal set is haploid (n).

Every chromosome in a eukaryotic cell that is about to divide is duplicated. Two sister chromatids, which constrict at their centromeres, make up a duplicated chromosome. The sibling chromatids share the same DNA molecules. During cell division (mitosis), the chromatids split off and become the chromosome of the new daughter cells.

Eukaryotic cell division consists of:

1. mitosis (division of the nucleus).
2. Cytokinesis (division of the cytoplasm).

The two cell division stages are frequently mixed together. Only the division of the chromosomes and organelles into daughter cells is the subject of mitosis. One stage of the cell cycle is mitosis. A significantly longer interphase that frequently makes up 90% of the cell cycle alternates with mitotic cell division. In order to prepare for cell division, the cell expands and duplicates its chromosomes during interphase.

*The time between cell divisions is known as **interphase**.
*The M (mitosis) phase, during which the cell doubles in size and DNA content, lasts a great deal longer.
• Interphase is divided into three distinct phases (**G1, S**, and **G2**).

Gap one phase (G1) might last for a few hours or several days. Following mitosis, this phase is when cells expand and proteins are made, bringing the

daughter cells' size and volume back to normal.

S phase (synthetic phase) lasts 8 to 12 hours in most cells. The chromosomes are duplicated as a result of the replication of DNA and the synthesis of proteins.

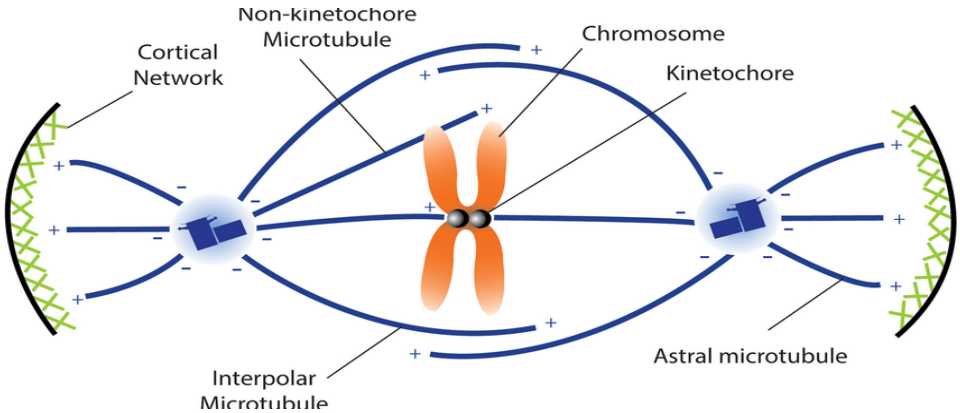
Animal cells have a centrosome, which is made up of two centrioles, with the exception of nematodes, a type of worms. Centrioles are absent in most eukaryotic species, including plants. Naturally, prokaryotes lack spindles and centrioles; during binary fission, the cell membrane fills in for these structures by pulling the then-replicated chromosomes apart. Also duplicated are the centrioles.

Gap two phase (G2) lasts for 2-4 hours. The centrioles mature, the energy needed to complete mitosis is saved, and the RNA and proteins required for mitosis, including tubulin protein for the microtubules of the spindle apparatus, are created as the cell gets ready to divide.

Mitosis lasts1-3 hours. By duplicating and dividing the initial chromosomes, mitosis is the process of creating daughter cells that are (typically) genetically identical to the parent cell.

A spindle apparatus's structure and key characteristics

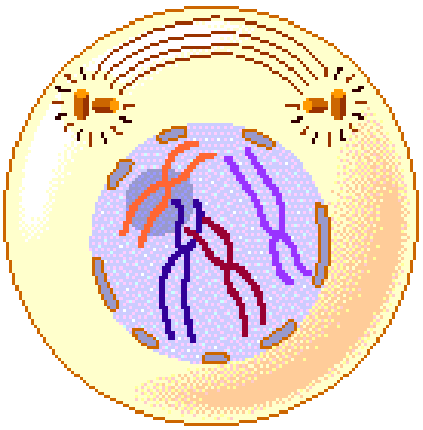
There are several interesting aspects of the condensed replicated chromosomes. The kinetochore, a complex protein structure where microtubules of the spindle apparatus attach, is on the outer borders of the centromere, which is the region where both sister chromatids are in contact with one another. Microtubules come in two varieties: **kinetochore microtubules**, which connect with the kinetochores of chromosomes, and **non-kinetochore microtubules (polar microtubules)**, which come from opposite poles and do not attach to the kinetochores but do overlap at the place where the two poles meet. The 9+2 pattern is seen in the microtubules. In addition to having centrioles, cells with centrioles also have a set of smaller microtubules called **asters** that connect the centrioles to the cell membrane. **The aster** is assumed to assist anchor the centrosome and act as a brace for the spindle fibers' proper operation. During anaphase, polar microtubules cause the entire cell to elongate



It is known that kinetochores have a molecular motor despite the fact that their structure and function are not completely understood. The motor starts working when a microtubule binds to the kinetochore and uses ATP energy to "crawl" along the tube in the direction of the starting centrosome. The tugging power required to later separate the two chromatids of the chromosome is supplied by the kinetochore.

