Week 3, Chapter 6: Cell Division & Cancer

Important Concepts

- all cells have to divide (w/o making mistakes)
- cell division (*mitosis*) is a timed event with specific phases
- all DNA has to be replicated prior to cell division
- cancer occurs dude to disrupted cell cycle control (mutation)
- cancer treatments try to kill off rapidly divididng cells

Bacterial Cell Division

1. DNA replicates to form additional copy of chromosome
2. Cell doubles its size
3. Cell splits into two by forming cell wall in between cells (binary fission)

rate of cell division is species specific:

- *E. Coli* divides every 20 minutes
- *C. perfringens* divides every 10 minutes (food poison)

Why is this a problem?

- bacterial cell numbers can accumulate very rapidly
- produces problems for infection treatment

Eukaryotic Cell Division

Four major *cell cycle phases*:

1. $\mathbf{G_1}$: Occurs after mitosis and cell begins to grow
2. **S**: DNA replication occurs
3. $\mathbf{G_2}$: Cell prepares for division
4. **Mitosis**: Cell division occurs and **equal DNA** is split between mother and daughter cells

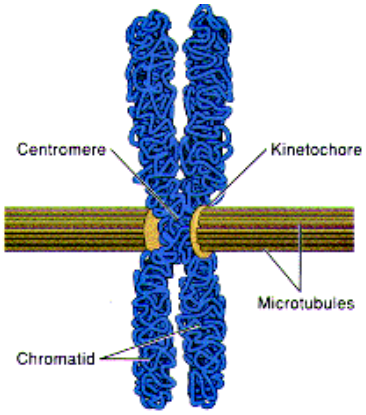
- average human cell cycle takes about 24 hours: G_1 = 11hrs, S = 8hrs, G_2 = 4hrs, M = 1hr

Why is Cell Cycle Important?

- has to produce **exact** copies of DNA instructions to the new cell
- if problems occur in mitosis, all future cells contain the same problem
- puts survival of organism at risk

How Are Chromosomes Pulled Apart in Mitosis?

- chromosomes attach to microtubules (spindle) at their centromere



Eukaryotic Cell Cycle

Mitosis is broken down into 4 stages:

1. **Prophase**: Chromosomes become thicker and spindle microtubules attach to the centromere of each chromosome
2. **Metaphase**: All chromosomes become aligned at the midpoint of spindle
3. **Anaphase**: Chromosomes separate from each other and one whole set of chromosomes go to each pole
4. **Telophase**: Chromosomes unwind and new nuclear membrane forms. Cytoplasm is divided.

Eukaryotic Cell Cycle Checkpoints

- cell has evolved times during the cell cycle to check for *mistakes* (called checkpoints)
  - **DNA damage**: G_1/S and G_2/M checkpoints
  - **Chromosome/spindle problems**: M checkpoint (anaphase)

