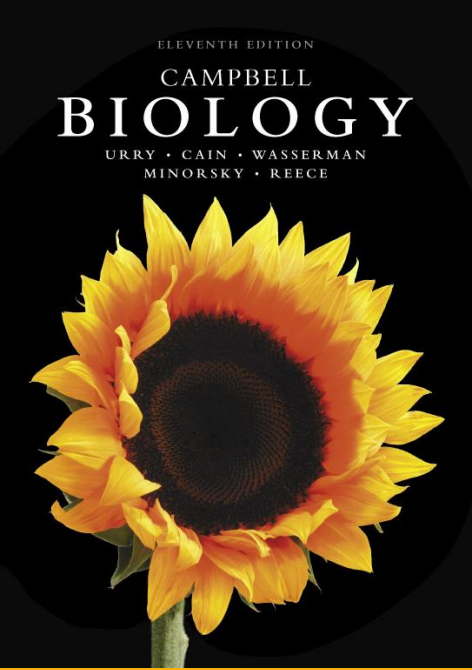


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Chapter 12

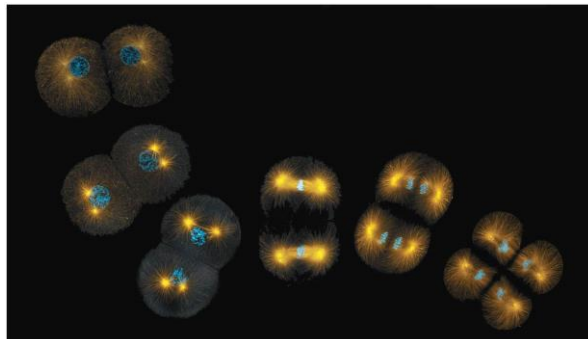
The Cell Cycle

Lecture Presentations by
Nicole Tunbridge and
Kathleen Fitzpatrick

The Key Roles of Cell Division

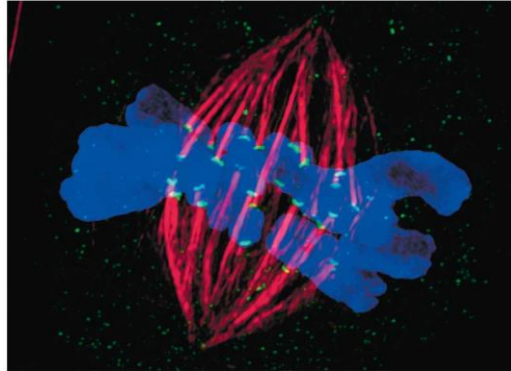
- The ability of organisms to produce more of their own kind best distinguishes living things from nonliving matter
- The continuity of life is based on the reproduction of cells, or **cell division**

*How do dividing cells
distribute chromosomes
to daughter cells?*



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Figure 12.1a



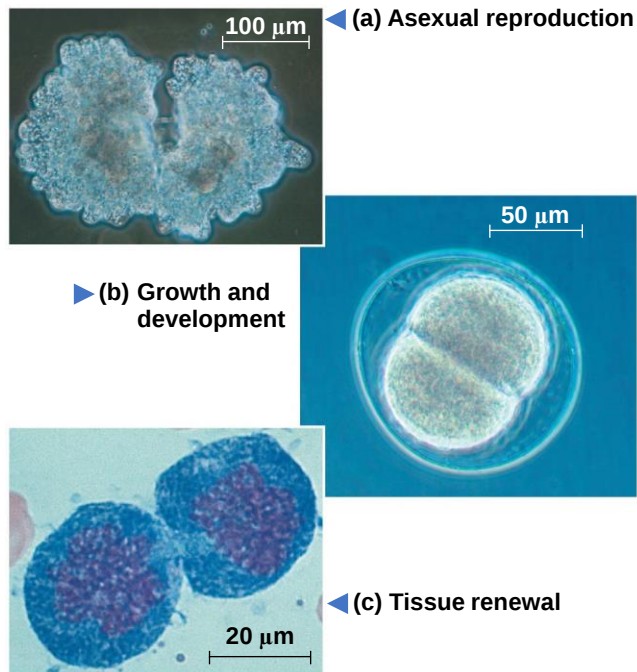
Chromosomes (blue) are attached by specific proteins (green) to cell machinery (red) and are moved during division of a rat kangaroo cell.

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- In unicellular organisms, division of one cell reproduces the entire organism
- Multicellular eukaryotes depend on cell division for
 - development from a fertilized egg
 - growth
 - repair
- Cell division is an integral part of the **cell cycle**, the life of a cell from formation to its own division

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Figure 12.2



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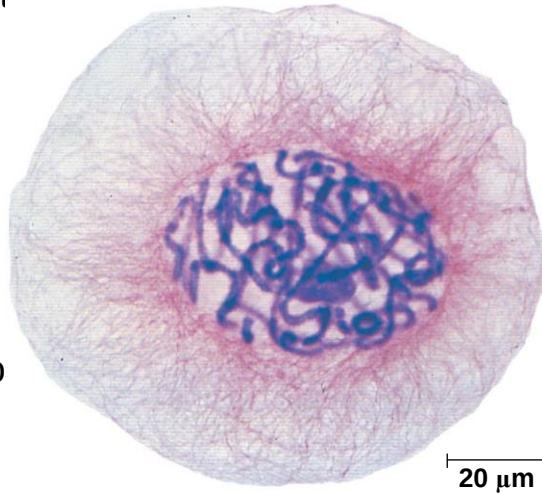
Concept 12.1: Most cell division results in genetically identical daughter cells

- Most cell division results in two daughter cells with identical genetic information, DNA
- *The exception is **meiosis**, a special type of division that can produce sperm and egg cells*

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Cellular Organization of the Genetic Material

