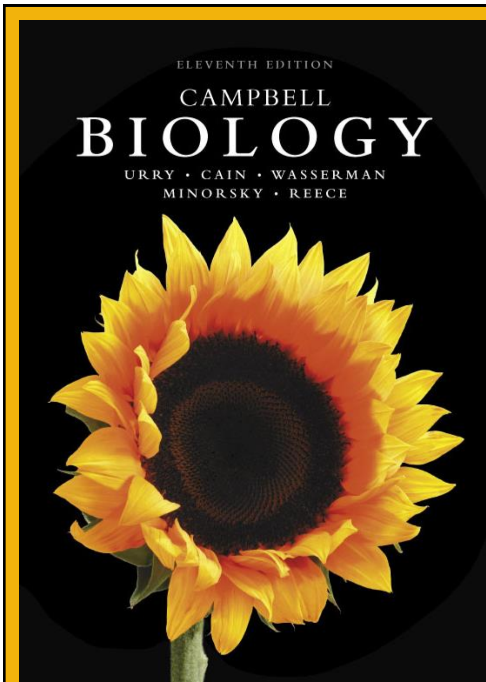


Chapter 12

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?

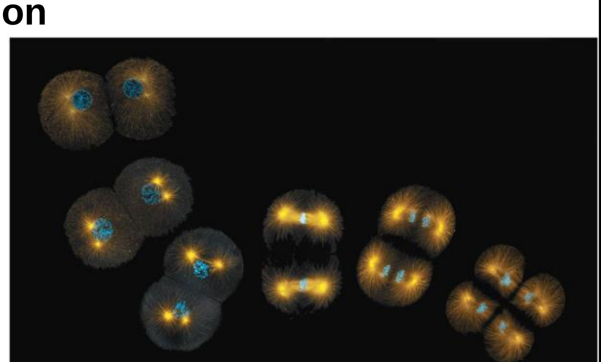
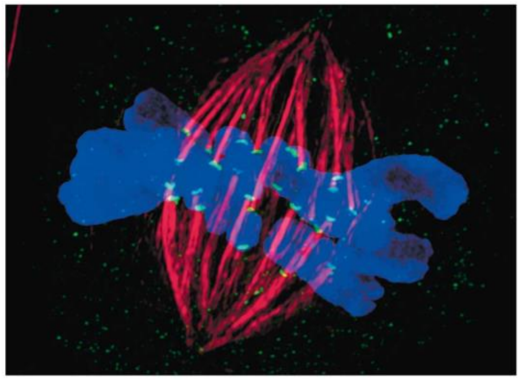


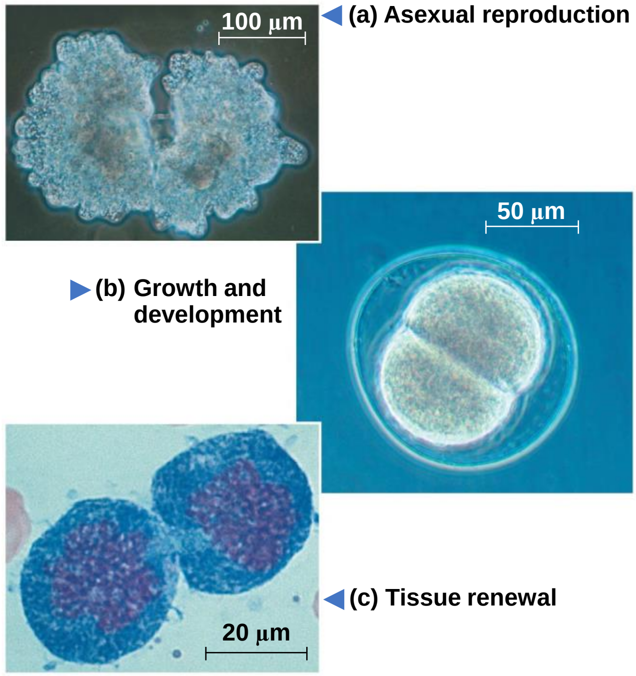
Figure 12.1a



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

- 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

Figure 12.2



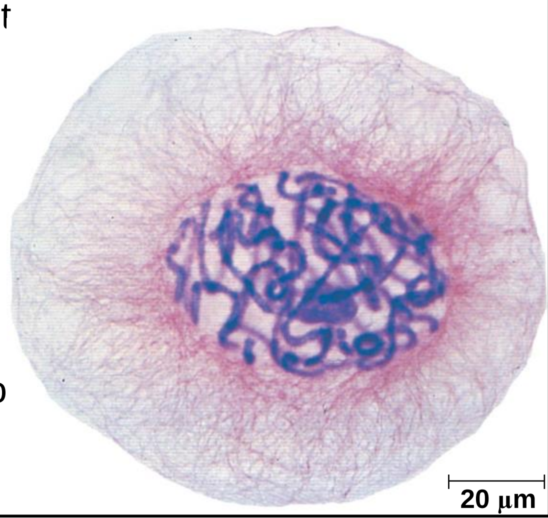
Concept 12.1: Most cell division results in genetically identical daughter cells

