

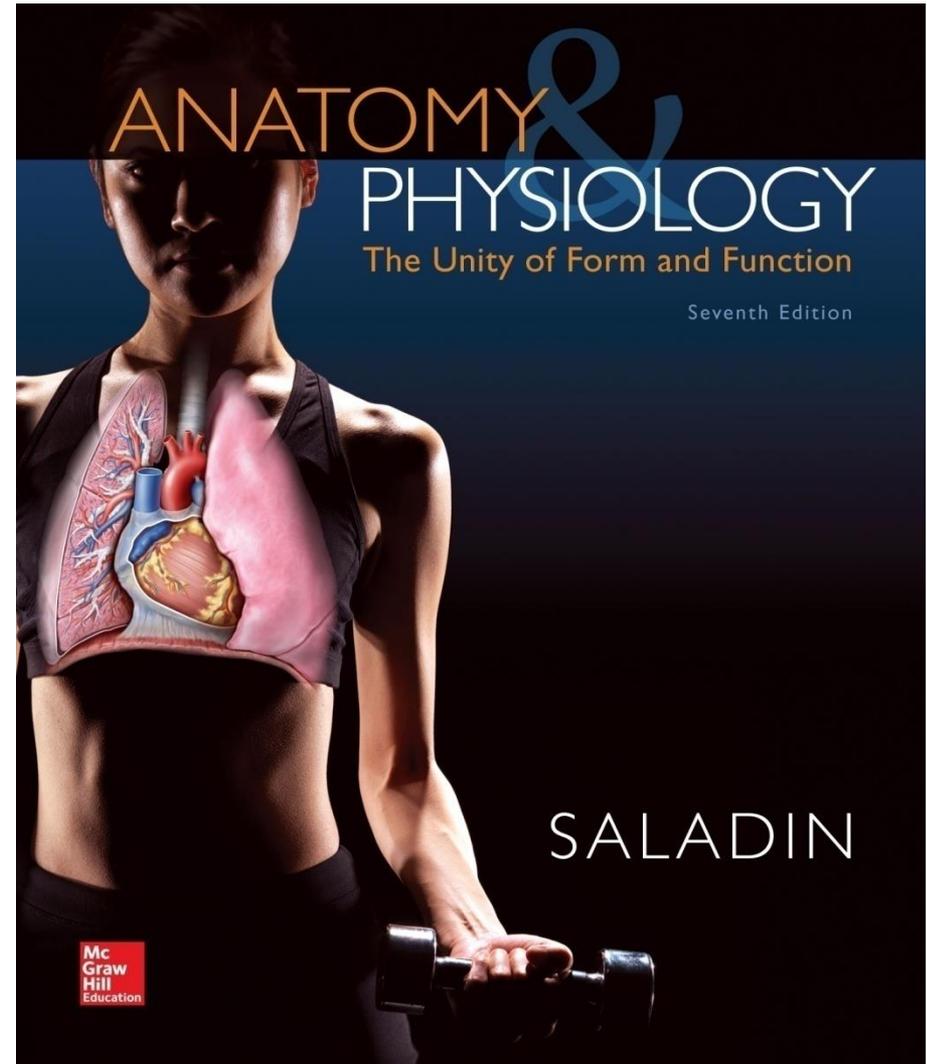
Chapter 04

Lecture and Animation Outline

To run the animations you must be in **Slideshow View**. Use the buttons on the animation to play, pause, and turn audio/text on or off.

Please Note: Once you have used any of the animation functions (such as Play or Pause), you must first click on the slide's background before you can advance to the next slide.

See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes and animations.



Introduction

- **Necessary to have some familiarity with DNA and genes in order to study genetic disorders that effect hereditary traits**
 - Color blindness, cystic fibrosis, diabetes mellitus, hemophilia
- **Mendelian genetics helps us discern and predict patterns of inheritance within a family line**

DNA and RNA—The Nucleic Acids

- **Expected Learning Outcomes**

- Describe the structure of DNA and relate this to its function.
- Explain how DNA and proteins are organized to form the chromosomes.
- Describe the types of RNA, their structural and functional differences, and how they compare with DNA.

