CHAPTER 9 CELLULAR REPRODUCTION AND THE CELL CYCLE

Chapter Outline

9.1 The Cell Cycle

A. Stages
   1. The cell cycle is an orderly set of stages from first division to the time the daughter cells divide.
   2. When a cell is going to divide, it grows larger, the number of organelles doubles, and the DNA replicates.

B. Interphase
   1. Most of a cell's life is spent in interphase where the cell performs its usual functions.
   2. Time spent in interphase varies by cell types: nerve and muscle cells do not complete the cell cycle and remain in $\mathbf{G_0}$ stage while embryonic cells complete a cycle every few hours.
   3. The **$\mathbf{G_1}$ stage** is just prior to DNA replication; a cell grows in size, organelles increase in number, and material accumulates for DNA synthesis.
   4. **S stage** is a DNA synthesis period where replication occurs; proteins associated with DNA are also synthesized; at the end of the S stage, identical pairs of chromosomes occur for each DNA molecule.
   5. **$\mathbf{G_2}$ stage** occurs just prior to cell division; the cell synthesizes proteins needed for cell division such as proteins in microtubules.
   6. **Interphase** therefore consists of G_1, S, and G_2 stages.

C. M (Mitotic) Stage
   1. **M stage (**M = mitosis) is the entire cell division stage, including both mitosis and cytokinesis.
   2. Cytokinesis is division of the cytoplasm.
   3. When division of the cytoplasm is complete, two daughter cells are produced.

D. Control of the Cell Cycle
   1. The cell cycle is controlled by both internal and external signals.
   2. A signal is a molecule that either stimulates or inhibits a metabolic event.
   3. Growth factors are external signals received at the plasma membrane.
   4. Cell Cycle Checkpoints
      a. There appear to be three checkpoints where the cell cycle either stops or continues onward.
      b. Researchers have identified cyclin, an internal signal that increases or decreases during the cell cycle.
      c. Cyclin must be present for the cell to move from G_1 stage ⇗ S stage and from G_2 stage ⇗ M stage.
      d. The cell cycle stops at the G_2 stage if DNA has not finished replicating.
      e. Stopping the cell are this stage allows time for repair of damaged DNA.
      f. The cycle also stops if chromosomes are not distributed accurately to daughter cells.
      g. DNA damage also stops the cycle at the G_1 checkpoint by the protein p53, if the DNA is not repaired, p53 triggers apoptosis.

E. Apoptosis
   1. Apoptosis is programmed cell death and involves a sequence of cellular events involving:
      a. fragmenting of the nucleus,
      b. blistering of the plasma membrane, and
      c. engulfing of cell fragments by macrophages and/or neighboring cells.
   2. Apoptosis is caused by cells harboring enzymes called caspases.
   3. Cells normally contain caspases by using inhibitors.
   4. Caspases are released by internal or external signals.
   5. Apoptosis and cell division are balancing processes that maintain the normal level of somatic cells.
   6. Cell death is a normal and necessary part of development: frogs must destroy tail tissue they used as tadpoles and the human embryo must eliminated webbing found between fingers and toes.
   7. Death by apoptosis prevents a tumor from developing.

9.2 Mitosis and Cytokinesis

A. Eukaryotic Chromosomes
    1. DNA in chromosomes of eukaryotic cells is associated with proteins; histone proteins organize chromosomes.
    2. When cell is not undergoing division, DNA in nucleus is a tangled mass of threads called **chromatin.**
    3. At cell division, chromatin becomes highly coiled and condensed and is now visible as chromosomes.
    4. Each species has a characteristic number of chromosomes.
        a. **Diploid (2n) number** includes two sets of chromosomes of each type.
            1) Found in all the non-sex cells of an organism's body (with a few exceptions).
            2) Examples include humans (46), crayfish (200), etc.
        b. **Haploid (n) number** contains one of each kind of chromosome.
            1) In the life cycle of many animals, only sperm and egg cells have the haploid number.
            2) Examples include humans (23), crayfish (100), etc.
    5. Cell division in eukaryotes involves nuclear division and cytokinesis (division of the cytoplasm).
        a. Somatic (body) cells undergo **mitosis** for development, growth, and repair.
            1) This nuclear division leaves the chromosome number constant.
            2) A 2n nucleus replicates and divides to provide daughter nuclei that are also 2n.
        b. A chromosome begins cell division with two sister chromatids.
            1) **Sister chromatids** are two strands of genetically identical chromosomes. .
            2) At the beginning of cell division, they are attached at a **centromere.**
            3) The **centromere** is a region of constriction on a chromosome where sister chromatids are attached.