- All the DNA in a cell constitutes the cell's **genome**
- A genome can consist of a single DNA molecule (common in prokaryotic cells) or a number of DNA molecules (common in eukaryotic cells)
- DNA molecules in a cell are packaged into **chromosomes**



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- Eukaryotic chromosomes consist of **chromatin**, a complex of DNA and protein that condenses during cell division
- Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus
- **Somatic cells (nonreproductive cells)** have two sets of chromosomes (23 x 2 in humans)
- **Gametes (reproductive cells: sperm and eggs)** have half as many chromosomes as somatic cells (23 in humans)

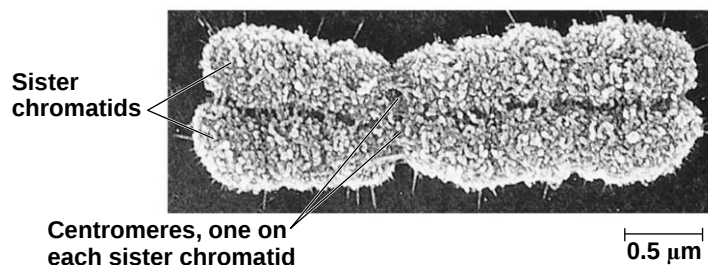
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Distribution of Chromosomes During Eukaryotic Cell Division

- In preparation for cell division, DNA is replicated and the chromosomes condense
- Each duplicated chromosome has two **sister chromatids** (joined copies of the original chromosome), attached along their lengths by proteins called *cohesins*
- The **centromere** is the narrow “waist” of the duplicated chromosome, where the two chromatids are most closely attached

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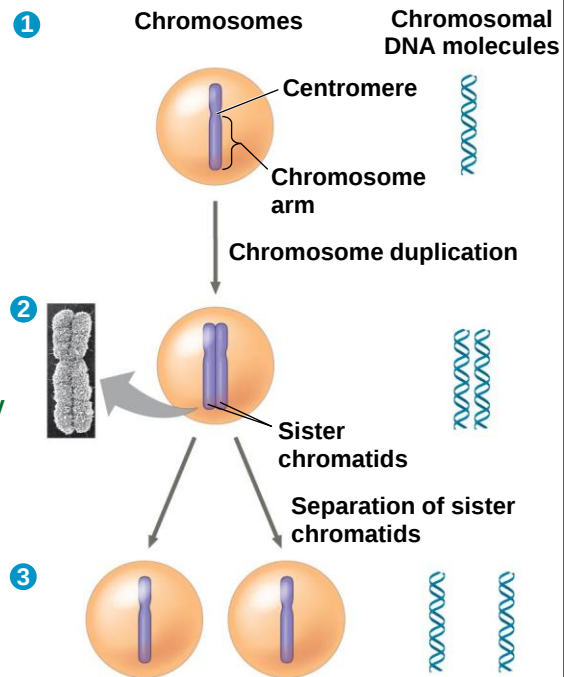
Figure 12.4



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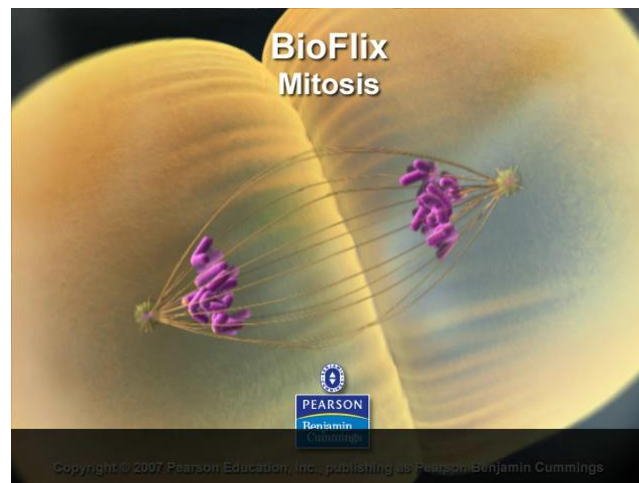
- During cell division, the two sister chromatids of each duplicated chromosome separate and move into two nuclei

- Once separate, the chromatids are called chromosomes



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BioFlix Animation: Chromosome Duplication



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- Eukaryotic cell division consists of
 - **mitosis**, the division of the genetic material in the nucleus
 - **cytokinesis**, the division of the cytoplasm
- Gametes are produced by a variation of cell division called *meiosis*
- Meiosis yields nonidentical daughter cells that have half as many chromosomes as the parent cell (Ch 13)

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Concept 12.2: The mitotic phase alternates with interphase in the cell cycle

Phases of the Cell Cycle

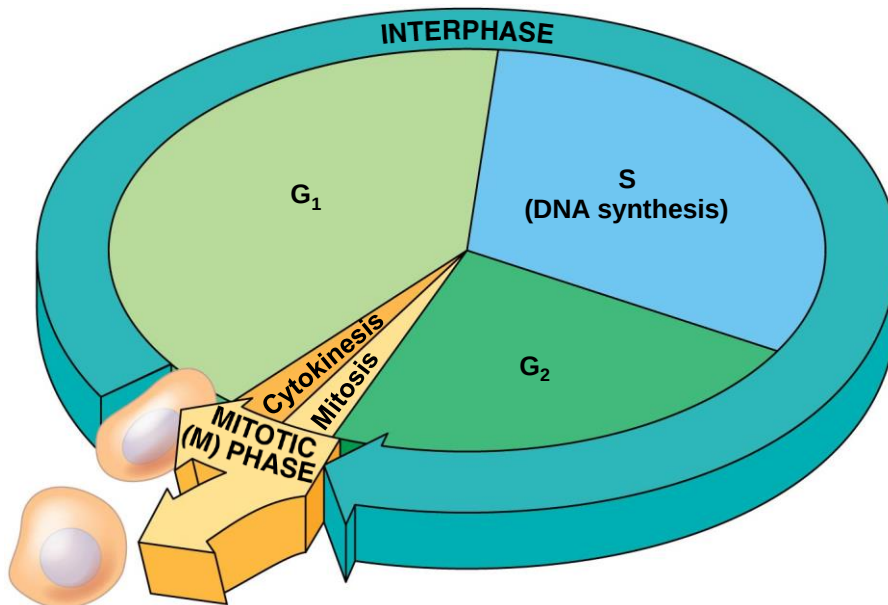
- The cell cycle consists of
 - **mitotic (M) phase** (mitosis and cytokinesis)
 - **interphase** (cell growth and copying of chromosomes in preparation for cell division)

