Chapter 11: Cell Communication.

- Cells communicate with each other through **cell-cell signaling**.
- **Signaling molecules** are the chemical messengers used (sometimes called **ligands**)

Why do cells need to signal?

Signal transduction pathways

•Are similar in microbes and mammals, suggesting an early origin

–Suggests an evolutionary connection.

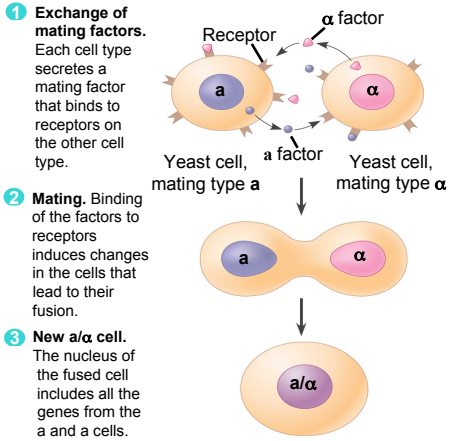
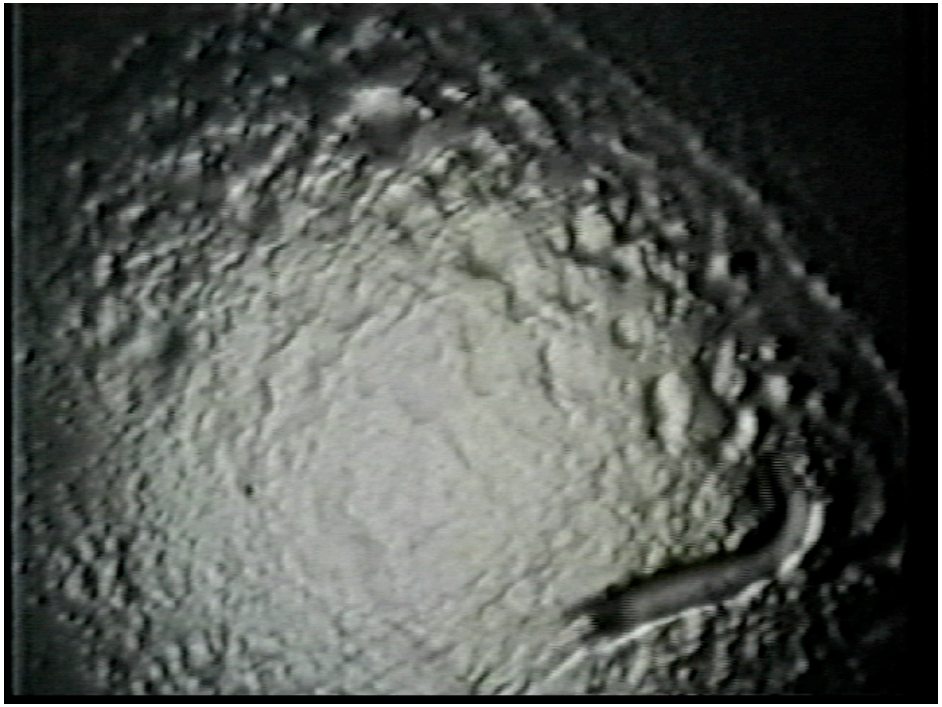