DNA and RNA—The Nucleic Acids

- **Johann Friedrich Miescher (1844–95)**
 - Swiss biochemist, studied the nuclei of white blood cells from pus extracted from bandages
 - Coined term *nuclein*, now called deoxyribonucleic acid (DNA), repository for genes
- **By 1900, components of DNA were known (sugar, phosphate groups, nitrogenous bases)**
- **In 1953 the overall structure of DNA was learned**

DNA Structure and Function

- **Deoxyribonucleic acid (DNA)**—long, thread-like molecule with uniform diameter, but varied length
 - **46** DNA molecules (chromosomes) in nucleus of most human cells
 - Average human DNA molecule about 2 inches long
- DNA and other nucleic acids are polymers of **nucleotides**
 - Nucleotide consists of a sugar, phosphate group, and nitrogenous base

DNA Structure and Function

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

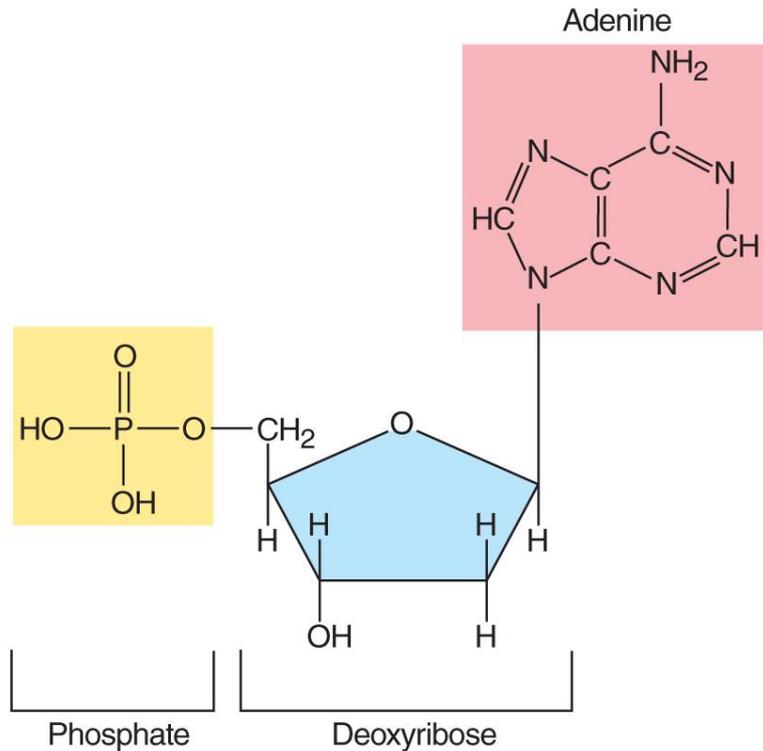


Figure 4.1a

- **A single nucleotide**
 - One sugar—deoxyribose
 - One phosphate group
 - One nitrogenous base

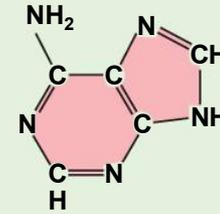
(a)

DNA Structure and Function

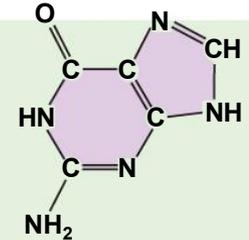
- Nitrogenous bases in nucleic acids are **purines** and **pyrimidines**
- **Purines—double ring**
 - Adenine (A)
 - Guanine (G)
- **Pyrimidines—single ring**
 - Cytosine (C)
 - Thymine (T)
 - Uracil (U)
- **DNA bases: A, T, C, G**

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

Purines

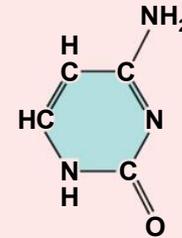


Adenine (A)