Prophase, **Prometaphase**, **Metaphase**, **Anaphase**, and **Telophase** are the **five** main stages of **mitosis**. Sometimes it's hard to tell them apart. The procedure is dynamic rather than static.

prophase is the start of the actual mitosis. Remember that chromatin and DNA duplicate during interphase. Chromatin condenses, and centrioles, if present, divide and move.

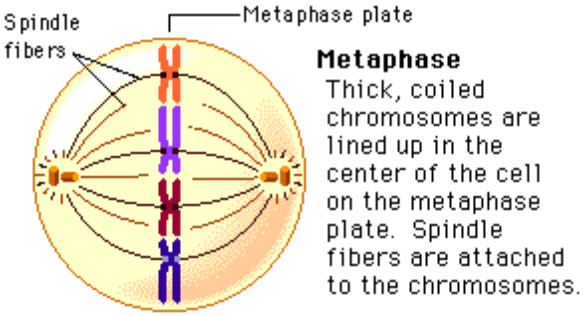


Prophase
The chromosomes appear condensed, and the nuclear envelope is not apparent.

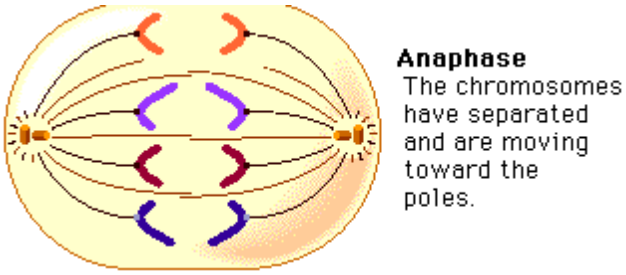
prometaphase is the mitotic phase that comes after prophase and before metaphase. The nuclear envelope disintegrates and vanishes. The

chromosomes, which are now tightly packed, are reached by microtubules that emerge from the centrosomes at the poles (ends) of the spindle. Chromosomes are stimulated into action when some spindle microtubles join the kinetochores. Microtubules coming from the opposing polarity make touch with other spindle microtubules. The chromosomes are propelled toward the center of the cell by forces generated by protein "motors" linked to spindle microtubules.

Metaphase. The chromosomes migrate to the spindle's equator, where the spindles connect with the kinetochore fibers. At this point, the chromosomes are made up of chromatids linked together by centromeres. Following the separation of the centromeres, chromosomes are pulled to the opposing poles of the spindle, where they are referred to as chromosomes.



Anaphase begins with the separation of the centromeres, and the pulling of chromosomes (we call them chromosomes after the centromeres are separated) to opposite poles of the spindle



Telophase is when the chromosomes uncoil into chromatin, the nuclear envelope reforms, the nucleolus, which had vanished during prophase, reforms, and the chromosomes reach the poles of their respective spindles. Two smaller cells with the exact same genetic makeup have appeared where there was once just one. The processes of development may then transform these cells into various adult forms.

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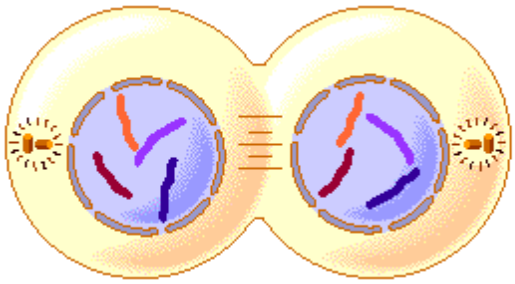
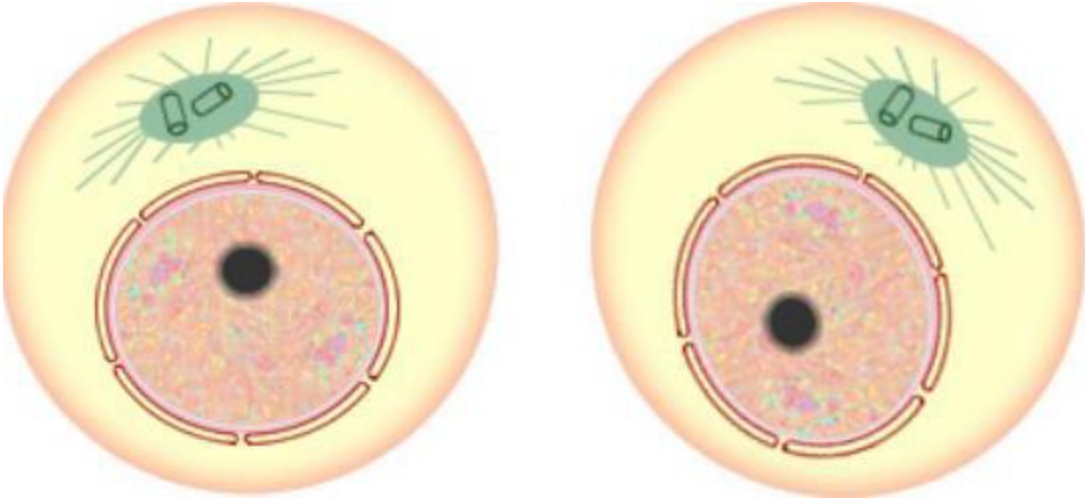


Telophase
The chromosomes are at the poles, and are becoming more difuse. The nuclear envelope is reforming. The cytoplasm may be dividing.

