Cell Biology: The Cell Cycle and Cell Division

AI-Generated Study Guide

(Based on lectures delivered by Dr. Ty C.M. Hoffman)

I. Understanding the Cell Cycle

A. Definition and Importance

- The cell cycle encompasses all events from the creation of a cell until it divides into two new cells.
- **Key purposes of cell division:Reproduction:** For unicellular organisms, cell division is the primary mode of reproduction. The parent cell ceases to exist, forming two new offspring cells.
- **Growth and Development:Growth:** In multicellular organisms, growth occurs by increasing the number of cells through cell division, not by individual cells growing to an enormous size. Even unicellular organisms grow by increasing in size between divisions.
- **Development:** Cells differentiate and specialize into various types (e.g., nerve, muscle cells) through controlled cell division and subsequent specialization from an initial single cell (zygote).
- **Tissue Renewal:** Replacing damaged, dead, or intentionally eliminated cells in multicellular organisms (e.g., red blood cells, skin cells). This process ensures the body maintains its structure and function.
- **Cell Theory Connection:** "All cells come from pre-existing cells" is a fundamental tenet of cell theory, directly supported by the process of cell division.

B. Genetic Material Organization

- **Chromatin:** The complex mixture of DNA and proteins (primarily histones) found within the nucleus of eukaryotic cells. It appears as a diffuse tangle during most of the cell cycle.
- **Chromosomes:** Condensed, discrete structures formed from chromatin, visible only when a cell is preparing for or undergoing division. A replicated chromosome typically has an "X" shape.

- **Sister Chromatids:** Two identical copies of a replicated chromosome, joined at the centromere. They are formed during DNA replication and separate during cell division.
- **Centromere:** The constricted region on a replicated chromosome where sister chromatids are joined. It also serves as the attachment point for kinetochore microtubules.
- **Kinetochore:** A complex of proteins located at the centromere of each sister chromatid, serving as the attachment site for kinetochore microtubules.

C. DNA's Role in the Cell Cycle

- **Two Major Functions of DNA:Replication:** The process of making an exact copy of the entire DNA genome. This is crucial before cell division to ensure each daughter cell receives a full and identical set of genetic material. Replication occurs during the S phase.
- **Transcription:** The process of synthesizing RNA from a DNA template. This is how genes are "read" to produce proteins, essential for the cell's normal functions throughout its lifetime (primarily in G1 and G2). DNA must be in a loose, unwound state (chromatin) for transcription to occur.

II. Phases of the Eukaryotic Cell Cycle

A. Major Divisions

- **Interphase:** The longest phase of the cell cycle, during which the cell grows, performs its normal functions, and prepares for division. It consists of three sub-phases:
- **G1 Phase ("First Gap"):** The primary growth phase where the cell performs its specific functions. DNA is in a loose chromatin state and actively transcribed. This is often the longest phase for a cell.
- **S Phase ("Synthesis"):** DNA replication occurs, resulting in duplicated chromosomes (each consisting of two sister chromatids). Centrosomes also replicate during this phase. The cell becomes committed to division after this phase.
- **G2 Phase ("Second Gap"):** The cell continues to grow and prepares for mitosis, synthesizing proteins and organelles necessary for cell division. DNA is still largely unwound, though condensation begins. Genes for cell division proteins are transcribed.
- **M Phase ("Mitotic Phase"):** The shortest phase, involving nuclear division (mitosis) and cytoplasmic division (cytokinesis).
- **Mitosis:** Division of the nucleus and its contents (chromosomes). Occurs only in eukaryotic cells.
- **Cytokinesis:** Division of the cytoplasm, leading to the formation of two separate daughter cells. It often overlaps with the telophase of mitosis.