- 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*

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**

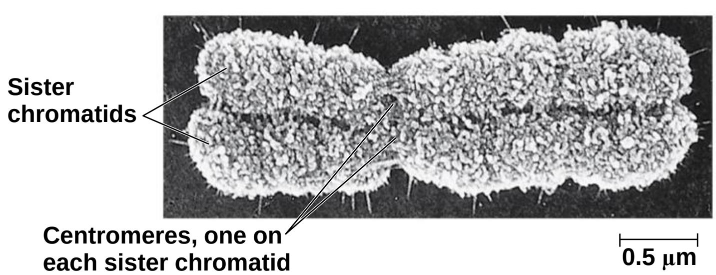


- Eukaryotic chromosomes consist of **chromatin**, a complex of DNA and protein that condenses during cell division
- Every eukaryotic species has a characteristic number of chromosomes in each cell nucleus
- **Somatic cells** (nonreproductive cells) have two sets of chromosomes (23 x 2 in humans)
-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

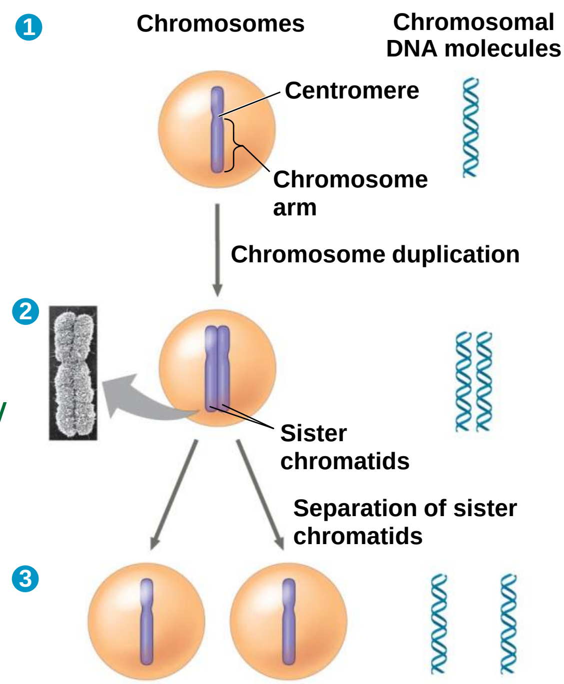
Distribution of Chromosomes During Eukaryotic Cell Division

- 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

Figure 12.4



- During cell division, the two sister chromatids of each duplicated chromosome *separate* and move into two nuclei
- *Once separate, the chromatids are called chromosomes*



BioFlix Animation: Chromosome Duplication

- 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)

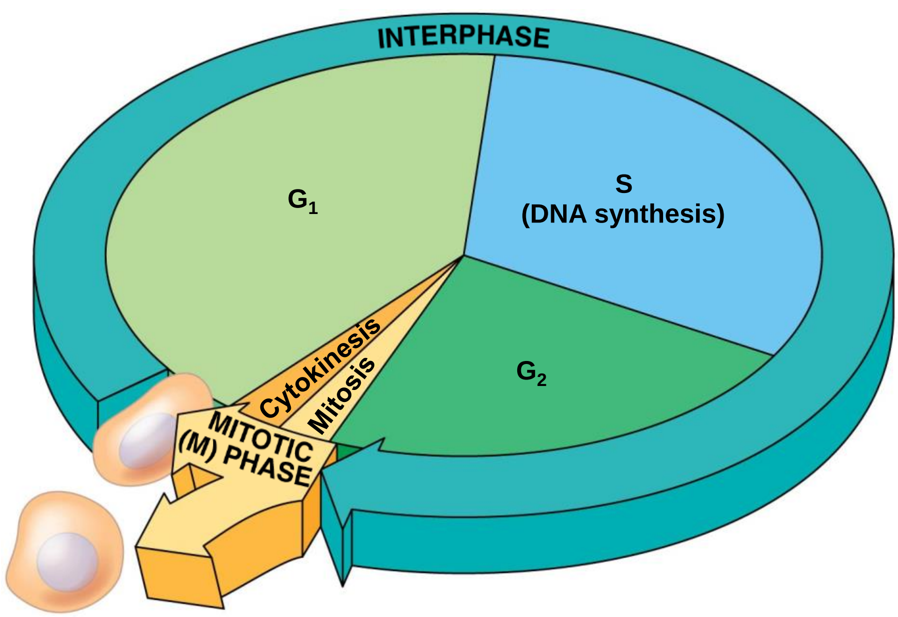
Concept 12.2: The mitotic phase alternates with interphase in the cell cycle

Phases of the Cell Cycle

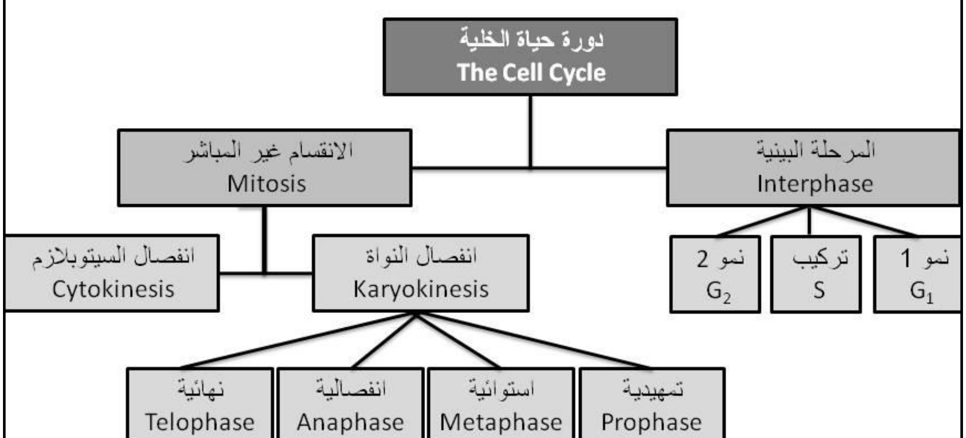
- The cell cycle consists of
  - **mitotic (M) phase** (mitosis and cytokinesis)
  - **interphase** (cell growth and copying of chromosomes in preparation for cell division)