A typical mitotic figure is symmetric and well formed. Cancer cells frequently have abnormal quantities of DNA and thus form abnormal or atypical mitotic figures.

Cytokinesis is the process of splitting the daughter cells apart. Whereas mitosis is the division of the nucleus, cytokinesis is the splitting of the cytoplasm and allocation of the Golgi, plastids and cytoplasm into each new cell.



The cell cycle varies in length in different types of cells, but is repeated each time a cell divides. Some cells divide rapidly (beans, for example, take 19 hours for the complete cycle; red blood cells must divide at a rate of 2.5 million per second). The cells that divide rapidly are also embryonic cells; marrow; cells of mucous tunics; skin cells (basal layer of epithelium); lymphoid tissue; cells of malignant neoplasms. Others, such as nerve cells, lose their capability to divide once they reach maturity. Some cells, such as liver cells (hepatocytes), retain but do not normally utilize their capacity for division. Liver cells will divide if part of the liver is removed. The division continues until the liver reaches its former size.

Distinctive cases of cell division:

1. It is temporarily suspended in non-dividing resting cells (e.g., peripheral lymphocytes), which are in the G0 state. Such cells may reenter the cycle and begin to divide again.

2. It is permanently interrupted in differentiated cells that do not divide (e.g., cardiac muscle cells and neurons).

Regulation of the cell cycle

Regulation of the cell cycle is accomplished in several ways:

I. A molecular control system drives the cell cycle.

II. Cyclical changes in regulatory proteins work as a mitotic clock.

As they divide, cells must proceed through the various stages of the cell cycle, including the G1, G2, and M phases. All phases are controlled by checkpoints – critical control points where stop and go- ahead signals can regulate the cycle. Triggers at each checkpoint assess the cell's readiness to proceed to the next stage. Regulation also ensures that each cell obtains the proper number and type of chromosomes and organelles.

Without the controlled timing of cell division, an organism would be a shapeless blob of uncoordinated cells. A cell uses 3 main checkpoints to both assess the internal state of the cell and integrate external signals.

1. The **G1/S** checkpoint is the primary point at which the cell decides to divide.

2. the **G2/M** checkpoint represents a commitment to mitosis.

3. the spindle checkpoint ensures that all chromosomes are attached to the spindle in preparation for anaphase.

Others checkpoints

4.G1 checkpoint The end of G1 phase

If conditions are not suitable for replication, the cell will not proceed to S phase but will instead enter a resting phase, G0.

5.G2 checkpoint The end of G2 phase

If conditions are not suitable, transition to the M phase will be delayed.

If DNA is damaged, cell division will be delayed to allow time for DNA repair.

6.M checkpoint

Between metaphase and anaphase stages of mitosis

If the chromosomes are aligned properly and ready for division, the cell will proceed from metaphase to anaphase, during which it will divide.

If the chromosomes are not aligned properly, the anaphase stage will be delayed

*Defects in the checkpoints that normally maintain the fidelity of the cell

cycle can lead to chromosomal instability and cancer.

Proteins that regulate the cell cycle

Cell cycle is paced by rhythmic fluctuations in the abundance and/or activity of control protein molecules.

Two main families of proteins involved in regulation of cell cycle are:

1. Cyclins

2. Cyclin-dependent protein kinases (Cdk's)

Cells also receive protein signals (growth factors) that affect cell division.

1. Cyclins are named such because these proteins undergo a constant cycle of synthesis and degradation during cell division. When cyclins are synthesized, they act as an activating protein and bind to cyclin dependent protein kinases forming a cyclin-Cdk complex. Eventually, the cyclin degrades, deactivating the Cdk, thus signaling exit from a particular phase. There are two classes of cyclins: mitotic cyclins and G1 cyclins.

2. Cyclin-dependent kinases (Cdks) are proteins (enzymes) which phosphorylate (add a phosphate, - PO4) other proteins to activate or inactivate them.

Now the group of protein kinases includes 11 proteins (Cdk1-Cdk11).

- Cdks levels are usually constant.
- Cdks are inactive in the absence of cyclin.
- Cdks are activated by binding to cyclins and regulated by phosphorylation and dephosphorylation.
- Cdks will be regulated the G1, G2 and M checkpoints.
- An example of cyclin-Cdk complexes is maturation promoting factor (MPF, also called mitosis- promoting factor or M-Phase promoting factor) which is composed of a regulatory subunit – cyclin B and a catalytic subunit – cyclin-dependent kinase (CDK1, also known as Cdc2 or p34 kinase) that stimulates the mitotic and meiotic cell cycles. MPF promotes the entrance into mitosis from the G2 phase by phosphorylating multiple proteins needed during mitosis. MPF is activated at the end of G2 by a phosphatase enzyme, which removes an inhibitory phosphate group added earlier.