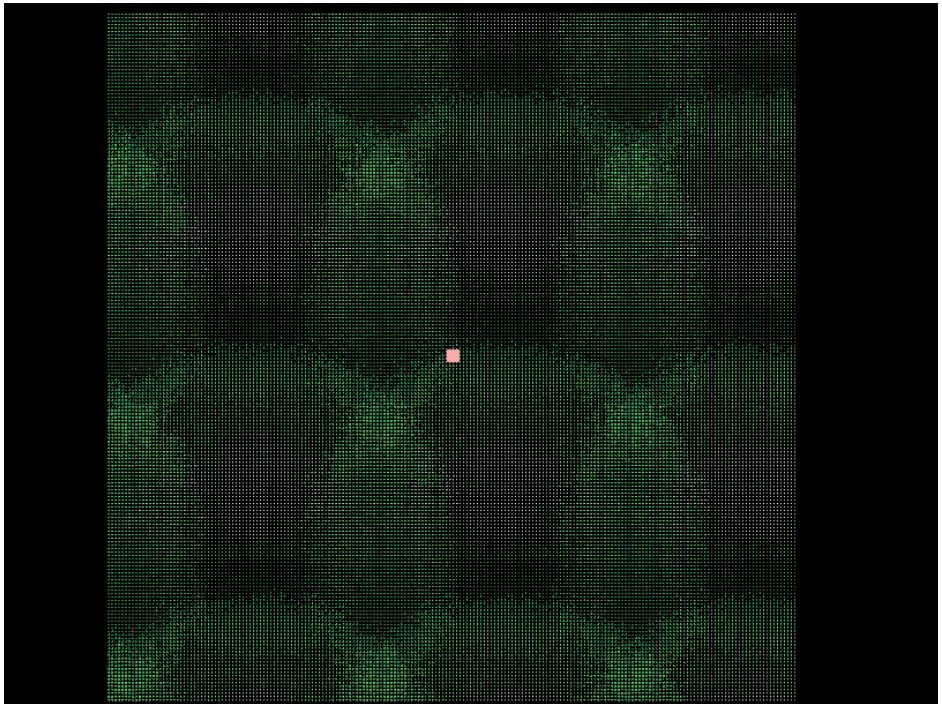
Figure 11.2

March 26 1996
Darkfield movie of DH1 and PDI ko #27

Density = $3.3 \times 10^7/cm^2$
DH1 is to the right

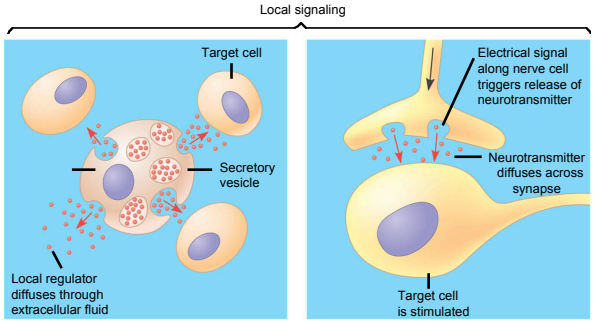
Non Subtracted Images





Signaling in multicellular organisms

- Can be both Local or Long-Distance
- **Local Signaling**
  - **Paracrine**: The signaling molecule is released and diffuses to the neighboring cells. This is local Signaling.
  - **Synaptic Signaling.** Nerve cells signal across a **synapse.**



(a) Paracrine signaling. A secreting cell acts on nearby target cells by discharging molecules of a local regulator (a growth factor, for example) into the extracellular fluid.

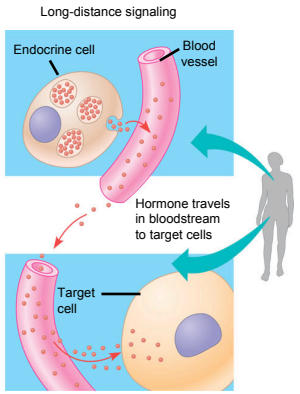
(b) Synaptic signaling. A nerve cell releases neurotransmitter molecules into a synapse, stimulating the target cell.

Figure 11.5 A B

Long Distance Signaling

•**Endocrine:** Signal is released into a carrier system, such as blood, which carries the molecules to the target cells, which can be far away.

– Examples of this are hormones.



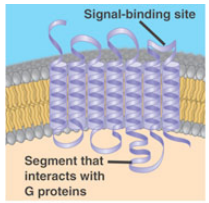
(c) Hormonal signaling. Specialized endocrine cells secrete hormones into body fluids, often the blood. Hormones may reach virtually all body cells.

Figure 11.5 C

- For most signals the signaling molecule does not enter the cell
  - The signal is relayed through the membrane, from the outside to the inside.

- **How is this done?**

- The **signaling molecule (ligand)** binds to a **membrane receptor** on the outside of the cell.
- This receptor spans the membrane and has both an **extracellular** and a **cytosolic** domain.
- The **cytosolic** domain **changes shape** when bound to ligand.
  - The **ligand** is not always a diffusible molecule



G-protein-linked receptor

The signal-transduction pathway

- **The response** of the cell to a signaling molecule is mediated through a **signal-transduction pathway.**
- This occurs through 3 steps.
  - **Reception**
  - **Transduction**
  - **Response**