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- Interphase (about 90% of the cell cycle) can be divided into three phases:
 - **G₁ phase** (“first gap”)
 - **S phase** (“synthesis”)
 - **G₂ phase** (“second gap”)
- *The cell grows during all three phases, but chromosomes are duplicated ONLY during the S phase*

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Figure 12.6



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- Mitosis is conventionally broken down into five stages:
 - **prophase**
 - **prometaphase**
 - **metaphase**
 - **anaphase**
 - **telophase**

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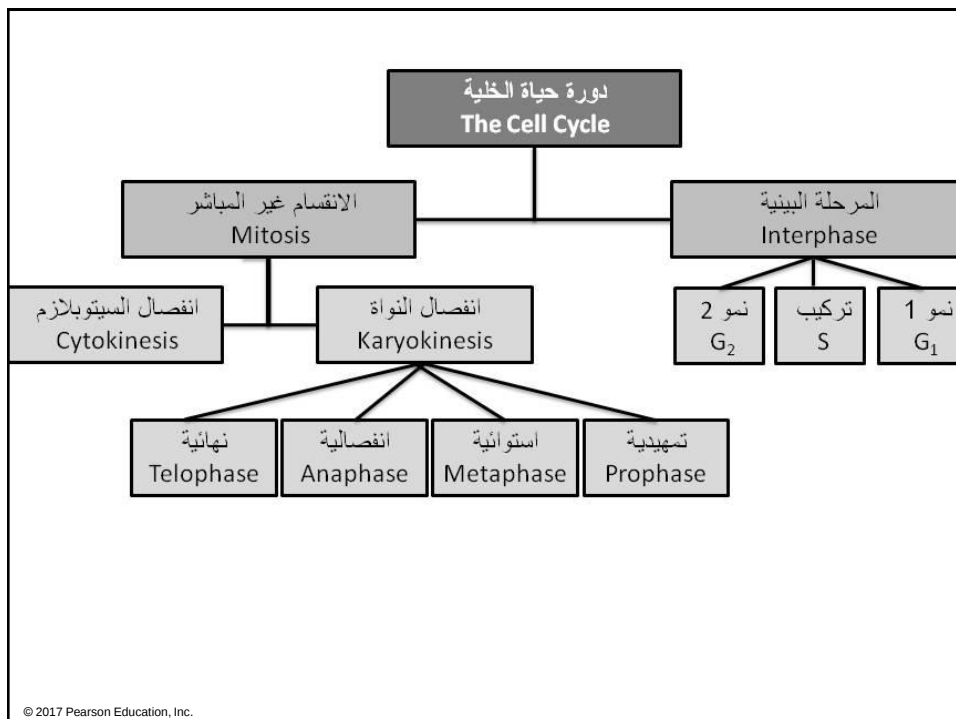