B. Stages of Mitosis (PMAT)

- **Prophase:**Chromatin condenses into visible chromosomes (each with two sister chromatids).
- The mitotic spindle (formed from microtubules) begins to form, with centrosomes moving apart.
- Nuclear envelope remains intact.
- **Prometaphase:**The nuclear envelope completely disintegrates, allowing the mitotic spindle to interact with chromosomes.
- Kinetochore microtubules attach to the kinetochores on each replicated chromosome.
- Non-kinetochore (polar) microtubules overlap and push against each other, elongating the cell.
- **Metaphase:**Replicated chromosomes are aligned at the **metaphase plate** (an imaginary equatorial plane equidistant from the two poles of the cell).
- Each replicated chromosome is attached to kinetochore microtubules from opposite poles.
- **Anaphase:**Sister chromatids separate at the centromere, becoming individual **unreplicated chromosomes**.
- These new unreplicated chromosomes are pulled by kinetochore microtubules towards opposite poles of the cell.
- The cell elongates further due to the pushing action of non-kinetochore microtubules.
- **Telophase:**Unreplicated chromosomes arrive at opposite poles of the cell.
- New nuclear envelopes form around each set of chromosomes, creating two new nuclei.
- Chromosomes begin to decondense and return to their chromatin state.
- Mitosis is complete. Cytokinesis typically begins during or immediately after telophase.

C. Cytokinesis (Cytoplasmic Division)

- **Animal Cells:**Occurs by **cleavage furrow** formation.
- A ring of actin microfilaments and motor proteins (like myosin) forms just inside the plasma membrane at the metaphase plate.
- This contractile ring constricts, pinching the cell into two.
- **Plant Cells:**Occurs by **cell plate** formation.
- Vesicles containing cell wall materials (e.g., cellulose) fuse at the metaphase plate, forming a cell plate.
- The cell plate grows outward until it fuses with the existing plasma membrane and cell wall, dividing the cell into two daughter cells, each with its own plasma membrane and a newly formed cell wall.

III. Regulation of the Cell Cycle

A. Checkpoints

- **Checkpoints:** Critical control points in the cell cycle where progression is regulated by specific conditions and molecular signals.

- **G1 Checkpoint (Restriction Point):** The most crucial checkpoint. If a cell passes this point, it is committed to dividing. If conditions are not met, the cell may enter a non-dividing state (G0 phase).
- **G0 Phase:** A non-dividing state where cells can remain indefinitely (e.g., mature nerve cells, muscle cells). They are essentially "stuck" in G1 and do not proceed to S phase.
- Other checkpoints exist (e.g., G2 checkpoint, M checkpoint) to ensure proper DNA replication and chromosome segregation.

B. Internal Molecular Signals

- **Cyclins:** Proteins whose concentrations fluctuate cyclically during the cell cycle. They bind to and activate CDKs.
- **Cyclin-Dependent Kinases (CDKs):** Enzymes that phosphorylate target proteins, thereby activating or inactivating them to promote progression through the cell cycle. CDKs are always present but are only active when bound to cyclins (hence "cyclin-dependent").
- **MPF (Maturation-Promoting Factor/M-Phase Promoting Factor):** A specific cyclin-CDK complex that triggers a cell's passage from the G2 phase into the M phase. Its activity peaks during mitosis and then drops rapidly as cyclins are degraded.

C. External Molecular Signals

- **Growth Factors:** Signaling molecules (often proteins) released by certain cells that stimulate other cells to divide. An example is Platelet-Derived Growth Factor (PDGF), which stimulates the division of fibroblasts.
- **Anchorage Dependence:** The requirement that most animal cells must be attached to a substratum (e.g., extracellular matrix) in order to divide. This provides a mechanical signal for division.
- **Density-Dependent Inhibition (Contact Inhibition):** A phenomenon in which crowded cells stop dividing. When cells come into contact with one another, they send signals that inhibit further cell division, preventing overgrowth in tissues.

IV. Cancer: Uncontrolled Cell Division

- **Cancer:** A disease characterized by uncontrolled cell division. It arises from genetic defects (mutations) in genes that regulate the cell cycle.
- **Loss of Control:** Cancer cells typically lose:
- **Density-dependent inhibition:** They continue to divide even when crowded, forming a multi-layered mass of cells (tumor).
- **Anchorage dependence:** They can grow and divide even when not attached to a surface, allowing them to spread.
- The need for external growth factors (some cancer cells produce their own or have hyperactive signaling pathways).

