I. Chapter 12 The Cell Cycle

- **Meiosis**: leads to the production of sperm and eggs cells "gametes."
- **Mitosis**: leads to the production of somatic cells.
- **Cytokinesis**: cell movement.

A. 12.1How do cells replicate?

- Simplified: 1. Copy DNA, 2. Separate the copies, 3. Divide the cytoplasm.
- Eukaryotic cell replication is responsible for three key events.
    - 1. Growth
    - 2. Wound repair
    - 3. Reproduction
- **Chromosome**: consists of a sing, long DNA double helix that is wrapped around proteins called *histones*.
- **Chromatid**: the DNA copies in a replicated chromosome.
- Before mitosis, sister chromatids are joined along their entire length by proteins called *cohesins*.
- **Centromere**: a specialized region of the chromosome where each chromatid is connecter to another.
- **M phase**: the dividing phase.
- **Interphase**: when the cell is growing, preparing to divide, or just doing its thing. The cell spends most of its time in this phase.
- **Synthesis (S) phase**: part of interphase; when DNA is being replicated. Replication of the genetic material is separated in time from the partitioning of the chromosome copies during M phase.
- **G1 phase**: the gap between the end of M and the start of S.
- **G2 phase**: the gap between the end of S and the start of M.
- Simplified cell cycle:
    - G1 phase
    - S phase
    - G2 phase
    - M phase
- Before the cell can begin mitosis, the cell must grow large enough to divide into two normal sized cells. The growing happens in the gap phases.

B. 12.2 What happens during M phase?

- **Chromatin**: DNA and protein material together.
- During interphase, chromatin is an uncondensed state, forming long thin strands.
- At the start of mitosis, each chromosome consists of two sister chromatids, each representing exact copies of the same genetic information, attached to each other at the centromere.
- During mitosis, the two sister chromatids separate to form two independent daughter chromosomes.
- Interphase is followed by the mitotic phases: prophase, prometaphase, metaphase, anaphase, telophase, and cytokinesis.
- **Prophase**: chromosome condense and spindle apparatus begins to form.

- **The spindle apparatus**: a structure that produced the mechanical forces that (1) move the replicated chromosomes during early mitosis and (2) pull chromatids apart in late mitosis.
- **Polar microtubules**: microtubules that extend from each spindle pole from the *microtubule organizing centers (MTOCs)* and overlap with one another.
- **MTOC is a centrosome**: a structure that contains a pair of centrioles.
- **Prometaphase**: nuclear envelope breaks down, microtubules contact chromosome at kinetochores.
- **Kinetochores**: specialized structures assembled at the centromere, there are 2 kinetochores on each side of the replicated chromosome.
- **Kinetochore microtubules**: microtubules attached to kinetochores.
- *Kinesin* and *dynein motors* are recruited to kinetochores and walk the chromosome up and down the microtubules.
- **Metaphase**: chromosomes complete migration to the middle of the cell.
- **Metaphase plate**: imaginary plane between the two spindle poles, where chromosome are lined up in metaphase.
- Spindle poles are held in place by astral microtubules that extend from MTOC and interact with the cell membrane.
- **Anaphase**: sister chromatids separate into daughter chromosomes and are pulled to opposite poles of the spindle apparatus.
- Two movements happen in anaphase:
    - 1. Daughter chromosomes move to opposite poles via the attachment of the kinetochore proteins and the shortening of the kinetochore microtubules.
    - 2. The two poles of the spindle are pushed and pulled further apart.
- When anaphase is complete, two complete collections of chromosomes are fully separated.
- **Telophase**: the nuclear envelope reforms and chromosomes uncondense.
- **Cytokinesis**: the cytoplasm divides to form two daughter cells.
    - In plants a *cell plate* forms.
    - In animals a *cleavage furrow* forms.
- Many bacteria divide using binary fusion: a ring forms between chromosome copies and pinches off the cells.

C. 12.3 Control of the cell

- **M phase-promoting factor (MPF)**: induces M phase in all eukaryotes.
- MPF is made up of *protein kinase*, which catalyzes the transfer of a P from ATP to a target protein, and a protein called *cyclin*.
- Cyclin concentrations build during interphase and peak at M phase *this is important because MPF is a **cyclin dependent kinase (Cdk).**
- Cyclin regulates the formation of MPF
- MPF starts M phase by phosphorylation of other proteins.
- MPF's Cdk subunit is further regulated by two phosphorylation events.
- How is MPF tuned off though?
    - Negative feedback:

        - Turned off by an enzyme complex that is activated in anaphase which attaches *ubiquitins* to MPF's cyclin subunit, which marks the cyclin subunit for destruction by a protein complex called a *proteasome*.
- There are three distinct check points in the cell cycle.
- Regulatory molecules decide whether the cell proceeds with cell division or *nahhhhh*.
- **G1 checkpoint**: occurs in late G1 phase.
    - Checks for size
    - Available nutrients.
    - Social signals: signaling molecules from other cells.
    - Damage to DNA.
- Some regulatory proteins are known as tumor suppressors.
- **G2 checkpoint**: occurs after S phase, between G2 and M.
    - Checks for mostly damage to chromosomes.
- **M phase checkpoints**:
    - 1. Regulate the onset of anaphase.
    - 2. Regulates the progression through M phase to G1

D. 12.4 Cancer: out of control cell division

- Cancer cells have two types of defects related to division:
    - 1. Defects that make proteins required for cell growth active when they shouldn't be.
    - 2. Defects that prevent tumor suppressors from shutting down the cell.
- Cells become malignant or cancerous if they gain the ability to detach from the original tumor and invade other tissues- this is called metastasis.
- Cancer cells can be cultures without the supply of growth factors.
- **Rb protein**: key molecule that enforce the G1 checkpoint.
- The G1 checkpoint is subject to social control:
    - 1. Growth factors arrive
    - 2. Growth factors cause an increase in cyclin and E2F concentrations.
    - 3. Cyclin binds to Cdk, which is then phosphorylated. RB inactivates E2F by binding to it.
    - 4. Inactivating phosphate is removed and active Cdk phosphorylates Rb.
    - 5. Phosphorylated Rb releases E2F
    - E2F triggers the production of S phase proteins.