Figure 12.7a

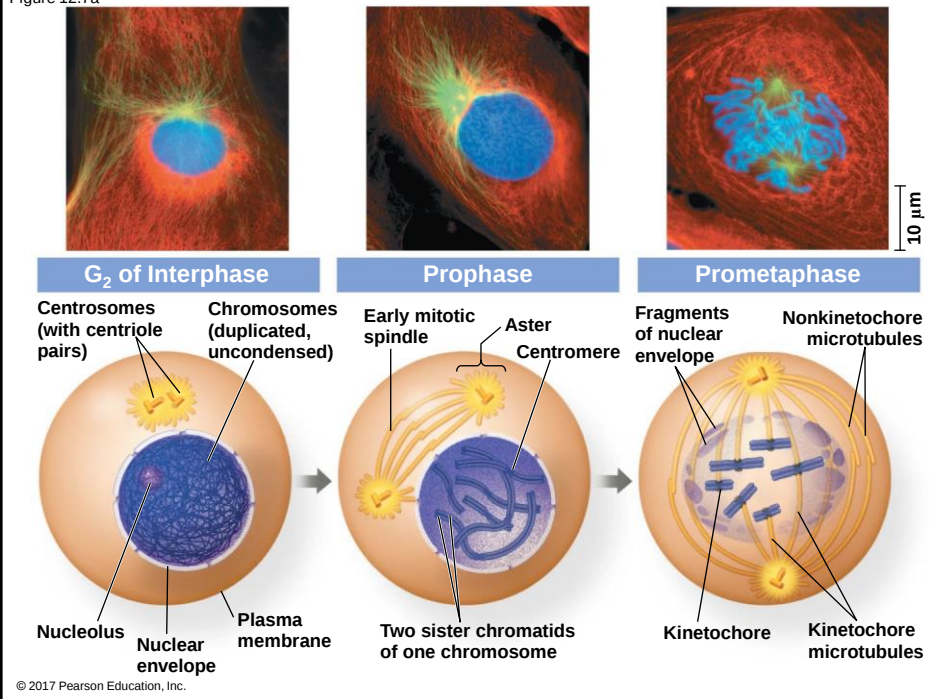
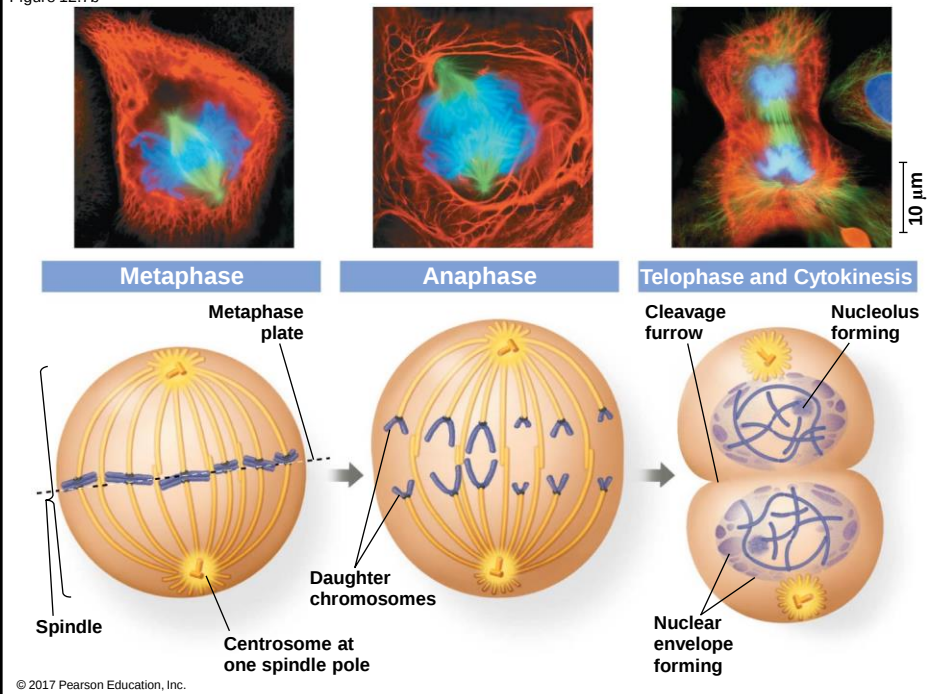
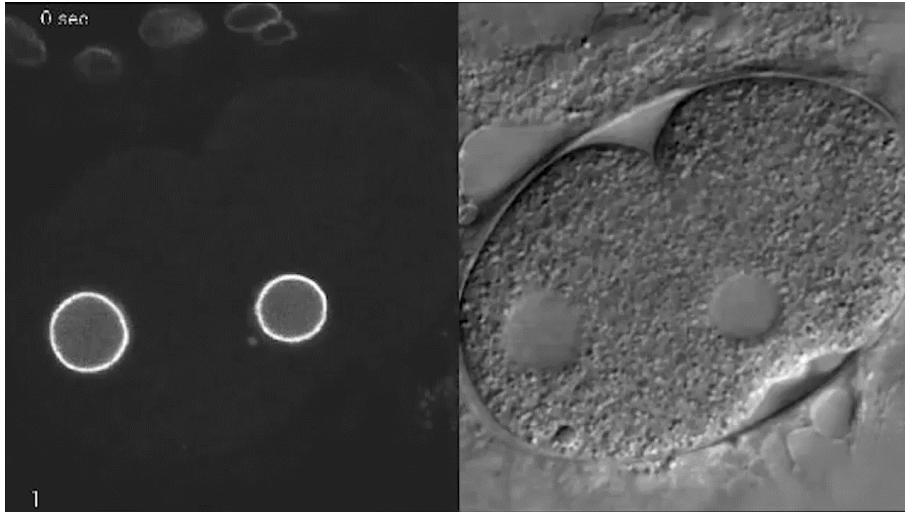


Figure 12.7b



Video: Nuclear Envelope Formation



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Video: Animal Mitosis (time-lapse)



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The Mitotic Spindle: *A Closer Look*

- The **mitotic spindle** is a structure made of microtubules that controls chromosome movement during mitosis
- In animal cells, assembly of spindle microtubules begins in the **centrosome**, the microtubule-organizing center
- The centrosome *replicates during interphase*, forming two centrosomes that migrate to opposite ends of the cell during prophase and prometaphase

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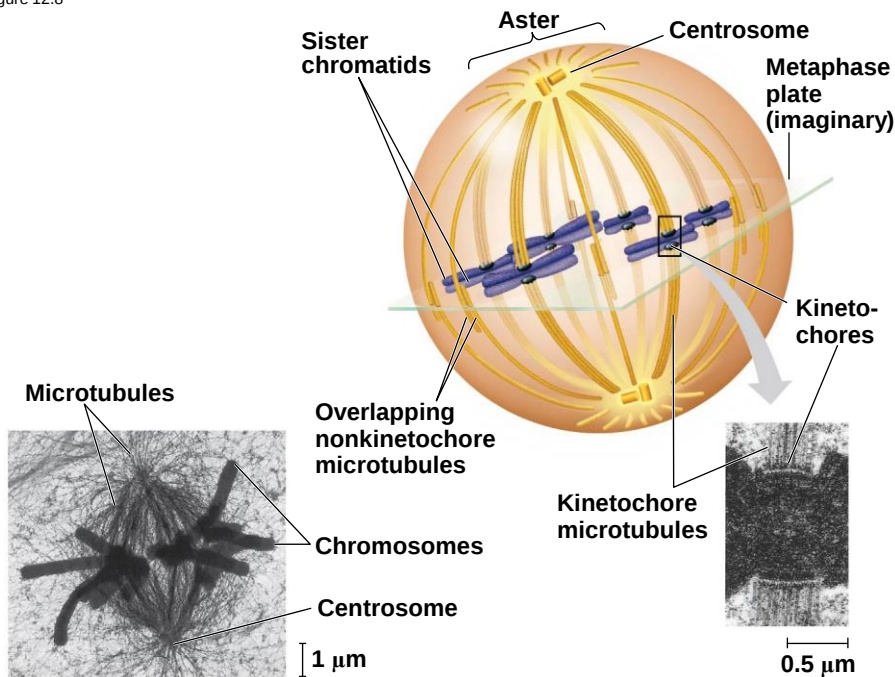
- An **aster** (a radial array of short microtubules) extends from each centrosome
- The spindle includes the centrosomes, the spindle microtubules, and the asters