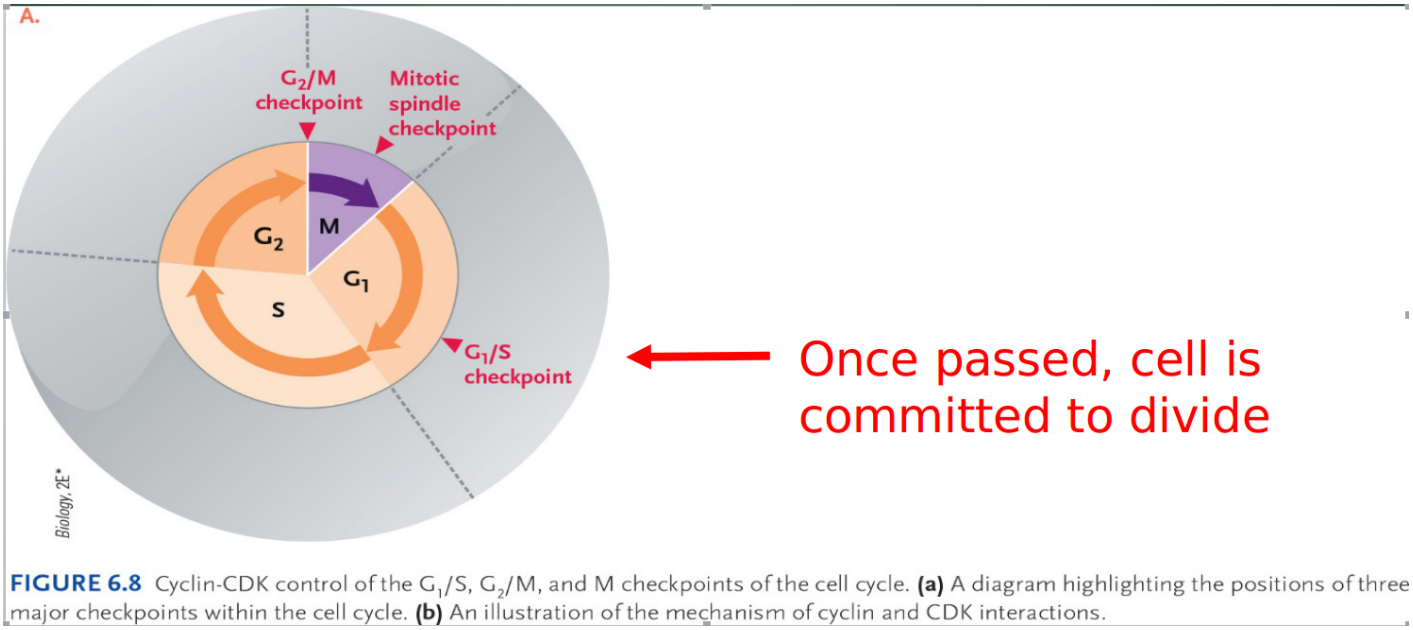


FIGURE 6.8 Cyclin-CDK control of the G_1/S, G_2/M, and M checkpoints of the cell cycle. **(a)** A diagram highlighting the positions of three major checkpoints within the cell cycle. **(b)** An illustration of the mechanism of cyclin and CDK interactions.