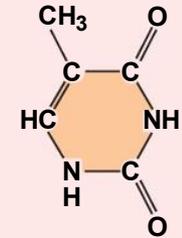


Guanine (G)

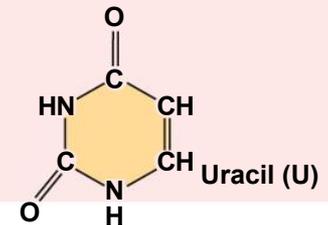
Pyrimidines



Cytosine (C)



Thymine (T)



Uracil (U)

(b)

Figure 4.1b

DNA Structure and Function

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

- **Double helix** shape of DNA (resembles spiral staircase)
 - Each sidepiece is a backbone of **phosphate groups** alternating with **deoxyribose**
 - Step-like connections between the backbones are **pairs of nitrogen bases**

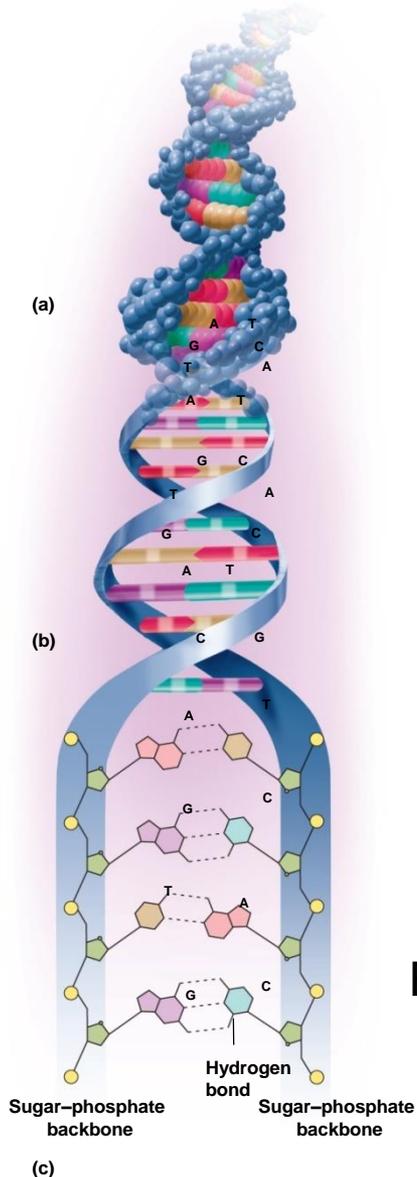
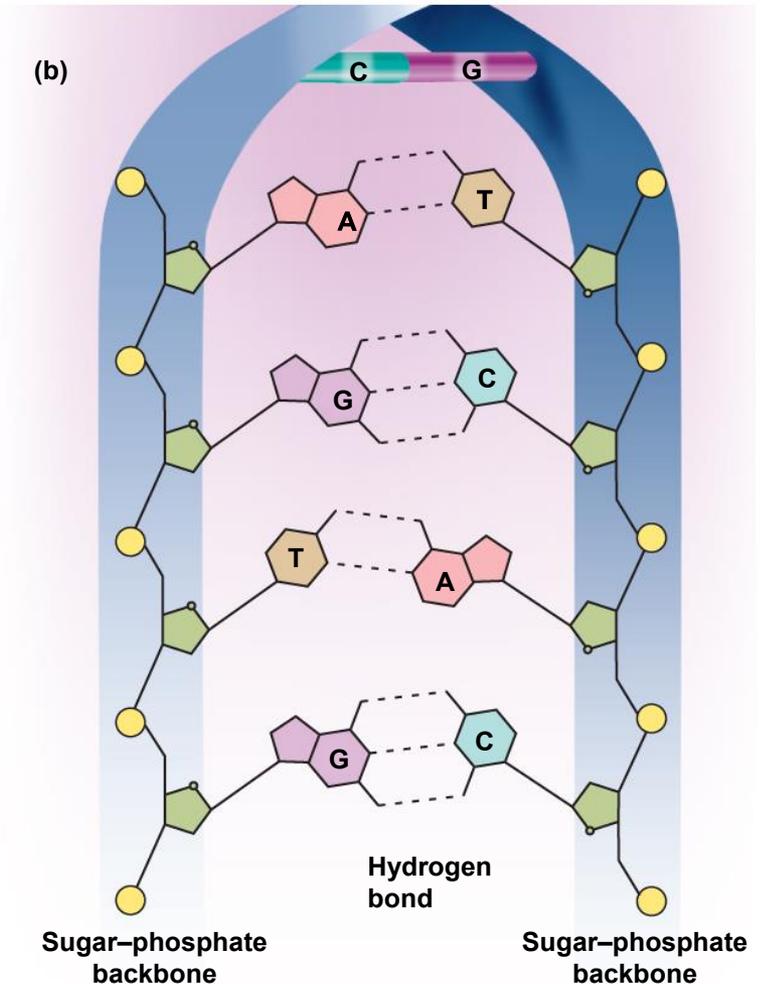


