Overview: 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**
• In unicellular organisms, division of one cell reproduces the entire organism

• Multicellular organisms depend on cell division for
  – Development from a fertilized cell
  – Growth
  – Repair

• Cell division is an integral part of the cell cycle, the life of a cell from formation to its own division
(a) Reproduction

(b) Growth and development

(c) Tissue renewal
(a) Reproduction
(b) Growth and development

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(c) Tissue renewal
Most cell division results in genetically identical daughter cells

- Most cell division results in 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.

**Gametes** (reproductive cells: sperm and eggs) have half as many chromosomes as somatic cells.
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), which separate during cell division.
- The centromere is the narrow “waist” of the duplicated chromosome, where the two chromatids are most closely attached.
Sister chromatids

Centromere

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

• Once separate, the chromatids are called chromosomes
Chromosomes

Centromere

Chromosome arm

Chromosomal DNA molecules
Chromosomes

1. Chromosome duplication (including DNA replication) and condensation

2. Sister chromatids

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1. Chromosome duplication (including DNA replication) and condensation.

2. Separation of sister chromatids into two chromosomes.
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 only one set of chromosomes, half as many as the parent cell
The mitotic phase alternates with interphase in the cell cycle

- In 1882, the German anatomist Walther Flemming developed dyes to observe chromosomes during mitosis and cytokinesis
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 subphases
  – **G\textsubscript{1} phase** (“first gap”)
  – **S phase** (“synthesis”)
  – **G\textsubscript{2} phase** (“second gap”)
• The cell grows during all three phases, but chromosomes are duplicated only during the S phase
INTERPHASE

$G_1$

$G_2$

$S$

(DNA synthesis)

MITOTIC (M) PHASE

Cytokinesis

Mitosis
• Mitosis is conventionally divided into five phases
  – Prophase
  – Prometaphase
  – Metaphase
  – Anaphase
  – Telophase
• Cytokinesis overlaps the latter stages of mitosis
G₂ of Interphase

- Centrosomes (with centriole pairs)
- Chromatin (duplicated)

Prophase

- Nucleolus
- Nuclear envelope
- Plasma membrane
- Early mitotic spindle
- Centrosome
- Aster
- Chromosome, consisting of two sister chromatids

Prometaphase

- Metaphase plate
- Fragments of nuclear envelope
- Nonkinetochore microtubules
- Kinetochore
- Kinetochore microtubule
- Centromere

Metaphase

- Anaphase
- Metaphase plate
- Centrosome at one spindle pole
- Daughters chromosomes
- Cleavage furrow

Anaphase

- Telophase and Cytokinesis
- Daughter chromosomes
- Nuclear envelope forming
- Nucleolus forming
G2 of Interphase

- Centrosomes (with centriole pairs)
- Chromatin (duplicated)
- Nucleolus
- Nuclear envelope
- Plasma membrane

Prophase

- Early mitotic spindle
- Centromere
- Chromosome, consisting of two sister chromatids

Prometaphase

- Fragments of nuclear envelope
- Nonkinetochore microtubules
- Kinetochore
- Kinetochore microtubule
Metaphase
- Metaphase plate
- Spindle
- Centrosome at one spindle pole

Anaphase
- Daughter chromosomes

Telophase and Cytokinesis
- Cleavage furrow
- Nuclear envelope forming
- Nucleolus forming
G₂ of Interphase  Prophase  Prometaphase

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Metaphase

Anaphase

Telophase and Cytokinesis

10 µm
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**, an imaginary structure at the midway point between the spindle’s two poles.
Sister chromatids

Aster

Centrosome

Metaphase plate (imaginary)

Kineto-chores

Overlapping nonkinetochore microtubules

Kinetochore microtubules

Microtubules

Chromosomes

Centrosome

0.5 µm

1 µm

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Kinetochores

Kinetochores microtubules

0.5 µm
Microtubules

Chromosomes

Centrosome

1 µm
• In anaphase, sister chromatids separate and move along the kinetochore microtubules toward opposite ends of the cell
• The microtubules shorten by depolymerizing at their kinetochore ends
**EXPERIMENT**

**RESULTS**

**CONCLUSION**
CONCLUSION

Chromosome movement

Microtubule

Motor protein

Chromosome

Kinetochore

Tubulin subunits

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• Nonkinetochore microtubules from opposite poles overlap and push against each other, elongating the cell
• In telophase, genetically identical daughter nuclei form at opposite ends of the 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
Video: Animal Mitosis

Video: Sea Urchin (Time Lapse)
(a) Cleavage of an animal cell (SEM)

- Cleavage furrow
- Contractile ring of microfilaments
- Daughter cells

100 µm

(b) Cell plate formation in a plant cell (TEM)

- Vesicles forming cell plate
- Wall of parent cell
- Cell plate
- New cell wall
- Daughter cells

1 µm
(a) Cleavage of an animal cell (SEM)

- Cleavage furrow
- Contractile ring of microfilaments
- Daughter cells

100 µm
Cell plate formation in a plant cell (TEM)

- Vesicles forming cell plate
- Wall of parent cell
- Cell plate
- New cell wall
- Daughter cells

Scale: 1 µm
Vesicles forming cell plate

Wall of parent cell

1 µm
Chromatin condensing
Nucleus
Nucleolus
Chromosomes
Cell plate

1. Prophase
2. Prometaphase
3. Metaphase
4. Anaphase
5. Telophase
Prophase

10 µm
Chromosomes

Prometaphase

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3 Metaphase
4 Anaphase
Telophase

Cell plate 10 µm
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
1 Chromosome replication begins.
1 Chromosome replication begins.