- **Tumor:** An abnormal mass of cells resulting from uncontrolled cell division.
- **Benign Tumor:** Cells remain at the original site; they can be surgically removed and usually do not cause serious problems (unless they interfere with organ function due to size).
- **Malignant Tumor:** Cells have the ability to invade surrounding tissues and metastasize.
- **Metastasis:** The spread of cancer cells from their original site to distant parts of the body, usually via the blood or lymph system. This makes cancer much more difficult to treat and is often life-threatening.
- **Genetic Basis:** Cancer is fundamentally a genetic disorder, meaning it involves changes in DNA. These changes can be inherited or, more commonly, acquired during a person's lifetime due to environmental factors (e.g., UV radiation, chemicals) or replication errors. The accumulation of these defects over time increases cancer risk, especially with age.

V. Prokaryotic Cell Division: Binary Fission

- **Binary Fission:** The method of asexual reproduction and cell division in prokaryotic cells (bacteria and archaea).
- **Process:**The single, circular prokaryotic chromosome replicates.
- The two identical chromosomes move to opposite ends of the cell.
- The plasma membrane pinches inward, and a new cell wall forms, eventually dividing the cell into two genetically identical daughter cells.
- **Key Differences from Eukaryotic Cell Division:**No nucleus or nuclear envelope to divide.
- Typically one circular chromosome, not multiple linear chromosomes.
- Does not involve mitosis or a mitotic spindle.

Quiz: The Cell Cycle

Instructions: Answer each question in 2-3 sentences.

1. Define the cell cycle.
2. Beyond reproduction, what are two other critical reasons for cell division in multicellular organisms?
3. Explain the difference between chromatin and a chromosome.
4. Why must DNA replication occur *before* a cell undergoes division?
5. What are the three sub-phases of interphase, and what is the primary event that occurs in each?
6. Describe the key event that occurs during anaphase of mitosis.
7. How does cytokinesis differ between animal cells and plant cells?
8. What is the significance of the G1 checkpoint in the cell cycle?
9. Explain the relationship between cyclins and CDKs in regulating the cell cycle.
10. What is metastasis, and why is it a significant concern in cancer?

Quiz Answer Key

1. **Define the cell cycle.** The cell cycle is the entire sequence of events in the life of a cell, from its creation to its division into two new daughter cells. It represents one generation of cells, encompassing periods of growth, DNA replication, and cell division.
2. **Beyond reproduction, what are two other critical reasons for cell division in multicellular organisms?** In multicellular organisms, cell division is crucial for growth and development, allowing an organism to increase in size and for its cells to differentiate into specialized tissues. It is also essential for tissue renewal, replacing old, damaged, or dead cells to maintain the integrity and function of tissues and organs.
3. **Explain the difference between chromatin and a chromosome.** Chromatin is the diffuse, tangled complex of DNA and proteins that makes up the genetic material inside the nucleus during interphase. A chromosome is a highly condensed, discrete structure formed from chromatin during cell division, becoming visible as individual units.
4. **Why must DNA replication occur *before* a cell undergoes division?** DNA replication is essential before cell division to ensure that each new daughter cell receives a complete and identical set of genetic material. Without replication, daughter cells would only receive half the necessary DNA, rendering them non-viable.
5. **What are the three sub-phases of interphase, and what is the primary event that occurs in each?** The three sub-phases of interphase are G1, S, and G2. In G1, the cell grows and performs its normal metabolic functions. In S phase, DNA replication occurs, synthesizing new DNA and duplicating chromosomes. In G2, the cell continues to grow and synthesizes proteins necessary for mitosis.
6. **Describe the key event that occurs during anaphase of mitosis.** During anaphase of mitosis, the sister chromatids of each replicated chromosome finally separate at the centromere. These newly separated chromatids are now considered individual unreplicated chromosomes and are pulled towards opposite poles of the cell by the shortening kinetochore microtubules.
7. **How does cytokinesis differ between animal cells and plant cells?** In animal cells, cytokinesis occurs by the formation of a cleavage furrow, where a contractile ring of actin microfilaments pinches the cell into two. In contrast, plant cells form a cell plate in the middle, which grows outward from fused vesicles containing cell wall materials until it divides the cell.
8. **What is the significance of the G1 checkpoint in the cell cycle?** The G1 checkpoint is highly significant because it is the primary "restriction point" where a cell makes the decision to divide or not. If conditions are favorable and signals are present, the cell proceeds to S phase; otherwise, it may enter a non-dividing G0 state.
9. **Explain the relationship between cyclins and CDKs in regulating the cell cycle.** Cyclins are proteins whose concentrations fluctuate throughout the cell cycle; they are required to bind to and activate CDKs. CDKs (Cyclin-Dependent Kinases) are enzymes that, once activated by cyclins, phosphorylate other proteins to drive the cell through different phases of the cell cycle.
10. **What is metastasis, and why is it a significant concern in cancer?** Metastasis is the process by which cancer cells spread from their primary tumor site to other parts of the