Figure 4.2

DNA Structure and Function

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

- Nitrogenous bases united by **hydrogen bonds**
 - A purine on one strand always bound to a pyrimidine on the other
 - **A–T** two hydrogen bonds
 - **C–G** three hydrogen bonds
- **DNA base pairing**
 - **A–T**
 - **C–G**
- **Law of complementary base pairing**
 - One strand determines base sequence of other



DNA Structure and Function

- **Gene**—a segment of DNA coding for the synthesis of a specific protein
- **Genome**—all the genes of one person
 - Humans have about 20,000 genes
 - Only about 2% of total DNA
 - Other 98% is noncoding DNA
 - Plays role in chromosome structure
 - Regulation of gene activity

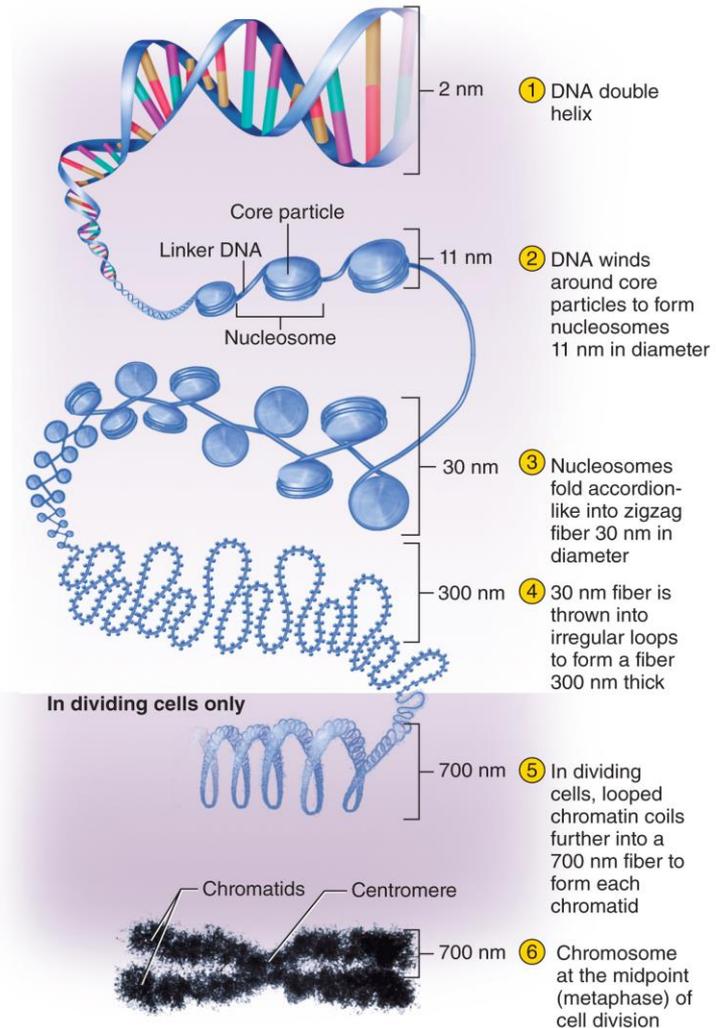
Discovery of the Double Helix

- **By 1900: components of DNA were known**
 - Sugar, phosphate, and bases
- **By 1953: X-ray diffraction determined geometry of DNA molecule**
- Nobel Prize awarded in 1962 to three men: **Watson, Crick, and Wilkins**, but not to Rosalind Franklin, who died of cancer at 37, after discovering the X-ray data that provided the answers to the double helix

Chromatin and Chromosomes

- **Chromatin**—fine filamentous DNA material complexed with proteins
 - Occurs as 46 chromosomes in most cells
 - 6 feet long thread packed in cell nucleus of 5 μm diameter
 - In **nondividing cells**, chromatin is so slender it cannot be seen with light microscope
 - Granular appearance under electron microscope

Copyright © McGraw-Hill Education. Permission required for reproduction or display.



(b)

Figure 4.4b

Chromatin and Chromosomes

- **Histones**—proteins crucial for DNA packing
 - Histones cluster in groups of eight molecules
 - DNA molecule winds around the cluster (like thread around spool)
 - Chromatin consists of thousands of repeating nucleosomes
- **Nucleosome** consists of:
 - **Core particle**—histone cluster with DNA (1.5 turns) around it
 - **Linker DNA**—short segment of DNA connecting core particles
- **Nucleosomes zigzag like an accordion**
- **Chromatin thrown into complex, irregular loops and coils**
 - 1,000 times shorter than original molecule