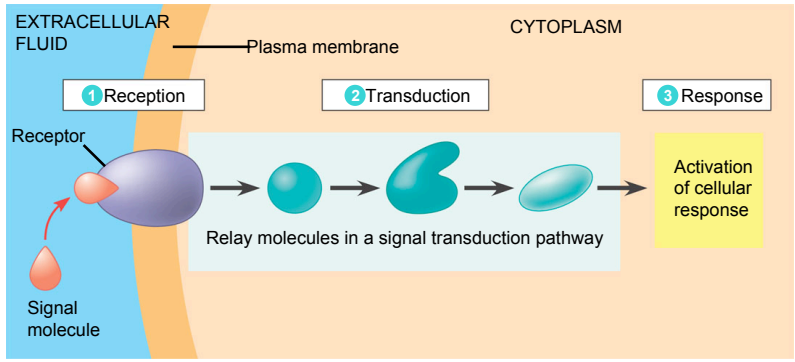


Figure 11.6

Receptors

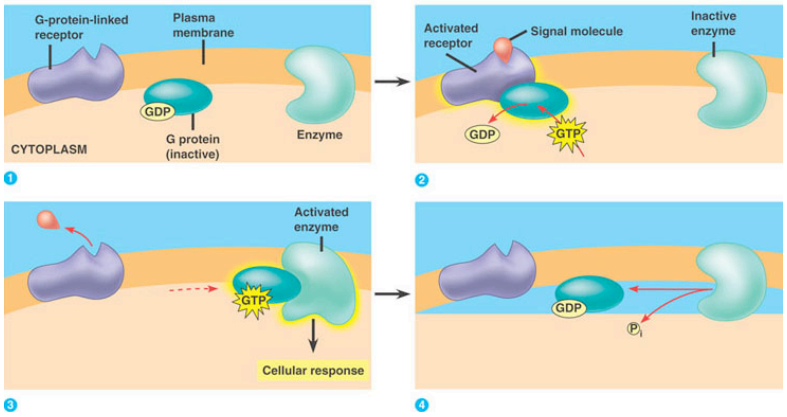
- *There are three major types of membrane receptors.*
  - **G-Protein** linked receptors. Figure 11.7a
  - **Tyrosine-Kinase** Receptors
  - **Ligand-gated** Ion channels.

Focus on the G-Protein linked receptors

Know the other pathways!

G-Protein linked receptors

- Are connected to a G-protein that is activated when a ligand binds to the receptor.
- The activation triggers the displacement of the GDP by GTP. This activated G-protein then goes on to activate other proteins.
- **Example:** Slime mold cAMP receptor system.



Tyrosine-Kinase Receptors.

- Form dimers.
- Phosphorylate the tyrosine amino acids on the other receptor
- This activates the receptor dimer
- Example: **Growth factor receptor**.

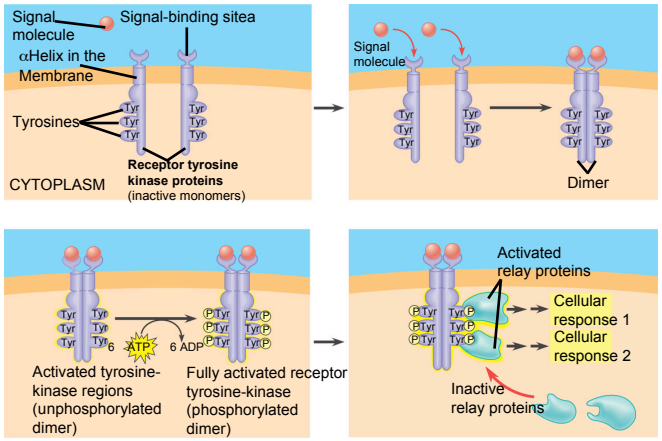


Figure 11.7

Ligand-gated Ion channels

- Binding of ligand opens up an ion channel.
- The opening of the channel leads to a net flow of ions into or out of the cell.
- This triggers an intracellular response. Na^+, Ca^{2+}

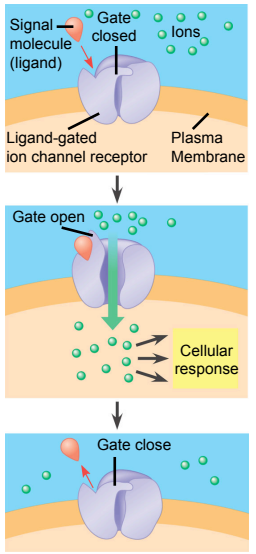


Figure 11.7

Intracellular Receptors.