body, forming new tumors. It is a significant concern because once cancer has metastasized, it becomes much more difficult to treat effectively, often leading to life-threatening conditions.

Essay Format Questions

1. Compare and contrast the processes of cell division in prokaryotic cells (binary fission) and eukaryotic cells (mitosis and cytokinesis). Discuss the underlying reasons for these differences in complexity.
2. Describe the interconnected roles of DNA replication and transcription throughout the eukaryotic cell cycle, emphasizing how the state of chromatin organization facilitates or inhibits these processes.
3. Discuss the intricate system of checkpoints and molecular signals (cyclins, CDKs, growth factors) that regulate the eukaryotic cell cycle. Explain the consequences of a cell's failure to adhere to these regulatory mechanisms.
4. Trace the journey of a replicated chromosome from its formation in S phase through its segregation into two daughter cells during mitosis. Detail the events in each mitotic sub-phase that contribute to the precise distribution of genetic material.
5. Explain how disruptions in the normal regulation of the cell cycle lead to cancer. Discuss specific mechanisms such as loss of anchorage dependence and density-dependent inhibition, and the implications of metastasis for cancer progression.

Glossary of Key Terms

- **Cell Cycle:** The entire sequence of events that takes place in a cell leading to its division and duplication.
- **Cell Division:** The process by which a parent cell divides into two or more daughter cells.
- **Reproduction:** The biological process by which new individual organisms are produced. For unicellular organisms, this is achieved by cell division.
- **Growth:** In multicellular organisms, an increase in size due to an increase in cell number through cell division. In unicellular organisms, an increase in cell volume.
- **Development:** The process by which a multicellular organism grows and differentiates from a single cell into a complex organism with specialized tissues and organs.
- **Tissue Renewal:** The process of replacing old, damaged, or dead cells in multicellular organisms through cell division.
- **Cell Theory:** A fundamental scientific theory stating that all living organisms are composed of cells, that cells are the basic unit of life, and that all cells come from pre-existing cells.
- **Chromatin:** The complex of DNA and proteins (histones) that forms chromosomes within the nucleus of eukaryotic cells. It exists in a relatively diffuse state during interphase.