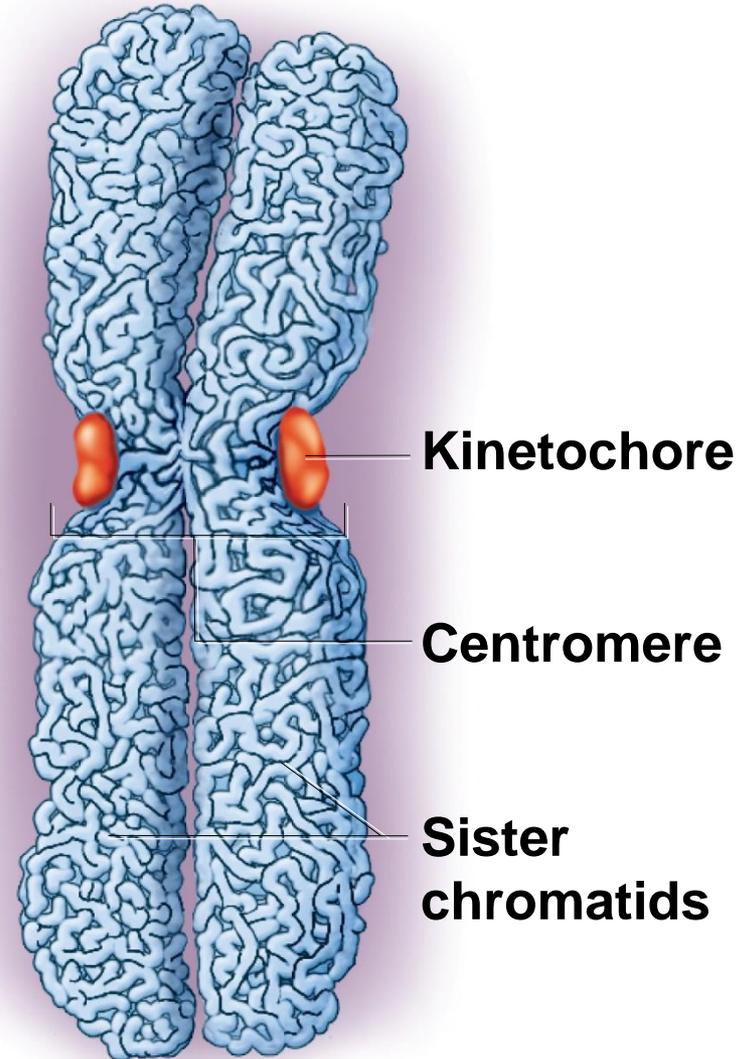
Chromatin and Chromosomes

- Each chromosome is packed into its own region of the nucleus—**chromosome territory**
 - Permeated with channels allowing regulatory chemicals to have access to the genes
- **In a nondividing cell, the chromatin is not static**
 - Changes moment to moment according to genetic activity of cell
 - Genes get turned off and on
 - Example: during development, chromosomes migrate, so that genes on different chromosomes can partner to bring about developmental changes in the cell

Chromatin and Chromosomes

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

- **When preparing to divide, cell makes copy of all nuclear DNA**
- Each chromosome then consists of two parallel filaments of identical DNA— **sister chromatids**
- **Becomes visible with light microscope**
- Chromatids are joined at constricted **centromere**
 - **Kinetochores**—protein plaques on each side of centromere



(a) Figure 4.5a

RNA Structure and Function

- **Ribonucleic acids (RNAs)**—smaller molecules that resemble DNA
 - Can have less than 100 or just over 10,000 bases per molecule
- Three important RNAs for protein synthesis
 - **Messenger RNA (mRNA)**
 - **Ribosomal RNA (rRNA)**
 - **Transfer RNA (tRNA)**
- **One nucleotide chain** (not a double helix)
- **Ribose** replaces deoxyribose as the sugar
- **Uracil** replaces thymine as a nitrogenous base
- **Functions mainly in cytoplasm**

RNA Structure and Function

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

TABLE 4.1		Comparison of DNA and RNA	
Feature	DNA	RNA	
Sugar	Deoxyribose	Ribose	
Types of nitrogenous bases	A, T, C, G	A, U, C, G	
Number of nitrogenous bases	Averages 10^8 base pairs	70–10,000 bases, mostly unpaired	
Number of nucleotide chains	Two (double helix)	One	
Site of action	Functions in nucleus; cannot leave	Leaves nucleus; functions mainly in cytoplasm	