- Interphase (about 90% of the cell cycle) can be divided into three phases:
  - **G_1 phase** ("first gap")
  - **S phase** ("synthesis")
  - **G_2 phase** ("second gap")
- *The cell grows during all three phases, but chromosomes are duplicated ONLY during the S phase*

Figure 12.6



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



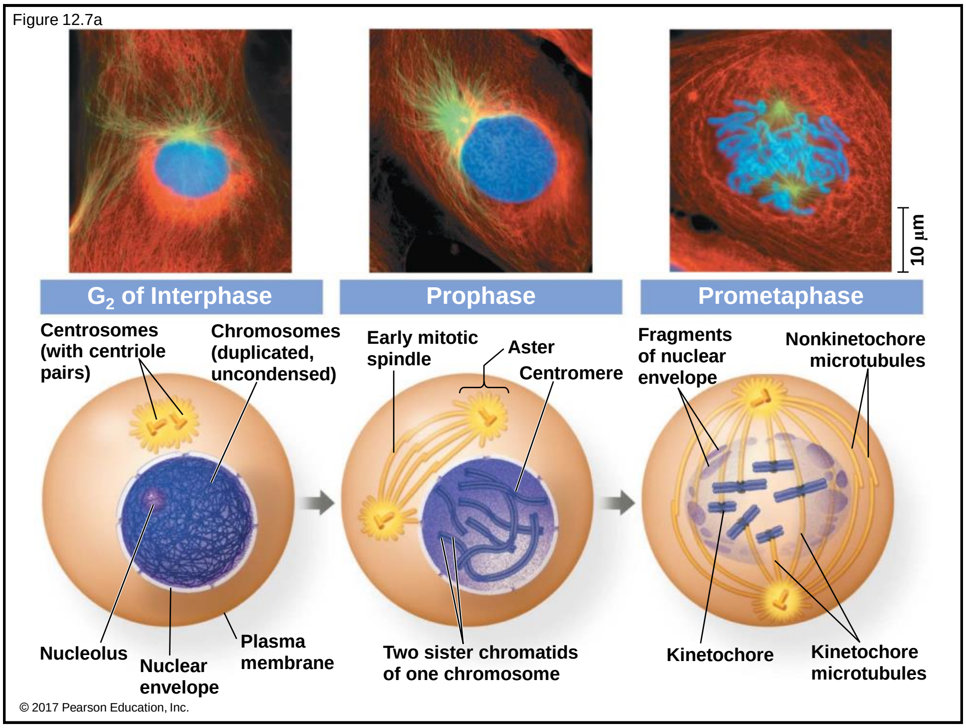


Figure 12.7a
10 µm
G_2 of Interphase
Prophase
Prometaphase
Centrosomes (with centriole pairs)
Chromosomes (duplicated, uncondensed)
Early mitotic spindle
Aster
Centromere
Fragments of nuclear envelope
Nonkinetochore microtubules