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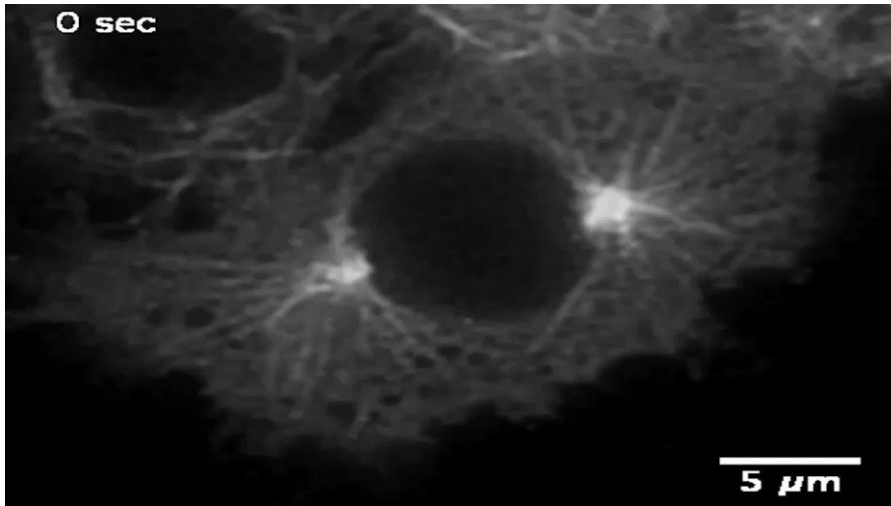
- During prometaphase, some spindle microtubules attach to the kinetochores of chromosomes and begin to move the chromosomes
- **Kinetochores** are protein complexes associated with centromeres
- At metaphase, the chromosomes are all lined up at the **metaphase plate**, a plane midway between the spindle's two poles

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Figure 12.8



Video: Spindle Formation During Mitosis



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- In anaphase the **cohesins** are cut by an enzyme called **separase**
- Sister chromatids separate and move along the kinetochore microtubules toward opposite ends of the cell
- The microtubules shorten by depolymerizing at their kinetochore ends

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- Nonkinetochore microtubules from opposite poles overlap and push against each other, elongating the cell
- At the end of anaphase, duplicate groups of chromosomes have arrived at opposite ends of the elongated cell
- Cytokinesis begins during anaphase or telophase, and the spindle eventually disassembles

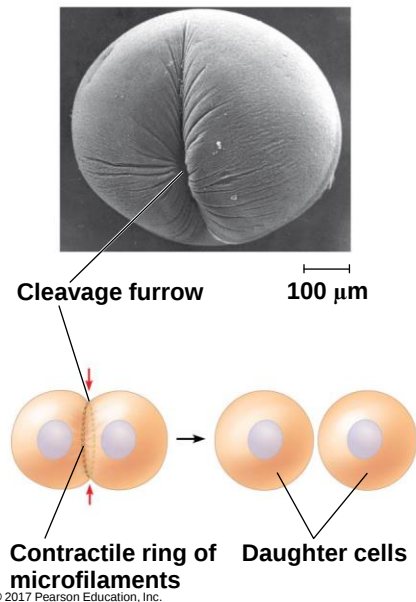
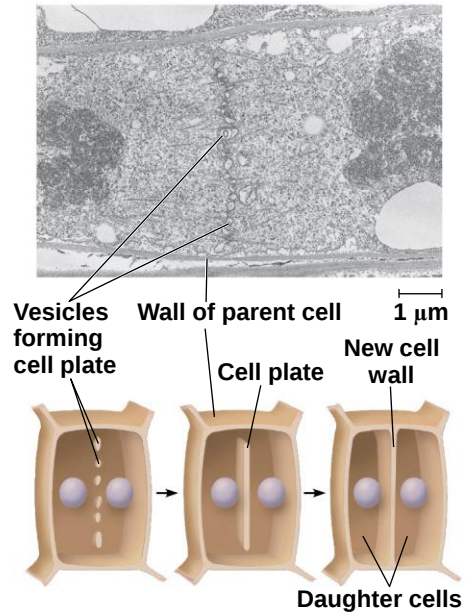
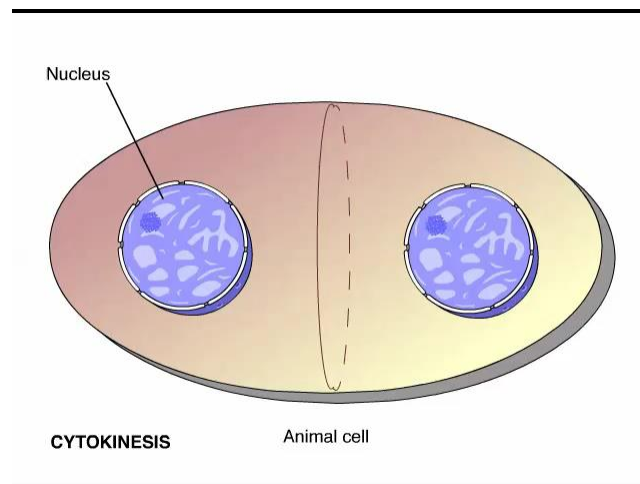
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Cytokinesis: *A Closer Look*

