Unit 8 Notes: The Cell Cycle

I. The Life of a Eukaryotic Cell

A. Eukaryotic cells divide at the end of a series of stages called the cell cycle.

1. Unicellular eukaryotes divide to produce a new organism.

2. Multicellular eukaryotes divide to increase cell surface area, produce specialized cells for tissues, and replace worn-out cells.

3. The cell cycle is very similar in all eukaryotes, suggesting a common origin.

B. The cell cycle has two major divisions, each of which has several subdivisions.

1. Interphase: period between cell divisions; takes up most of the cell cycle.

a. G1 (gap 1): prereplication; cell grows, makes RNA, proteins, etc.; performs tissue's specific function(s).

i. G0: a stopping point in G1; not gearing up for division; nerve cells; most adult cells.

ii. R (restriction point): cell in G1 or G0 receives signals to divide and begins process – no turning back.

b. S (DNA synthesis): DNA of each chromosome is replicated, doubling each gene in the nucleus.

c. G2: cell prepares for mitosis by making specific types of RNA and proteins.

2. Mitosis: even nuclear division ensures each daughter cell gets a full set of chromosomes; cytokinesis splits the cells apart.

II. DNA Replication

A. The synthesis of DNA depends on the structure of nucleotides and a host of enzymes and other proteins.

1. Special proteins bind to specific regions of chromosomes called replication origins.

2. At the replication origin, helicase unwinds the DNA while single-strand binding proteins hold the strands apart.

3. Primase attaches 5 – 15 nucleotides of RNA at the origin, running 5′ to 3′.

4. DNA polymerase adds complimentary nucleotides to the RNA primer, also in the 5′ to 3′ direction.

a. The leading strand can be made as one long polymer.

b. The lagging strand must be made in short (100 - 300 nucleotide) segments called Okazaki fragments.

i. When DNA polymerase reaches an RNA primer, it replaces the RNA with DNA.

ii. DNA ligase joins the new fragment to the old one.

5. Replisomes (DNA polymerases, associated enzymes, and proteins) move in both directions from replication origins, speeding the process of replication.

6. Each "new" DNA strand is half "old" – semiconservative.

B. DNA repair mechanisms exist to fix base mismatches and other problems.

1. DNA polymerase is only about 99.99% accurate at matching base pairs during replication (1 mistake per 10,000 nucleotides).

a. To improve accuracy, DNA polymerase checks its work and pauses to replace mismatches.

b. Accuracy is improved to 99.99999% (1 mistake per 10 million nucleotides).

2. Mutations caused during interphase by mutagenic chemicals or radiation are fixed through excision repair.

a. A repair enzyme cuts out the damaged section.

b. DNA polymerase replaces the nucleotides and DNA ligase links them to the old DNA.

3. These are only 2 of many ways to repair DNA.

4. Without these mechanisms, DNA would degrade fairly quickly, making life and reproduction impossible.

III. Mitosis and Cell Division

A. After the S and G2 stages of interphase, the cell has organized itself for mitosis.

1. Each chromosome has been copied resulting in two sister chromatids held together by a centromere.

a. The centromere helps to organize the sister chromatids for even chromosome segregation in mitosis.

b. Uneven division results in aneuploidy which can lead to cancer, an inability to perform mitosis again, etc.

2. Mitosis is a continuous process which is considered to have four distinct steps.

a. Prophase can be recognized by condensed, unorganized chromosomes.

i. Microtubules form around the nucleus, creating a mitotic spindle.

ii. Centrioles (or an equivalent) are pushed to either side of the cell and are surrounded and anchored by spindle poles that form around them.

iii. Microtubules attached to the centrioles bind to a protein complex called a kinetochore within the centromere of each sister chromatid.

b. The beginning of metaphase is defined by the chromosomes lining up at the cell's equator.

i. Sister chromatids are pushed to the equator region by the spindle fibers they are attached to.

ii. The metaphase plate helps ensure that each daughter cell gets one copy of each chromosome.

c. Sister chromatids separate during anaphase.

i. Enzymes break down the centromeres.

ii. Motor proteins of the kinetochores pull the chromatids along the spindle microtubules to opposite spindle poles.

iii. Cytokinesis may begin.

d. In telophase, the chromosomes begin to expand, nuclear envelopes form (creating two new nuclei), and cytokinesis advances until the daughter cells separate.

B. Some small differences exist between eukaryotes.

1. Primitive eukaryotes attach their chromosomes to the nuclear envelope for division (similar to prokaryotes).

2. Plants have no centrioles and form a cell plate in the middle of the cell during telophase.

3. Some fungi bud a new nucleus with imbedded spindle poles.

IV. Regulation of the Cell Cycle

A. All eukaryotes use the same basic mechanism to regulate the progression of the cell cycle – cyclins.

1. Cyclins work by varying their concentration, causing specific kinase enzymes to become active or inactive.

a. Kinase enzymes transfer phosphate groups from ATP to specific enzymes or other proteins, activating them.

b. Activated proteins perform their job until their phosphate is transferred elsewhere.

c. The concentration of the various kinases and proteins remains constant in the cell, but they are not active during all of the cell cycle.

2. G1 cyclins activate replication, accumulating late in G1 and peaking in S.

3. Mitotic cyclins control the order of mitotic events.

    a. Low mitotic cyclin levels in G2 activate kinases that activate the breakdown of the nuclear membrane and condensation of chromosomes.

    b. As more cyclins build up, other kinases activate pathways controlling the stages of mitosis.

    c. The last pathway activated breaks down specific proteins including centromeres and the mitotic cyclins themselves.

B. Cell cycle regulators prevent the reproduction of defective cells and control when cells leave G0.

1. If checkpoint control proteins find defects, the cell is brought into cell cycle arrest until the problem is fixed.

    a. If p53 finds mismatched bases, it activates cell cycle inhibitors that keep the G1 cyclin-kinase system from activating S.

    b. other arrest points: S (unreplicated DNA), G2 (damaged DNA), and mitosis (spindle problems).

2. Certain genes can encourage or dissuade a cell from leaving G0.

    a. Protooncogenes (signal receivers, transcription regulators, etc.) promote while tumor suppressor genes (checkpoint proteins) inhibit cell division.

    b. A mutation to one type of G0 control gene is kept in check by the other, but mutations to both = cancer.

3. Cancer cells reproduce as quickly as possible, neglecting their G0 duties.

    a. Constant division leads to a tumor which can interfere with the functionality of the tissue it invades.

    b. Some types of cancer metastasize into the blood stream, are deposited in other tissues, and start tumors there.