Nucleolus
Nuclear envelope
Plasma membrane
Two sister chromatids of one chromosome
Kinetochore
Kinetochore microtubules
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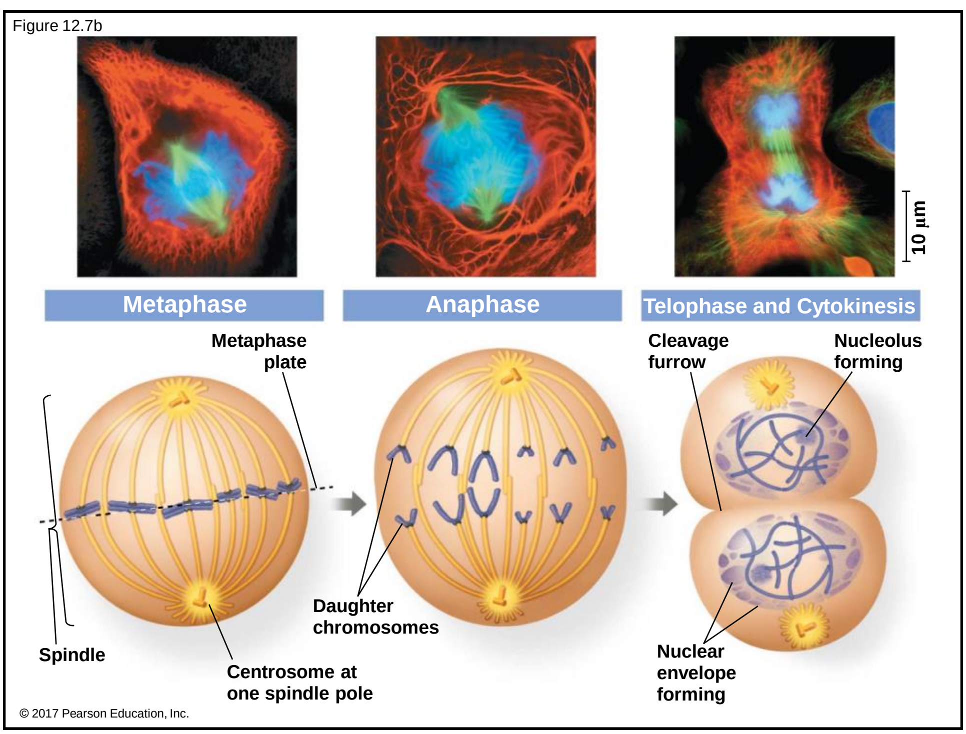
Figure 12.7b
10 µm
Metaphase
Anaphase
Telophase and Cytokinesis
Metaphase plate
Cleavage furrow
Nucleolus forming
Spindle
Centrosome at one spindle pole
Daughter chromosomes
Nuclear envelope forming
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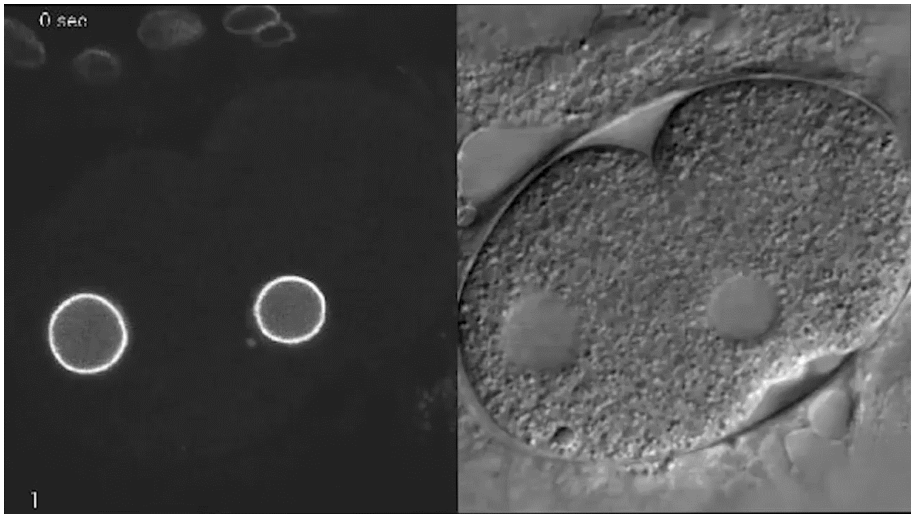
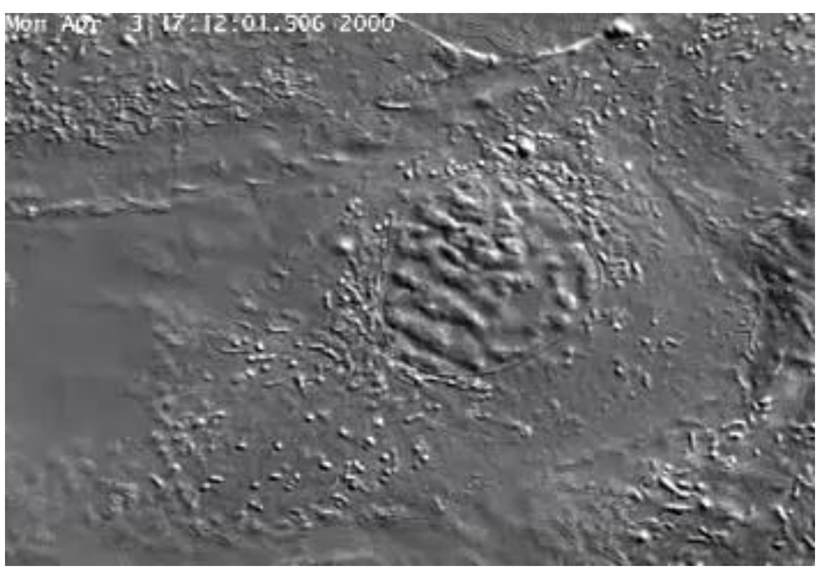
Video: Nuclear Envelope Formation



Video: Animal Mitosis (time-lapse)