- Small **non polar** molecules, **Hormones**, can travel through the membrane where they can bind to an **internal receptor protein**
- Usually activates a transcription factor.

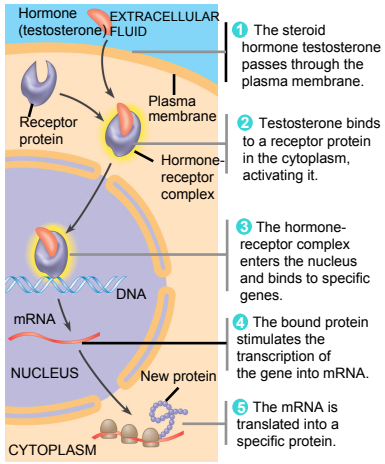


Figure 11.6

Transduction

The signal is relayed via cascades of molecular interactions in the cell.

- **Amplification** of the signal can be achieved by **phosphorylation cascades** and **second messengers**
- Adding or removing phosphate groups regulates protein activity.
- **Kinases** use ATP to phosphorylate molecules.
- **Phosphatases** remove phosphate groups from molecules.

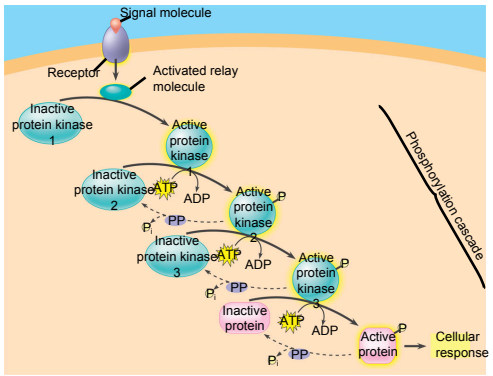


Figure 11.9

Second messengers

– cAMP and Ca^{2+} or other small molecules (IP3, DAG)

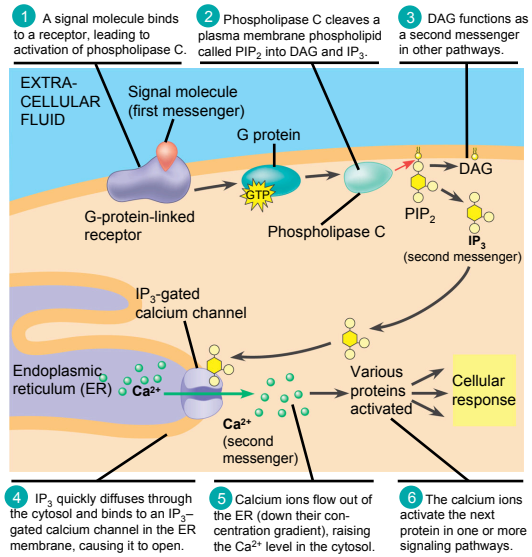


Figure 11.13

Nuclear response to a signal

Regulate genes by activating transcription factors that turn genes on or off

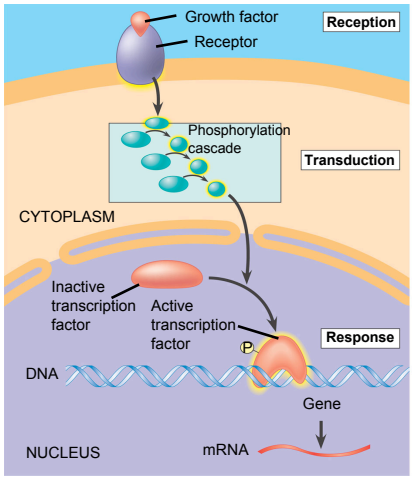


Figure 11.14

The **signaling** is very **specific**

- **Receptors** only bind to a specific ligand.

- The same signaling molecule can lead to different responses in different types of cells.
  - **Example:** Epinephrine
  - In liver it triggers breakdown of glycogen
  - In the heart it increase the heart beat.