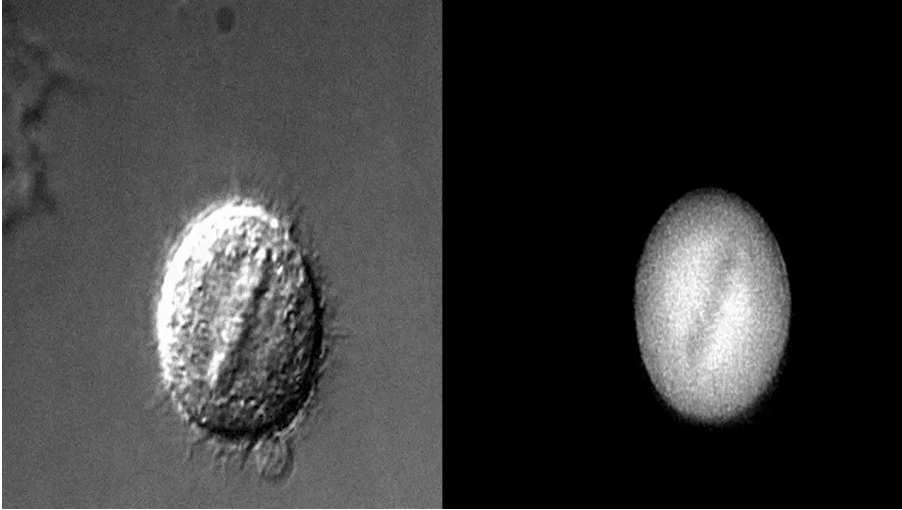
- In animal cells, cytokinesis occurs by a process known as **cleavage**, forming a **cleavage furrow**
- In plant cells, a **cell plate** forms during cytokinesis

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Figure 12.10

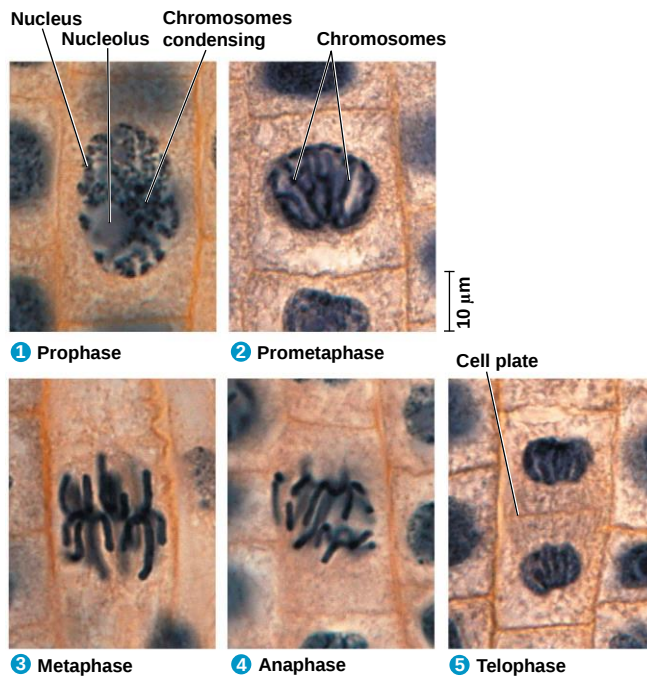
(a) Cleavage of an animal cell (SEM)**(b) Cell plate formation in a plant cell (TEM)****Animation: Cytokinesis**

Video: Myosin and Cytokinesis



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Figure 12.11



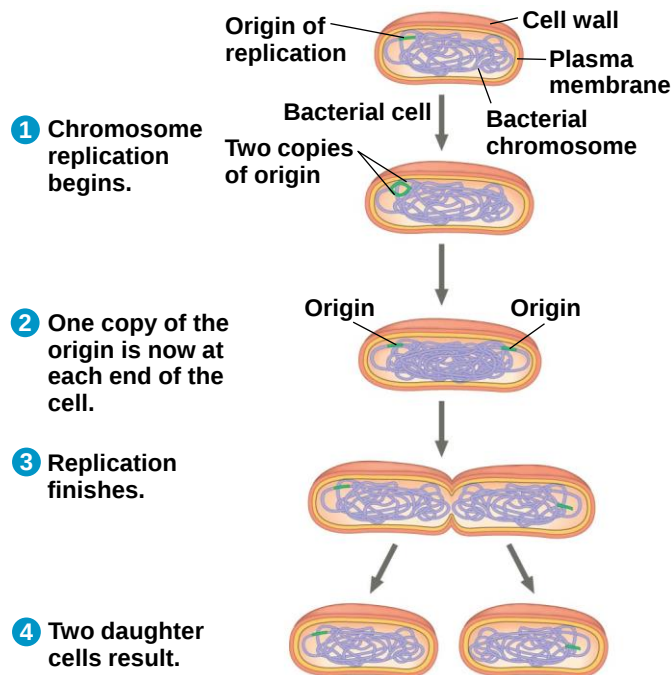
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Binary Fission in Bacteria

- Prokaryotes (bacteria and archaea) reproduce by a type of cell division called **binary fission**
- In binary fission, the chromosome replicates (beginning at the **origin of replication**), and the two daughter chromosomes actively move apart
- The plasma membrane pinches inward, dividing the cell into two

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Figure 12.12_4



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Concept 12.3: The eukaryotic cell cycle is regulated by a molecular control system

- The frequency of cell division varies with the type of cell
- These differences result from regulation at the molecular level
- Cancer cells manage to escape the usual controls on the cell cycle

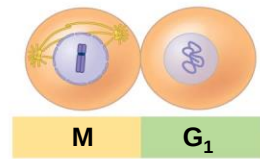
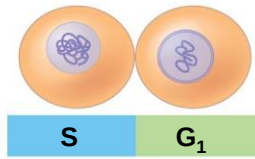
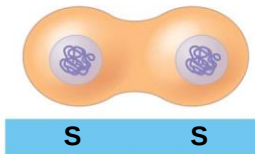
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The Cell Cycle Control System

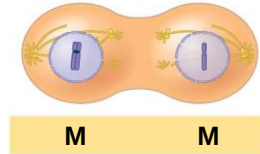
- The cell cycle appears to be driven by specific chemical signals present in the cytoplasm
- Some evidence for this hypothesis comes from experiments in which cultured mammalian cells at different phases of the cell cycle were fused to form a single cell with two nuclei

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Figure 12.14

Experiment**Experiment 1****Experiment 2****Results**

G_1 nucleus immediately entered S phase and DNA was synthesized.