- **Chromosome:** A thread-like structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes. Chromosomes become highly condensed and visible during cell division.
- **Sister Chromatids:** Two identical copies of a single replicated chromosome that are joined together at the centromere.
- **Centromere:** The constricted region of a replicated chromosome that links the sister chromatids and serves as the attachment point for spindle microtubules during cell division.
- **Kinetochore:** A protein structure on chromatids where the spindle fibers attach during cell division to pull sister chromatids apart.
- **DNA Replication:** The biological process of producing two identical replicas of DNA from one original DNA molecule. Occurs during the S phase.
- **Transcription:** The process by which the information in a strand of DNA is copied into a new molecule of messenger RNA (mRNA).
- **Interphase:** The longest phase of the cell cycle during which the cell grows, performs its normal functions, and prepares for division, consisting of G1, S, and G2 phases.
- **G1 Phase (First Gap):** The first growth phase of the cell cycle, where the cell increases in size and synthesizes proteins and organelles, but does not replicate its DNA.
- **S Phase (Synthesis):** The phase of the cell cycle during which DNA replication occurs, resulting in the duplication of chromosomes.
- **G2 Phase (Second Gap):** The second growth phase of the cell cycle, occurring after DNA replication and before mitosis, during which the cell prepares for division.
- **M Phase (Mitotic Phase):** The phase of the cell cycle that includes both mitosis (nuclear division) and cytokinesis (cytoplasmic division).
- **Mitosis:** The process of nuclear division in eukaryotic cells, resulting in two identical daughter nuclei each containing the same number of chromosomes as the parent nucleus.
- **Cytokinesis:** The division of the cytoplasm and its contents following nuclear division (mitosis or meiosis), resulting in two separate daughter cells.
- **Prophase:** The first stage of mitosis, characterized by the condensation of chromatin into visible chromosomes and the formation of the mitotic spindle.
- **Prometaphase:** The second stage of mitosis, where the nuclear envelope disintegrates, and kinetochore microtubules attach to the kinetochores of chromosomes.
- **Metaphase:** The third stage of mitosis, where replicated chromosomes align at the metaphase plate (equatorial plane) in the center of the cell.
- **Metaphase Plate (Equatorial Plane):** An imaginary plane equidistant from the two poles of a cell where the replicated chromosomes align during metaphase.
- **Anaphase:** The fourth stage of mitosis, during which sister chromatids separate and move towards opposite poles of the cell, becoming individual unreplicated chromosomes.
- **Telophase:** The final stage of mitosis, where new nuclear envelopes form around the separated chromosomes at each pole, and chromosomes begin to decondense.
- **Cleavage Furrow:** A shallow groove in the cell surface near the old metaphase plate, which signals the beginning of cytokinesis in animal cells.

- **Cell Plate:** A structure formed in the cytoplasm of a plant cell during cytokinesis, which develops into a new cell wall separating the two daughter cells.
- **Centrosome:** A microtubule-organizing center in animal cells, which replicates during the S phase and forms the poles of the mitotic spindle.
- **Mitotic Spindle:** A macromolecular machine that segregates chromosomes to two daughter cells during mitosis. Composed of microtubules and associated proteins.
- **Kinetochore Microtubules:** Microtubules of the mitotic spindle that attach to the kinetochores of replicated chromosomes and pull them towards the poles.
- **Non-kinetochore Microtubules (Polar Microtubules):** Microtubules that overlap and push against each other, elongating the cell during mitosis.
- **Checkpoints:** Control points in the cell cycle where stop and go-ahead signals can regulate progression.
- **G1 Checkpoint (Restriction Point):** The most important cell cycle checkpoint, determining whether a cell will divide or enter G0.
- **G0 Phase:** A non-dividing state entered by cells that have exited the cell cycle, typically from G1, often indefinitely.
- **Cyclins:** A family of proteins that control the progression of cells through the cell cycle by activating cyclin-dependent kinase (CDK) enzymes.
- **Cyclin-Dependent Kinases (CDKs):** A family of protein kinases that are activated by binding to cyclins, essential for regulating the cell cycle by phosphorylating target proteins.
- **Growth Factor:** A naturally occurring substance capable of stimulating cell proliferation, healing, and differentiation.
- **Platelet-Derived Growth Factor (PDGF):** A specific type of growth factor that stimulates cell division, particularly in fibroblasts.
- **Anchorage Dependence:** The requirement that most animal cells must be attached to a substratum in order to divide.
- **Density-Dependent Inhibition (Contact Inhibition):** The phenomenon whereby cell division stops when cells become too crowded, typically observed in normal animal cells growing in culture.
- **Cancer:** A disease caused by an uncontrolled division of abnormal cells in a part of the body.
- **Tumor:** An abnormal mass of tissue that forms when cells grow and divide more than they should or do not die when they should.
- **Metastasis:** The spread of cancer cells from the place where they first formed to another part of the body.
- **Binary Fission:** The primary method of asexual reproduction and cell division used by prokaryotic organisms (bacteria and archaea).