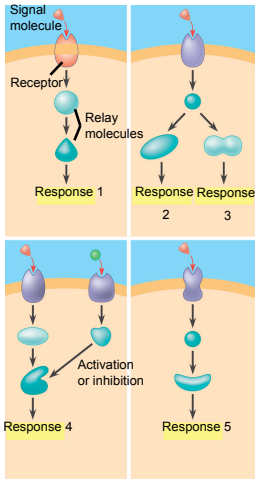
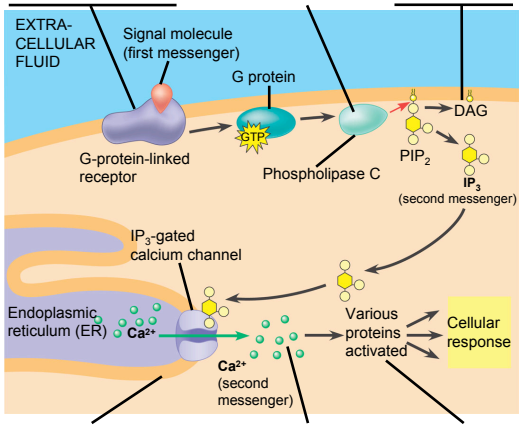


Figure 11.17

Signal Transduction



Summary of signaling.

- Via membrane proteins.
  - **G-Protein linked receptors. Many different G-proteins**
  - **Tyrosine-Kinase Receptors.**
  - **Ligand-gated Ion channels.**
- Directly **Intracellular Receptors**
  - Non-polar molecules that bind to receptors inside cells. Usually activate transcription factors.
- Both can lead to amplification of signal.
  - **Branching**: Binding of signaling molecule can trigger several different responses inside cell.
  - Combination of two different signals.

Chapter 12 The Cell Cycle.

Every living organism must be able to **reproduce** in order to survive.

- Reproduction occurs by **Cell Division.**
  - It is part of the **Cell Cycle**.
  - It results in genetically identical daughter cells
- The **Cell Cycle** is the foundation of life.
- Unicellular organisms
  - Reproduce by cell division
- Multicellular organisms depend on cell division for
  - Development from a fertilized cell
  - Growth
  - Repair

- Eukaryotic cell division consists of
  - **Mitosis**, the division of the nucleus
  - **Cytokinesis**, the division of the cytoplasm
- In **meiosis**
  - **Sex cells** are produced after a **reduction** in **chromosome number**

Genome

Brief review

- The cells genetic information is called its **genome**.
- The genome contains the recipe for running and building the cell.
- The genome contains all the **chromosomes.**
- The chromosome is made up of a very long linear **DNA strand** containing up to thousands of **genes**, each gene specifying a specific protein.
- This strand is associated with various proteins that maintain the structure and control the activity of genes.
- This DNA protein complex is called **chromatin.**
  - A cell can have 3 m long DNA strands even though it is only 10 µm long.

The Cell Cycle is divided into Two Phases
Interphase and **Mitosis (Mitotic phase)**

- Interphase is split into 3 phases
- **G_1, S, G_2**
- After G_2 the cell enters mitosis.

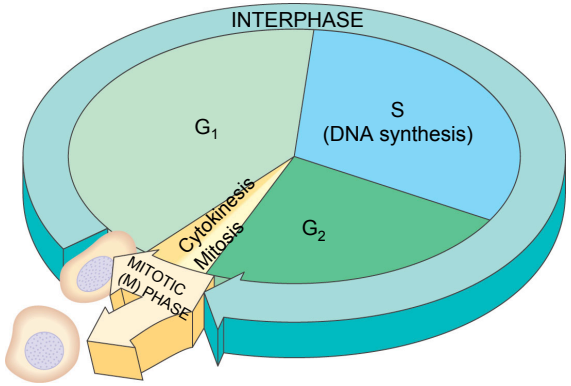


Figure 12.5

- DNA is **Duplicated** in **S** phase! **Not** in **mitosis**.
- After the S phase each chromosome has an identical copy, the pair are called **sister chromatids.**
- They are joined at the **Centeromere,** a waist like region near the center of the chromosome.
- **Kinetochores,** where the microtubules attach, are formed here as well.