G_1 nucleus began mitosis without chromosome duplication.

Conclusion

Molecules present in the cytoplasm control the progression to S and M phases.

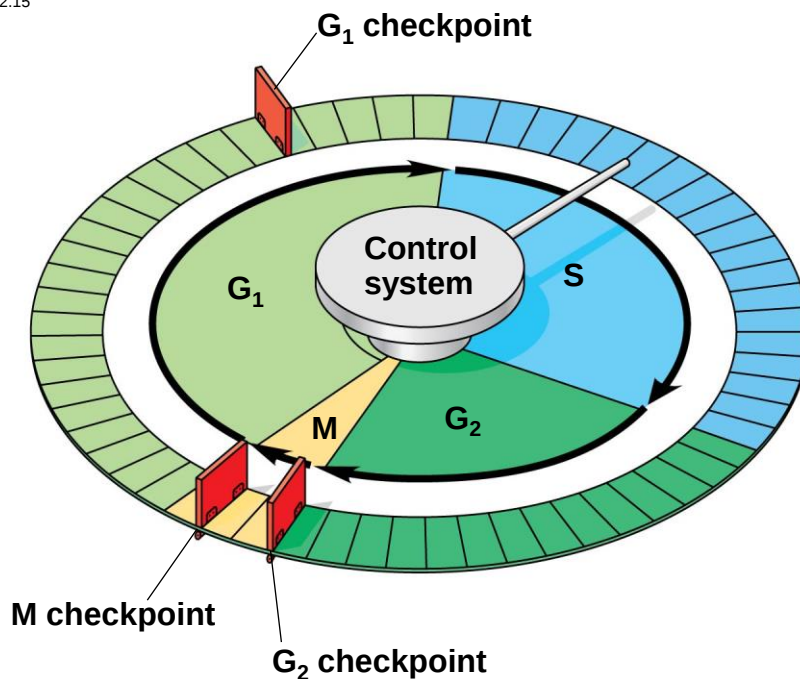
Data from R. T. Johnson and P. N. Rao, Mammalian cell fusion: Induction of premature chromosome condensation in interphase nuclei, *Nature* 226:717–722 (1970).

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- The sequential events of the cell cycle are directed by a distinct **cell cycle control system**, which is similar to a clock
- The cell cycle control system is regulated by both internal and external controls
- The clock has specific **checkpoints** where the cell cycle stops until a go-ahead signal is received

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Figure 12.15



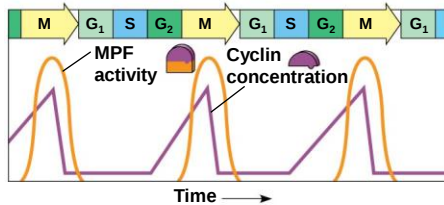
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The Cell Cycle Clock: Cyclins and Cyclin-Dependent Kinases

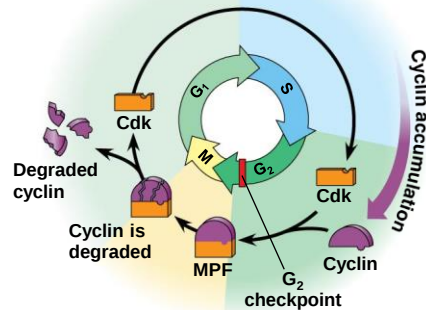
- Two types of regulatory proteins are involved in cell cycle control: **cyclins** and **cyclin-dependent kinases (Cdks)**
- The activity of a Cdk rises and falls with changes in concentration of its cyclin partner
- **MPF** (maturation-promoting factor) is a cyclin-Cdk complex that triggers a cell's passage past the G₂ checkpoint into the M phase

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Figure 12.16



(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle



(b) Molecular mechanisms that help regulate the cell cycle

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Stop and Go Signs: Internal and External Signals at the Checkpoints

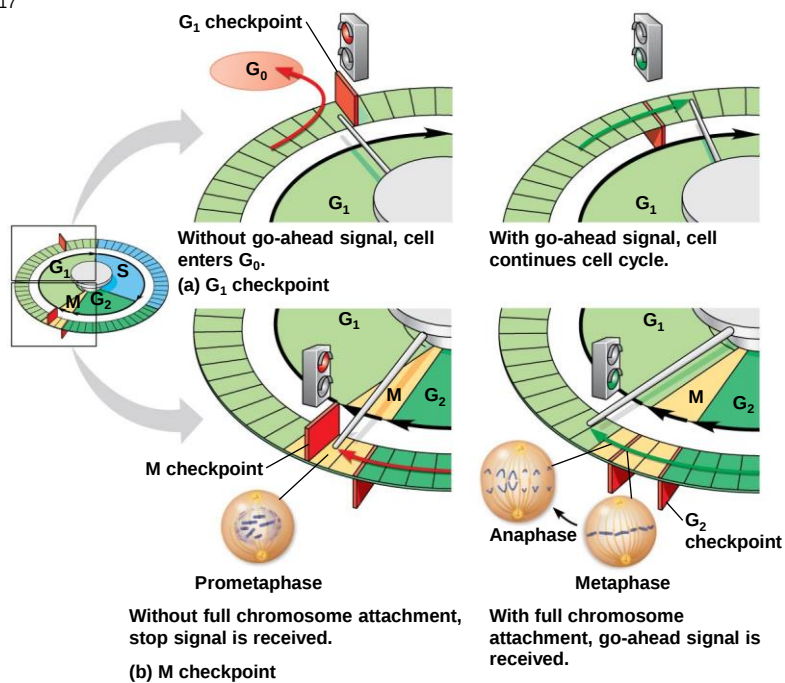
- Many signals registered at checkpoints come from cellular surveillance mechanisms within the cell
- Checkpoints also register signals from outside the cell
- Three important checkpoints are those in the G_1 , G_2 , and M phases