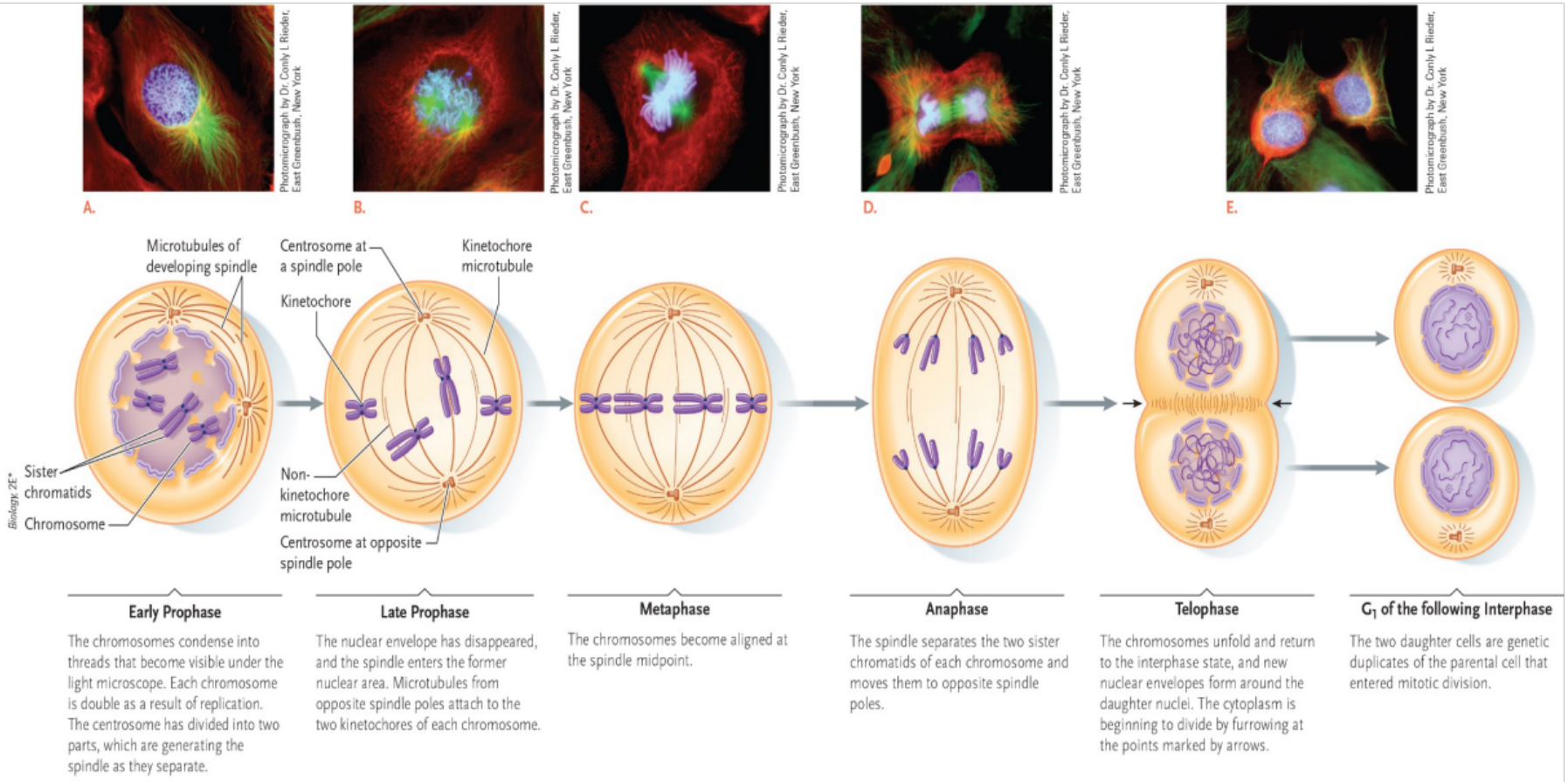


FIGURE 6.5 The stages of mitosis. Immunofluorescent light micrographs show mitosis in an animal cell (salamander lung). The chromosomes are blue, the spindle and cytoplasmic microtubules are yellow-green, and the intermediate filaments are red. **(a)** Early prophase. Chromosomes are condensed, and the nuclear envelope is intact. **(b)** Late prophase. The nuclear envelope has broken down to allow the chromosomes to interact with the microtubules originating from two separate centrosomes. **(c)** Metaphase. All of the replicated chromosomes are aligned on the metaphase plate. **(d)** Anaphase/telophase. Chromosomes have been equally segregated and have decondensed to form two independent daughter nuclei. This cell has just begun cytokinesis. **(e)** The end result of mitosis: two genetically identical daughter cells.

Cancer

- unregulated growth of cells, forms masses (tumors)
- **benign** tumors NOT cancerous
  - cells don't spread to other organs
- **malignant** tumor cells are able to spread
  - can break away from 1 site and enter bloodstream
  - form another tumor at 2 site (METASTASIS)
- Caused by:
  - smoking, diet, sun, age, etc
  - some viruses cause cancer (cervical, Human Papilloma Virus)
  - genetic inheritance (BRCA 1/2) ALL cancers have a genetic cause

Types of Cancer

1. **Carcinomas**: 85%; cancers of the epithelium skin, lining of organs (lung, prostate, breast)
2. **Sarcomas**: 6%; cancers of connective tissue, muscle, bone
3. **Leukemias/lymphomas**: 5%; cancers of bone marrow, lymph glands, blood (eg: chronic myelogenous lukemia)
4. **Other**: 4%; Brain, other rare cancers

What Causes Cancer?

Carcinogens: chemicals, radiation, viruses, etc can cause mutations
Random mutation: sometimes mutations happen on their own (>60% of ALL cancers have nothing to do with lifestyle choices)
Generally, mutations result in errors in the *cell cycle*

Genetic Mutation: changes in DNA sequence of genes
Two types of cancer causing genes:
Oncogenes: causes cells to speed up through cell cycle (accelerator)

- over 400 known genes that cause cancer
- mutations in normal genes (proto-oncogenes) trigger uncontrolled cell division and growth (cancer)
- cells cannot stop dividing

Tumor Supressors: causes cells to stop cell cycle (brake)

- normally provide negative signals for cell proliferation
- mutations in these genes abolish normal function
- cells divide without control (checkpoints not allowed)

Cancer Progression

- single cells undergoes mutation that leads to lack of cell cycle control (no checkpoints-oncogenes and tumor supressors)
- eventually cell contains many mutations (>100!) that cause tumor growth (occurs in most cancers)

Cancer Metastasis

FIGURE 6.12 Cancer metastasis. An illustration of the various steps leading to the metastasis (spreading) of cancer cells through the circulatory system from a primary to a secondary site.