B. Mitosis in Animal Cells
    1. Centrosomes are believed responsible for organizing the spindle.
    2. The centrosome is the main microtubule organizing center of the cell.
    3. The centrosome has divided before mitosis begins.
    4. Each centrosome contains a pair of barrel-shaped organelles called **centrioles**.
    5. The spindle contains many fibers, each composed of a bundle of microtubules.
    6. Microtubules are made of the protein **tubulin.**
        a. Microtubules assemble when tubulin subunits join, disassemble when tubulin subunits become free, and form interconnected filaments of cytoskeleton.
        b. Microtubules disassemble as spindle fibers form.
    7. Mitosis is divided into five phases: prophase, prometaphase, metaphase, anaphase, and telophase.
    8. **Prophase**
        a. Nuclear division is about to occur because chromatin condenses and chromosomes become visible.
        b. The nucleolus disappears and the nuclear envelope fragments.
        c. Already duplicated chromosomes are composed of two sister chromatids held together by a centromere.
            1) This configuration in diagrammatic drawings gives accurate chromosome number.
            2) Chromosomes have no particular orientation in cell at this time.
        d. Spindle begins to assemble as pairs of centrosomes migrate away from each other.
    9. **Prometaphase**
        a. Specialized protein complexes (kinetochores) develop on each side of centromere for future chromosome orientation.
        b. An important event during prometaphase is attachment of chromosomes to the spindle and their movement as they align at the metaphase plate (equator) of the spindle.
        c. The kinetochores of sister chromatids capture **kinetochore spindle fibers**.
        d. Chromosomes move back and forth toward alignment at the metaphase plate.
    10. **Metaphase**
        a. Chromosomes, attached to kinetochore fibers, are now aligned at the **metaphase plate**.
        b. Non-attached spindle fibers, called **polar spindle fibers**, can reach beyond the metaphase plate and overlap.
    11. **Anaphase**
        a. Two sister chromatids of each duplicated chromosome separate at centromere.
        b. Daughter chromosomes, each with a centromere and single chromatid, move to opposite poles.
            1) Polar spindle fibers lengthen as they slide past each other.

2) Kinetochore spindle fibers disassemble at the kinetochores; this pulls daughter chromosomes to poles.
3) The motor molecules kinesin and dynein are involved in this sliding process.

12. **Telophase**
    a. Spindle disappears in this stage.
    b. The nuclear envelope reforms around the daughter chromosomes.
    c. The daughter chromosomes decondense and return to chromatin.
    d. The nucleolus reappears in each daughter nucleus.

C. Mitosis in Plant Cells
1. Plant meristematic tissue in tips of roots and shoots of stems retains ability to divide throughout life.
2. The stages are essentially the same as in animal cells.
3. Although plant cells have a centrosome and spindle, there are no centrioles and asters do not form.

D. Cytokinesis in Plant and Animal Cells
1. When mitosis occurs but cytokinesis doesn't occur, it results in a multinucleated cell; this occurs in skeletal muscle cells and the embryo sac in flowering plants.
2. Cytokinesis in Animal Cells
    a. **Cleavage furrow** indents the plasma membrane between the two daughter nuclei at a midpoint; this deepens to divide the cytoplasm during cell division.
    b. Cytoplasmic cleavage begins as anaphase draws to a close and organelles are distributed.
    c. The cleavage furrow deepens as a band of actin filaments, called the contractile ring, constricts between the two daughter cells.
    d. A narrow bridge exists between daughter cells during telophase until constriction completely separates the cytoplasm..
3. Cytokinesis in Plant Cells
    a. The rigid cell wall that surrounds plant cells does not permit cytokinesis by furrowing.
    b. The Golgi apparatus produces vesicles that move to the midpoint between the daughter nuclei.
    c. Vesicles fuse forming a **cell plate**; their membranes complete the plasma membranes of the daughter cells.
    d. The new membrane also releases molecules form the new plant cell walls.
    e. The cell walls are strengthened by the addition of cellulose fibrils.

9.3 The Cell Cycle and Cancer

A. Characteristics of Cancer Cells
1. Cancer cells lack differentiation.
    a. Unlike normal cells that differentiate into muscle or nerves cells, cancer cells have a general abnormal form and are nonspecialized.
    b. Normal cells enter the cell cycle only about 50 times; cancer cells are immortal.
2. Cancer cells have abnormal nuclei.
    a. The nuclei may be enlarged and may have an abnormal number of chromosomes.
    b. The chromosomes have mutated; some chromosomes may be duplicated or deleted.
    c. Gene amplification, extra copies of genes, is more frequent in cancerous cells.
    d. Ordinary cells with DNA damage ultimately undergo apoptosis; cancer cells do not.
3. Cancer cells form tumors.
    a. Normal cells are anchored and stop dividing when in contact with other cells.
    b. Cancer cells invade and destroy normal tissue and their growth is not inhibited.
    c. Cancer cells no longer respond to inhibitory growth factors and do not need as much stimulatory growth factors.
    d. Cancer cells pile on top of each other to form a **tumor**.
4. Cancer cells undergo angiogenesis and metastasis.
    a. A benign tumor is encapsulated and does not invade adjacent tissue.
    b. Angiogenesis, the formation of new blood vessels, is triggered when some cancer cells release a growth factor that causes nearby blood vessels to grow and bring more nutrients and oxygen to the tumor.
    c. Cancer *in situ* is still in its place of origin and has not spread to other tissues.
    d. Malignancy occurs when metastasis spreads new tumors distant from the primary tumor.
    e. Cancer prognosis depends on whether the tumor has invaded surrounding tissue, if there is lymph node involvement, and whether there are metastatic tumors elsewhere in the body.