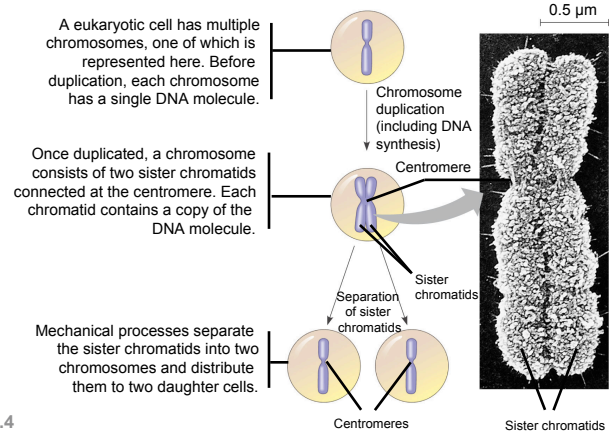


Figure 12.4

Mitosis is split into five subphases
It is made up of **mitosis** and **cytokinesis**

- **Prophase**
  - Two centerosomes already formed begin to move towards opposite poles of the cell. Microtubules grow from the centerosomes. Chromosomes begin to condense and sister chromatid pairs become visible.
- **Prometaphase**
  - Nuclear envelope begins to break down.
  - Each of the two sister chromatids has now a structure called **Kinetochore** located at the centeromer region. Microtubules begin to attach to the kinetochores.
- **Metaphase**
  - Centerosomes are at opposite poles. Chromosomes convene in the center between the two centerosomes .
- **Anaphase**
  - The two sister chromatids are separated as the microtubules shorten.
- **Telophase**
  - Two daughter nuclei form and the nuclear envelope arises from the fragments of the parents nuclear envelope. The chromosomes become less tightly coiled.

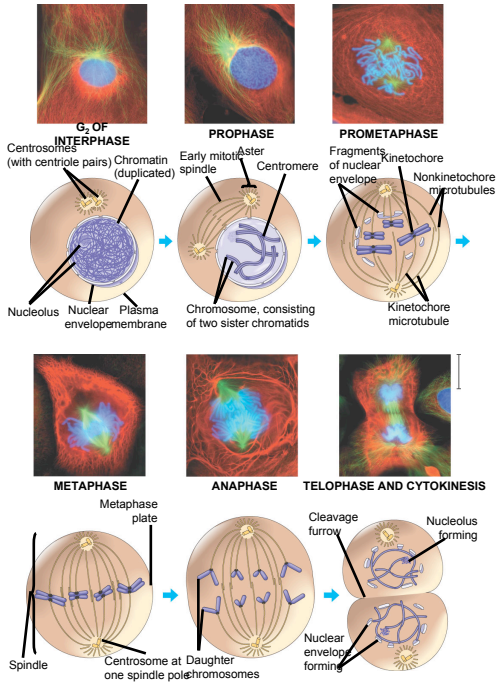
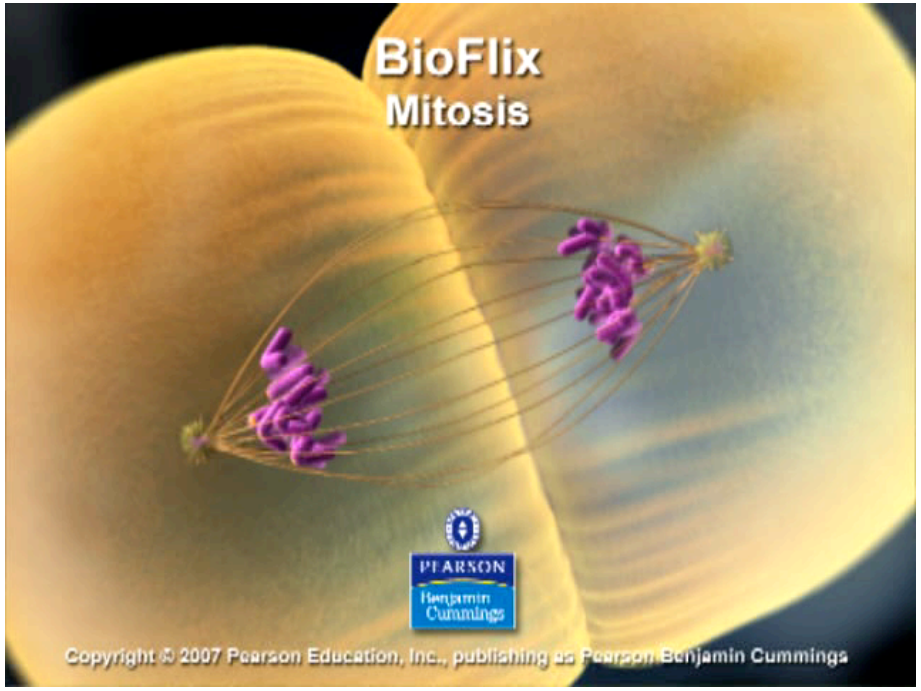


Figure 12.6



- Every **Eukaryotic** cell has a characteristic number of chromosomes.
  - **Diploid** cells have **pairs** of homologous chromosomes.
  - **Haploid** cells have **single** chromosomes. The only haploid cells in humans are the gametes.