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- For many cells, the G_1 checkpoint seems to be the most important
- If a cell receives a go-ahead signal at the G_1 checkpoint, it will usually complete the S, G_2 , and M phases and divide
- If the cell does not receive the go-ahead signal, it will exit the cycle, switching into a nondividing state called the **G_0 phase**

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Figure 12.17



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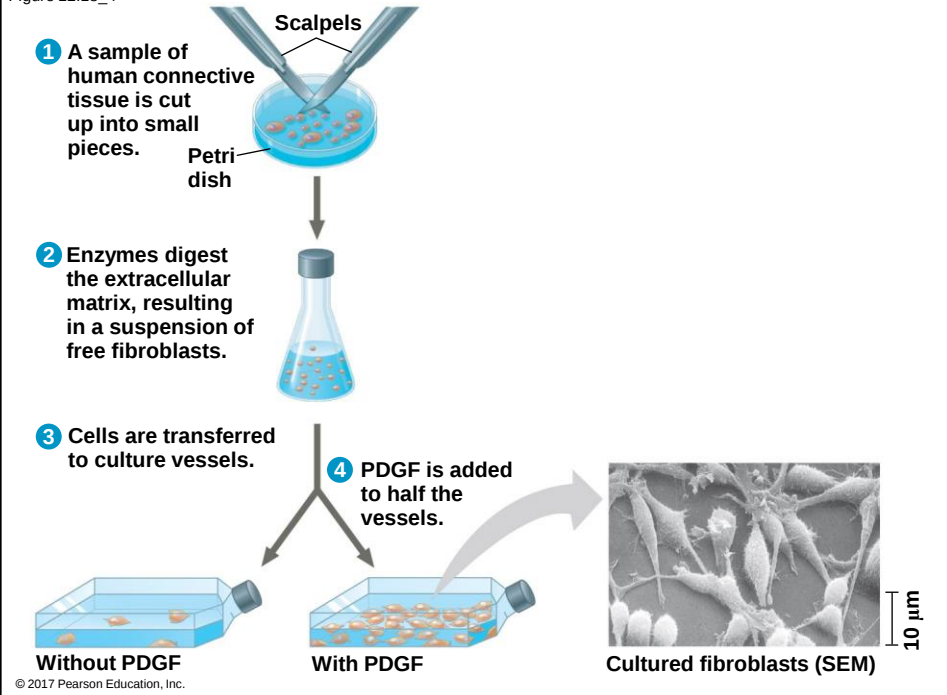
- An example of an internal signal is that cells will not begin anaphase until all chromosomes are properly attached to the spindle at the metaphase plate
- This mechanism ensures that daughter cells have the correct number of chromosomes

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- External factors that influence cell division include specific growth factors
- **Growth factors** are released by certain cells and stimulate other cells to divide
- Platelet-derived growth factor (PDGF) is made by blood cell fragments called platelets
- In **density-dependent inhibition**, crowded cells will stop dividing

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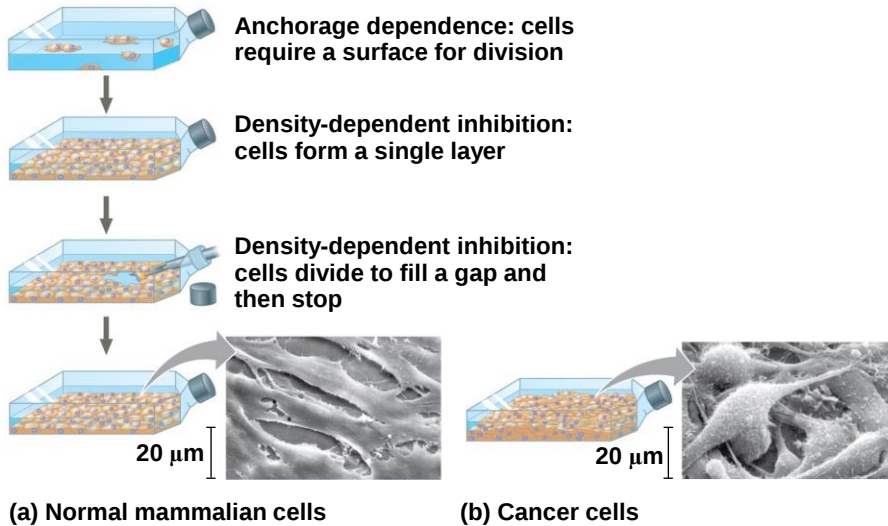
Figure 12.18_4



- Most cells also exhibit **anchorage dependence**—to divide, they must be attached to a substratum
- Density-dependent inhibition and anchorage dependence check the growth of cells at an optimal density
- Cancer cells exhibit neither type of regulation of their division

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Figure 12.19



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Loss of Cell Cycle Controls in Cancer Cells

- Cancer cells do not respond normally to the body's control mechanisms
- Cancer cells do not need growth factors to grow and divide:
 - They may make their own growth factor
 - They may convey a growth factor's signal without the presence of the growth factor
 - They may have an abnormal cell cycle control system

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- Cells that acquire the ability to divide indefinitely are undergoing **transformation**
- Cancer cells that are not eliminated by the immune system form tumors, masses of abnormal cells within otherwise normal tissue
- If abnormal cells remain only at the original site, the lump is called a **benign tumor**

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- **Malignant tumors** invade surrounding tissues and can undergo **metastasis**, the spread of cancer cells to other parts of the body, where they may form additional tumors
- Localized tumors may be treated with high-energy radiation, which damages the DNA in the cancer cells
- To treat metastatic cancers, chemotherapies that target the cell cycle may be used

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Figure 12.20