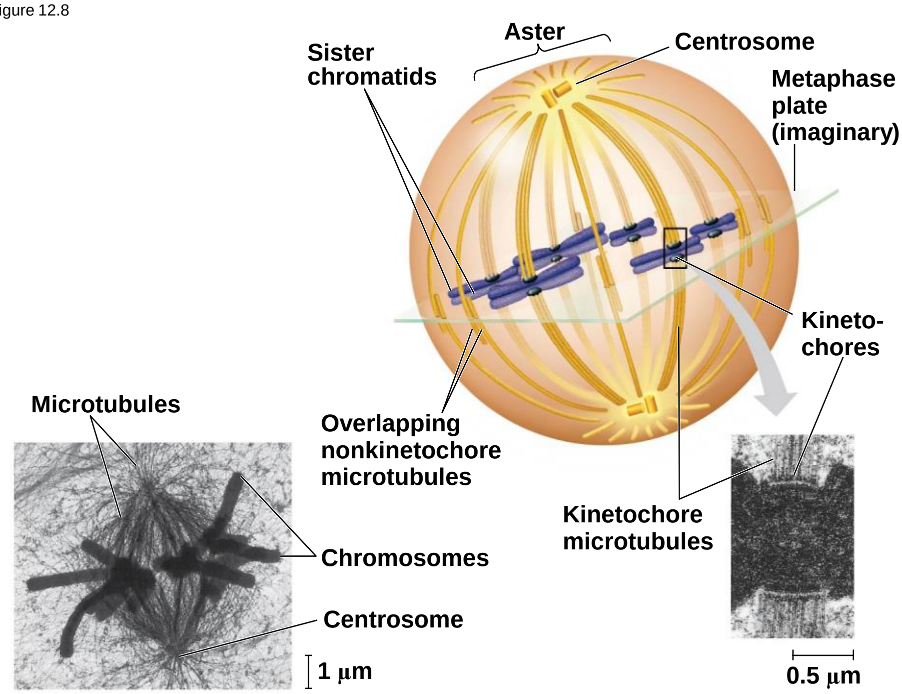
The Mitotic Spindle: *A Closer Look*

- 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

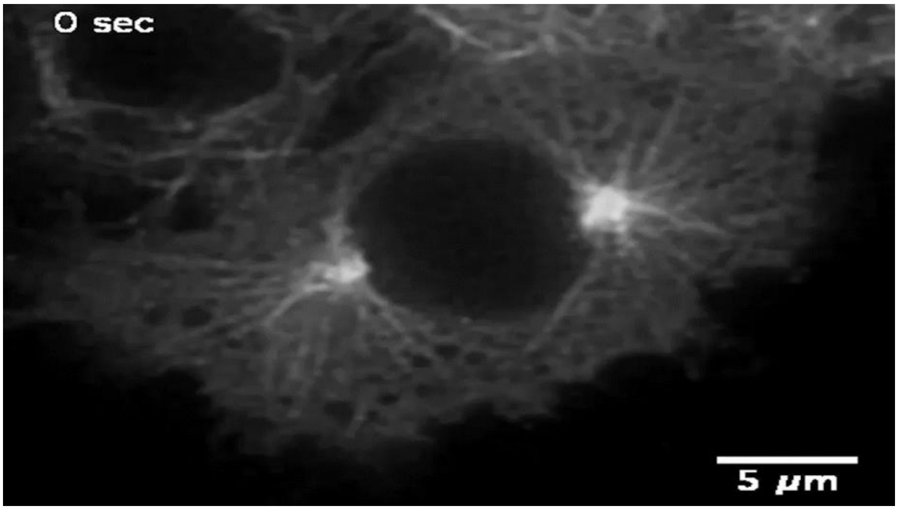
- An **aster** (a radial array of short microtubules) extends from each centrosome
- The spindle includes the centrosomes, the spindle microtubules, and the asters

- 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

Figure 12.8



Video: Spindle Formation During Mitosis



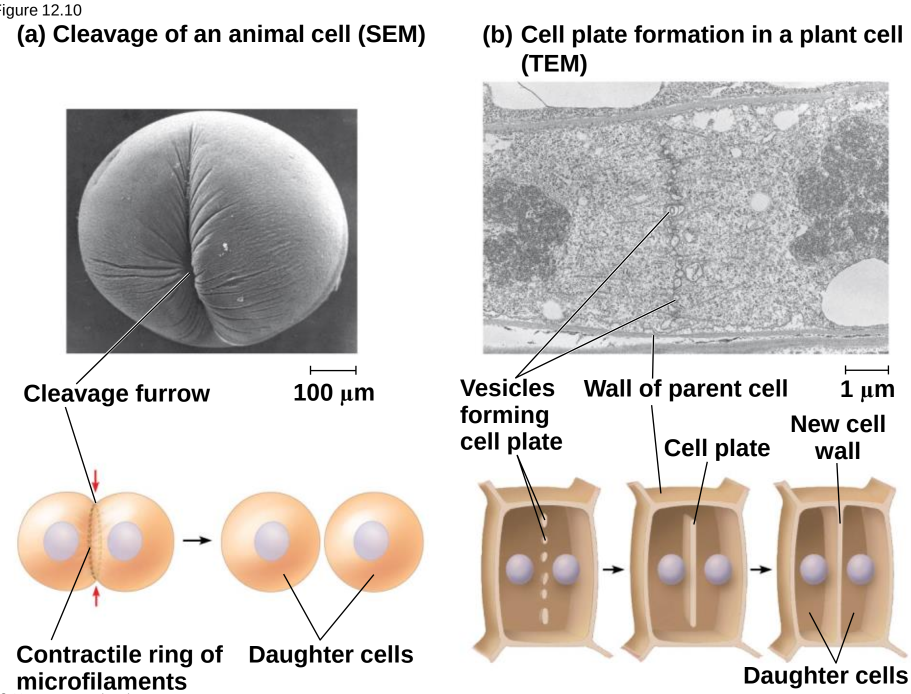
- In anaphase the **cohesins** are cut by an enzyme called **separase**
- Sister chromatids separate and move along the kinetochore microtubules toward opposite ends of the cell
- The microtubules shorten by depolymerizing at their kinetochore ends