Plant and animal Cytokinesis

- **Cytokinesis,** the division of the cytoplasm usually finishes at the end of telophase.

•In animal cells
  –Cytokinesis occurs by a process known as cleavage, forming a cleavage furrow

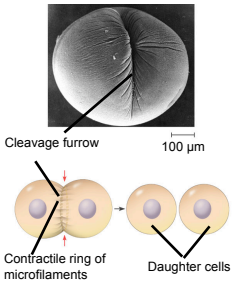


Figure 12.9 A **(a) Cleavage of an animal cell** (SEM)

- In plant cells, during cytokinesis
  - A cell plate forms

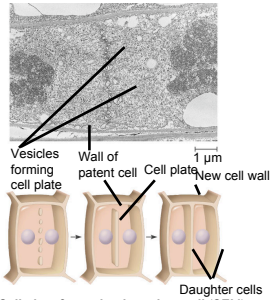


Figure 12.9 B **(b) Cell plate formation in a plant cell** (SEM)

Bacteria divide by binary fission

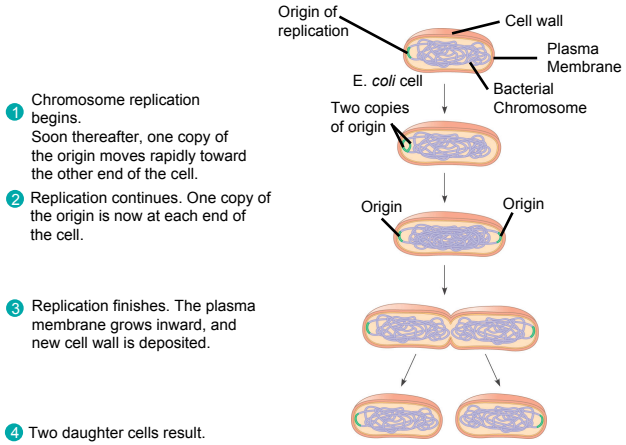


Figure 12.11

How many chromatids does a human cell have after undergoing S-phase?

A) 46

B) 19

C) 23

D) 32

E) 92

Can the repeated cycle of cell divisions continue unchecked?

Cell check points

- The cell cycle is regulated by a molecular control system
- There are **3 major checkpoints** during the cell cycle.
  - The **G_1** checkpoint goes into S or into G_0
  - The **G_2** checkpoint
  - And the **Mitotic** checkpoint.
- Why are checkpoints necessary?

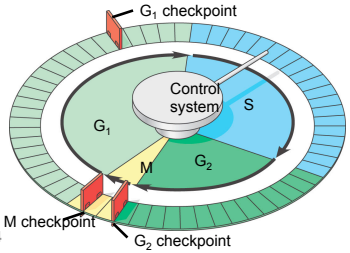


Figure 12.14

Cell cycle clock

- **Cyclins** proteins whose concentrations cycles during the cell cycle
- **Cyclin-dependent-Kinases (CDK's)** that are activated when bound to the cyclins.
- **MPF maturation (mitotic) promotion factor** at the G_2 checkpoint, a cdk-cyclin complex.