2 Replication continues.
1 Chromosome replication begins.

2 Replication continues.

3 Replication finishes.
1. Chromosome replication begins.

2. Replication continues.

3. Replication finishes.

4. Two daughter cells result.
The Evolution of Mitosis

- Since prokaryotes evolved before eukaryotes, mitosis probably evolved from binary fission
- Certain protists exhibit types of cell division that seem intermediate between binary fission and mitosis
(a) Bacteria

(b) Dinoflagellates

(c) Diatoms and some yeasts

(d) Most eukaryotes

- Bacterial chromosome
- Intact nuclear envelope
- Chromosomes
- Microtubules
- Kinetochore microtubule
- Intact nuclear envelope
- Kinetochore microtubule
- Fragments of nuclear envelope
(a) Bacteria

(b) Dinoflagellates

- Bacterial chromosome
- Chromosomes
- Microtubules
- Intact nuclear envelope
(c) Diatoms and some yeasts

(d) Most eukaryotes
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
Evidence for Cytoplasmic Signals

• 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
When a cell in the S phase was fused with a cell in G₁, the G₁ nucleus immediately entered the S phase—DNA was synthesized.

When a cell in the M phase was fused with a cell in G₁, the G₁ nucleus immediately began mitosis—a spindle formed and chromatin condensed, even though the chromosome had not been duplicated.
The Cell Cycle Control System

- 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.
G₁ checkpoint

M checkpoint

G₂ checkpoint

S

Control system
• For many cells, the G₁ checkpoint seems to be the most important
• If a cell receives a go-ahead signal at the G₁ checkpoint, it will usually complete the S, G₂, 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 G₀ phase
(a) Cell receives a go-ahead signal.

(b) Cell does not receive a go-ahead signal.
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 (Cdns)**
- Cdns activity fluctuates during the cell cycle because it is controled by cyclins, so named because their concentrations vary with the cell cycle
- **MPF** (maturation-promoting factor) is a cyclin-Cdk complex that triggers a cell’s passage past the G₂ checkpoint into the M phase
(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle

(b) Molecular mechanisms that help regulate the cell cycle
(a) Fluctuation of MPF activity and cyclin concentration during the cell cycle
(b) Molecular mechanisms that help regulate the cell cycle

Cdk

Degraded cyclin

Cyclin is degraded

MPF

Cdk

Cyclin

G1

S

G2

M

G2 checkpoint

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

- An example of an internal signal is that kinetochores not attached to spindle microtubules send a molecular signal that delays anaphase.

- Some external signals are growth factors, proteins released by certain cells that stimulate other cells to divide.

- For example, platelet-derived growth factor (PDGF) stimulates the division of human fibroblast cells in culture.
1. A sample of human connective tissue is cut up into small pieces.

2. Enzymes digest the extracellular matrix, resulting in a suspension of free fibroblasts.

3. Cells are transferred to culture vessels.

4. PDGF is added to half the vessels.
• A clear example of external signals is **density-dependent inhibition**, in which crowded cells stop dividing.

• Most animal cells also exhibit **anchorage dependence**, in which they must be attached to a substratum in order to divide.

• Cancer cells exhibit neither density-dependent inhibition nor anchorage dependence.
Anchorage dependence

Density-dependent inhibition

Density-dependent inhibition

(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 may 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
A normal cell is converted to a cancerous cell by a process called **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 **metastasize**, exporting cancer cells to other parts of the body, where they may form additional tumors.
A tumor grows from a single cancer cell.

Cancer cells invade neighboring tissue.

Cancer cells spread through lymph and blood vessels to other parts of the body.

Cancer cells may survive and establish a new tumor in another part of the body.
Recent advances in understanding the cell cycle and cell cycle signaling have led to advances in cancer treatment
Mitosis and Cytokinesis

MITOTIC (M) PHASE

- Prometaphase
- Metaphase
- Anaphase
- Telophase and Cytokinesis

INTERPHASE

- G₁
- S
- G₂

Cytokinesis

Mitosis
One sister chromatid
Interphase

Chromatin
Nuclear envelope

Prometaphase

Metaphase

Anaphase

Microtubules

Nuclear envelope forming

Telophase and cytokinesis

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