- 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

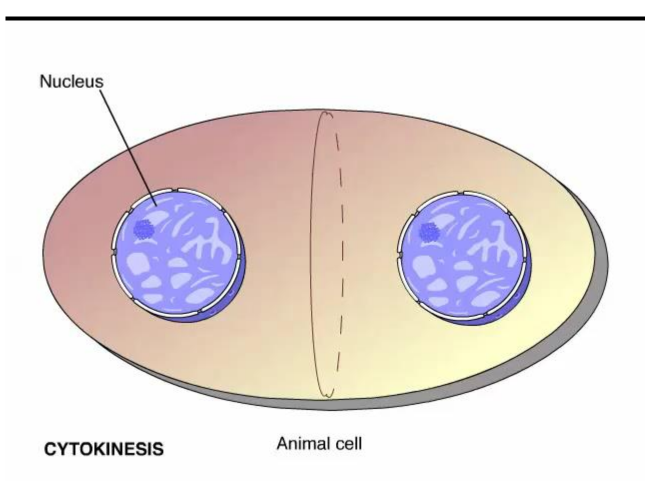
Cytokinesis: *A Closer Look*

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

Figure 12.10



Animation: Cytokinesis



Video: Myosin and Cytokinesis

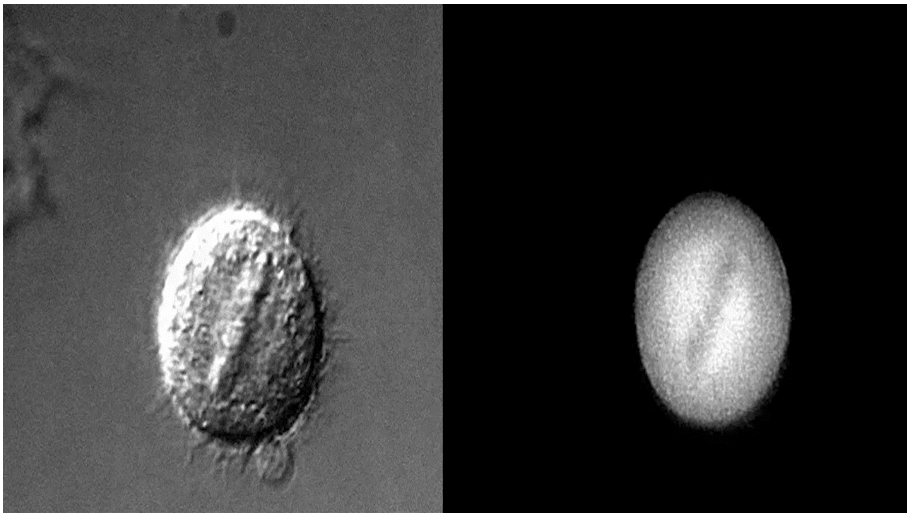
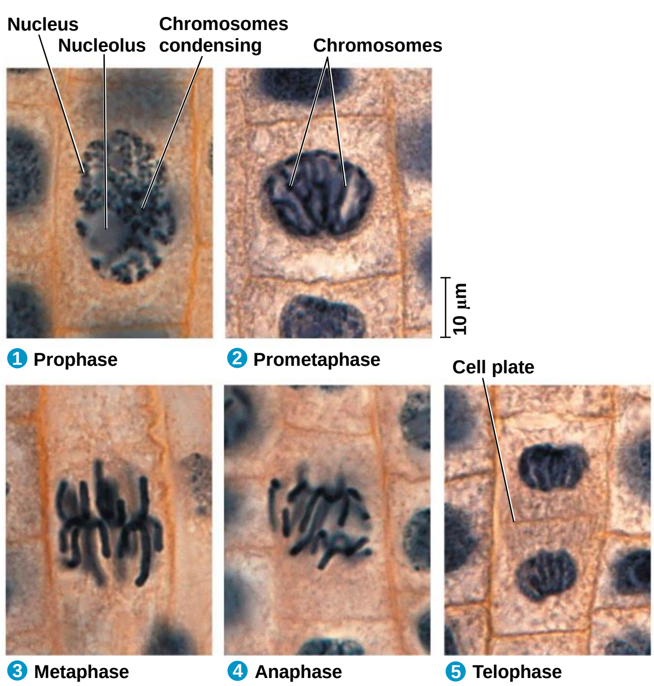


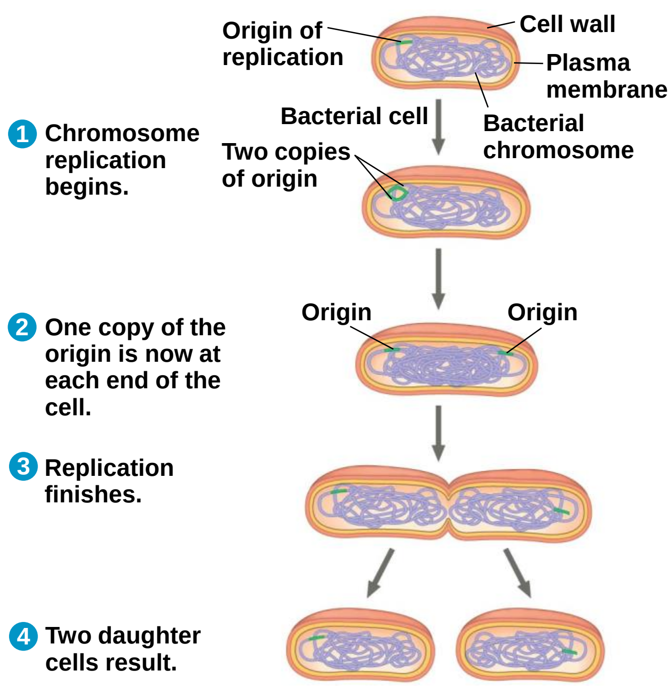
Figure 12.11



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

Figure 12.12_4



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

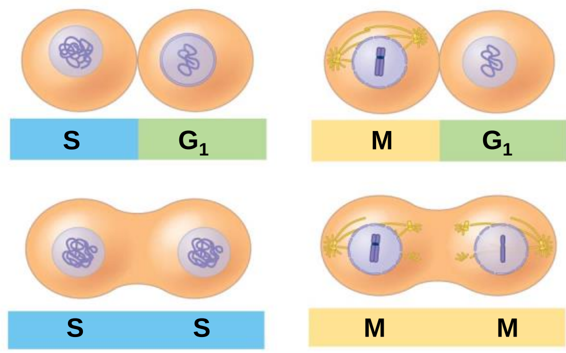
The Cell Cycle Control System

- 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

Figure 12.14

Experiment

Experiment 1 | **Experiment 2**



Results

G_1 nucleus immediately entered S phase and DNA was synthesized.