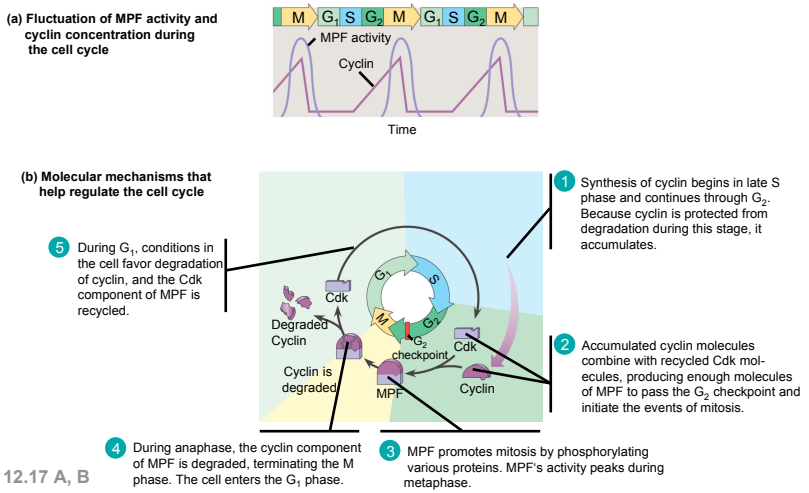


Figure 12.17 A, B

- **Growth factors**
- PDGF (Platelet derived growth factor) for fibroblasts affect the G_1 checkpoint.
- **Density dependence and anchorage dependence inhibition.**
  - Can lower density of growth factors.
  - There is also contact inhibition.

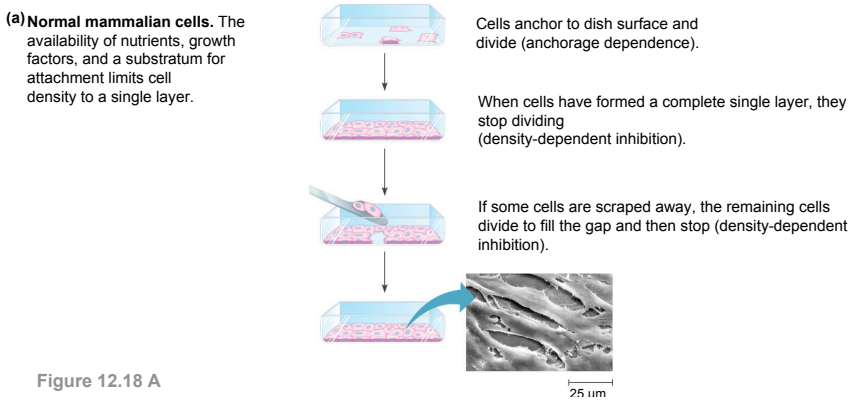


Figure 12.18 A

Control of Cell growth

- **Growth factors**
  - PDGF (Platelet derived growth factor) for fibroblasts affect the G_1 checkpoint.
- **Density dependence and anchorage dependence inhibition.**
  - Can lower density of growth factors.
  - There is also contact inhibition.

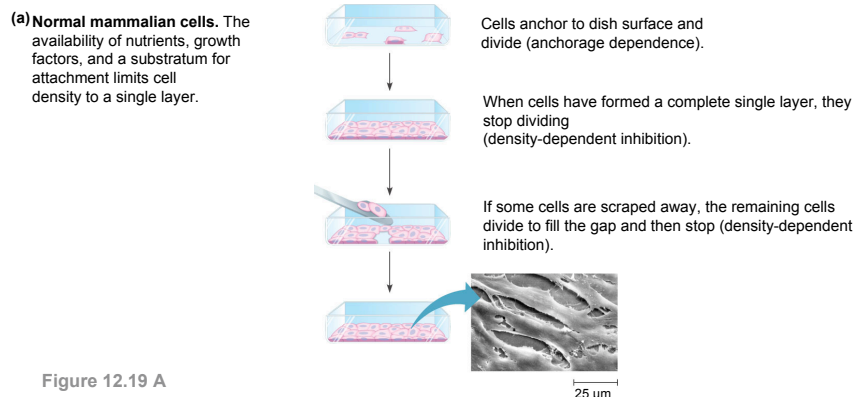


Figure 12.19 A

Cancer

- Cancer cells
  - Exhibit neither density-dependent inhibition nor anchorage dependence
  - Have escaped from cell cycle control
  - Make excessive amounts of GF
  - Have lost the ability to be controlled by GF.
  - GF signaling pathway abnormal.

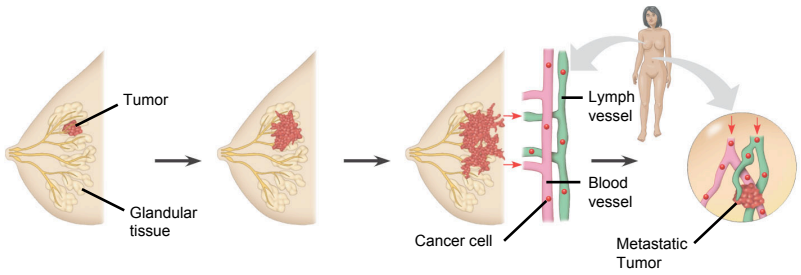


Figure 12.20