B. Origin of Cancer
  1. The DNA repair system corrects mutations during DNA replication; mutations in genes encoding the various enzymes of repair can cause cancer.
  2. **Proto-oncogenes** specify proteins that stimulate the cell cycle while **tumor-suppressor genes** specify proteins that inhibit the cell cycle; mutations of either of these genes can cause cancer.
  3. DNA segments called **telomeres** form the ends of chromosomes and shorten with each replication, eventually signaling the cell to end all division; cancer cells produce **telomerase** that keeps telomeres long and cells continue dividing.

C. Regulation of the Cell Cycle
  1. Proto-oncogenes are that the end of a stimulatory pathway from the plasma membrane to the nucleus; a growth factor can result in turning on an oncogene.
  2. Tumor-suppressor genes are at the end of an inhibitory pathway that also extends from the plasma membrane to the nucleus; a growth-inhibitory factor can result in turning on a tumor suppressor gene that inhibits the cell cycle.
  3. A balance between stimulatory signals and inhibitory signals determines whether proto-oncogenes are active or tumor-suppressor genes are active.

D. Oncogenes
  1. Proto-oncogenes can undergo mutation to become oncogenes (cancer-causing genes).
  2. An oncogene can code for a faulty receptor in the stimulatory pathway.
  3. An oncogene can specify an abnormal protein product or abnormally high levels of a normal product that stimulates the cell cycle.
  4. About 100 oncogenes have been described; the *ras* gene family includes variants associated with lung, colon, and pancreatic cancers as well as leukemias and thyroid cancers.

E. Tumor-suppressor Genes
  1. Mutation of a tumor-suppressor gene results in unregulated cell growth.
  2. Researchers have identified a half dozen tumor-suppressor genes.
  3. The *RB* tumor-suppressor gene prevents retinoblastoma, a cancer of the retina, and has been found to malfunction in cancers of the breast, prostate, bladder, and small-cell lung carcinoma.
  4. The *p53* tumor-suppressor gene is more frequently mutated in human cancers than any other known gene; it normally functions to trigger cell cycle inhibitors and stimulate apoptosis.

9.4 Prokaryotic Cell Division

A. Prokaryotes reproduce with asexual reproduction resulting in identical offspring that have received genetically identical chromosomes.

B. The Prokaryotic Chromosome
  1. Prokaryotic cells (bacteria and archaea) lack a nucleus and other membranous organelles.
  2. The prokaryotic chromosome contains DNA and associated proteins, but much less protein than eukaryotic chromosomes.
  3. The chromosome consists of **nucleoid**, an irregularly-shaped region that is electron-dense and not enclosed by a membrane.
  4. The chromosome, when stretched out, is a circular loop attached to the inside of the plasma membrane; it is about 1,000 times the length of the cell.

C. Binary Fission
  1. **Binary fission** of prokaryotic cells produces two genetically identical daughter cells by division (fission).
  2. Before cell division, DNA is replicated so two chromosomes are attached to a special site inside the plasma membrane.
  3. Following DNA replication, the two chromosomes separate as a cell lengthens and pulls them apart.
  4. When the cell is approximately twice its original length, the plasma membrane grows inward, a new cell wall and plasma membrane forms dividing the cell into two approximately equal daughter cells.
  5. The generation time of *Escherichia coli* is 20 minutes; other bacteria need up to one hour to beyond a day to divide.

D. Comparing Prokaryotes and Eukaryotes
  1. Both binary fission and mitosis ensure that each daughter cell is genetically identical to the parent.
  2. Bacteria and protists use asexual reproduction to produce identical offspring.
  3. In multicellular fungi. Plants, and animals, cell division is part of the growth process that produces and repairs the organism.

4. Prokaryotes have a single chromosome with mostly DNA and some associated protein; there is no spindle apparatus.
5. Eukaryotic cells have chromosomes with DNA and many associated proteins, especially histone that organizes the chromosome.
6. The spindle is involved in distributing the daughter chromosomes to the daughter nuclei.