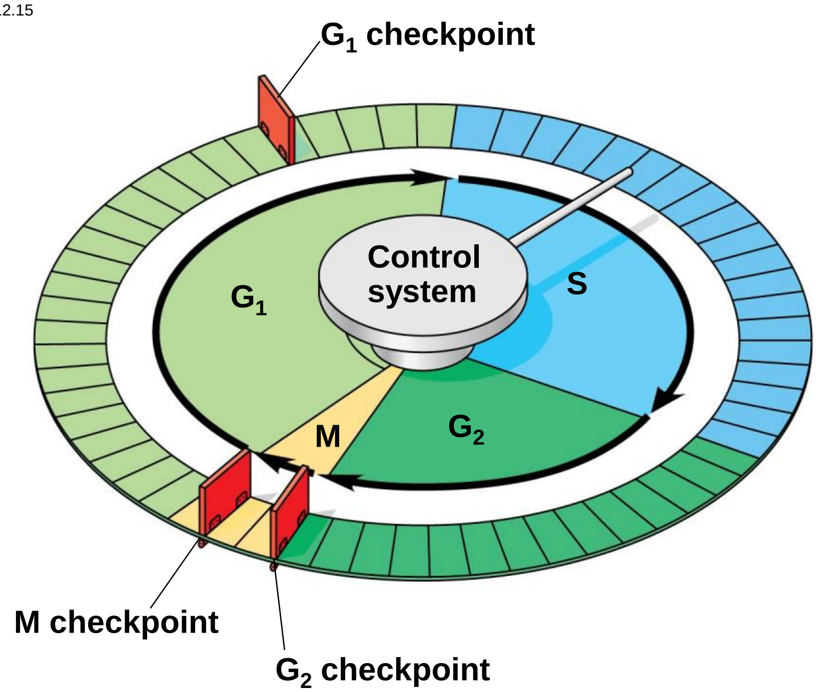
G_1 nucleus began mitosis without chromosome duplication.

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).

- 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

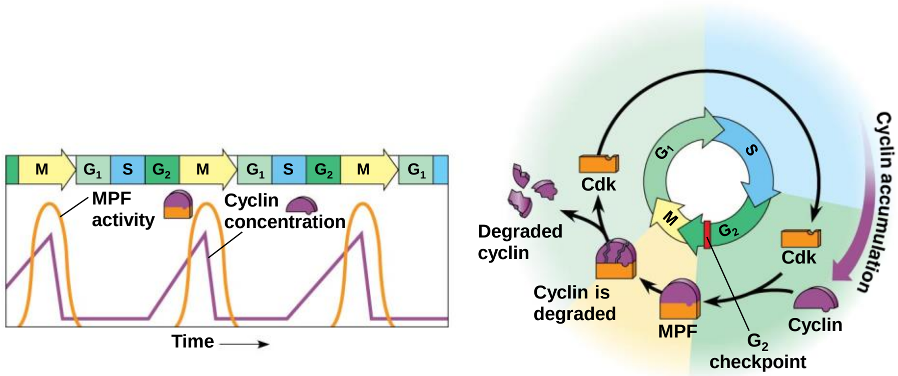
Figure 12.15



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 G_2 checkpoint into the M phase

Figure 12.16



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

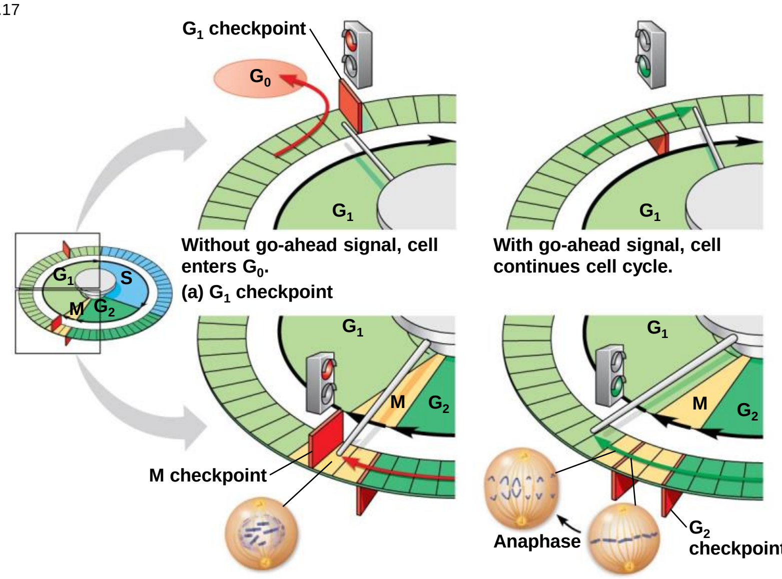
(b) Molecular mechanisms that help regulate the cell cycle

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

- 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**

Figure 12.17



Without go-ahead signal, cell enters G_0.

With go-ahead signal, cell continues cell cycle.

(a) G_1 checkpoint

Without full chromosome attachment, stop signal is received.

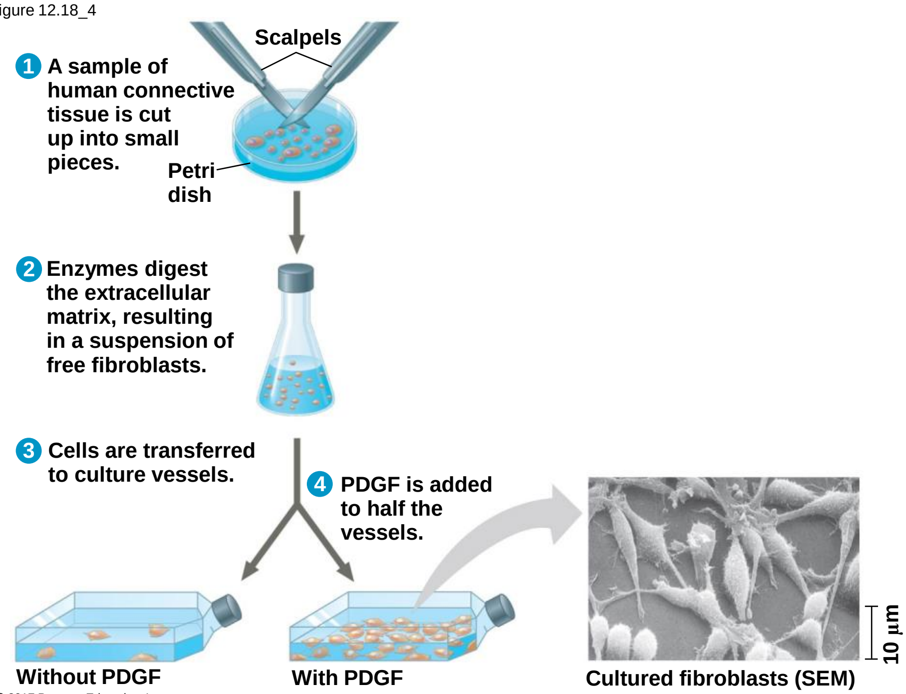
With full chromosome attachment, go-ahead signal is received.

(b) M checkpoint

- 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

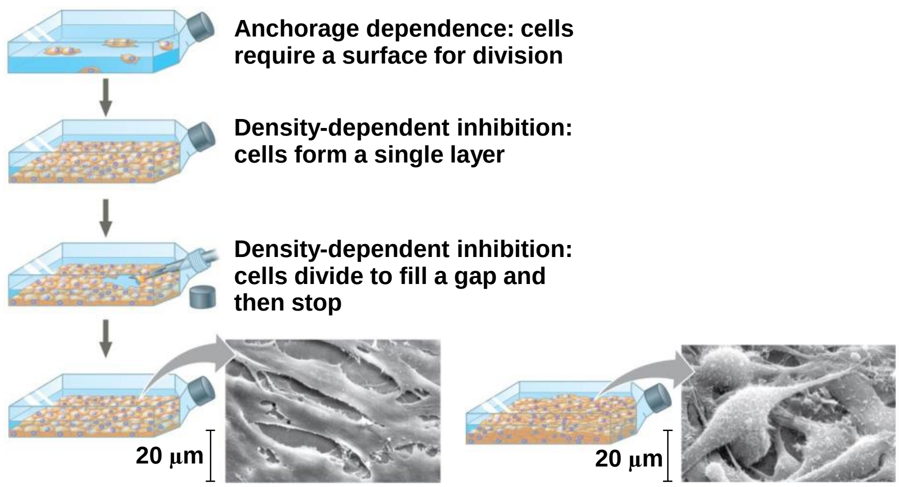
- External factors that influence cell division include specific growth factors
- **Growth factors** are released by certain cells and stimulate other cells to divide
- Platelet-derived growth factor (PDGF) is made by blood cell fragments called platelets
- In **density-dependent inhibition**, crowded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

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

Figure 12.19



(a) Normal mammalian cells

(b) Cancer cells

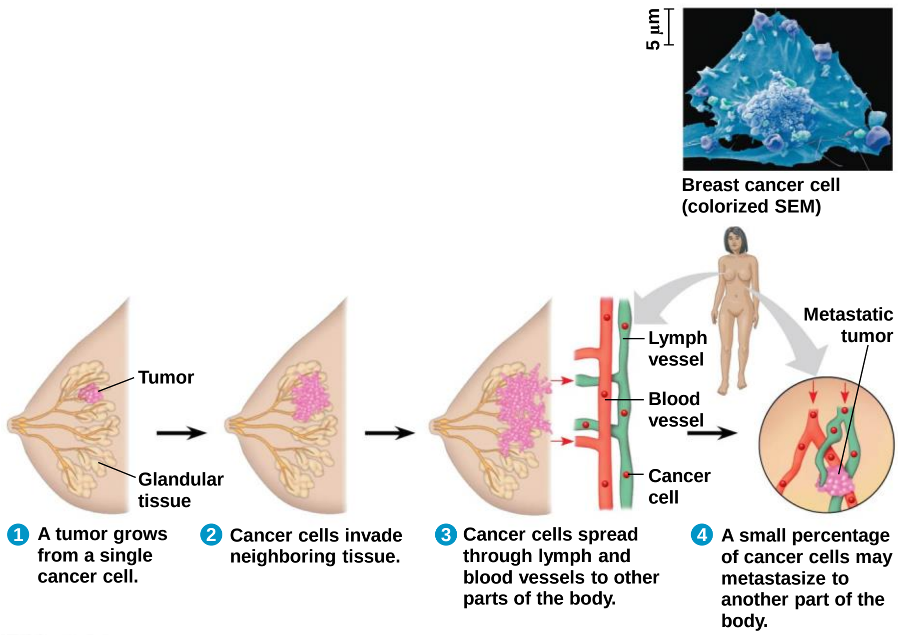
Loss of Cell Cycle Controls in Cancer Cells

- 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

- 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**

- **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

Figure 12.20



5 µm
Breast cancer cell (colorized SEM)
Tumor
Glandular tissue
Lymph vessel
Blood vessel
Cancer cell
Metastatic tumor
1 A tumor grows from a single cancer cell.
2 Cancer cells invade neighboring tissue.
3 Cancer cells spread through lymph and blood vessels to other parts of the body.
4 A small percentage of cancer cells may metastasize to another part of the body.