Function	Codes for synthesis of RNA and protein	Carries out the instructions in DNA; assembles proteins	

Genes and Their Action

- **Expected Learning Outcomes**

- Give a working definition of the *gene*.
- Explain what the human genome is and its relationship to health sciences.
- Define *genetic code* and describe how DNA codes for protein structure.
- Describe the assembly of amino acids into a protein.
- Explain what happens to a protein after its amino acid sequence has been synthesized.
- Describe ways a gene can be turned on or off.
- Explain how DNA indirectly regulates the synthesis of nonprotein molecules.

What Is a Gene?

- Previous definition: **gene**—a segment of DNA that carries the code for a particular protein
 - But body has millions of proteins and only about 20,000 genes
- Current definition: **gene**—an information-containing segment of DNA that codes for the production of a molecule of RNA that plays a role in synthesizing one or more proteins
- **Amino acid sequence of a protein is determined by the nucleotide sequence in the DNA**

The Genome

- **Genome**—all the DNA in one 23-chromosome set
 - 3.1 billion nucleotide pairs in human genome
- **46 human chromosomes come in two sets of 23 chromosomes**
 - One set of 23 chromosomes came from each parent
- **Human Genome Project (1990–2003)** identified the base sequences of 99% of the human genome
 - **Genomics**—study of the whole genome and how its genes and noncoding DNA interact to affect structure and function of the whole organism

The Genome

- **Findings of Human Genome Project:**
 - *Homo sapiens* has fewer than 100,000 genes
 - A single gene can code for many different proteins
 - A gene is on average 3,000 bases long (can be up to 2.4 million bases long)
 - All humans are at least 99.99% genetically identical
 - Still, two individuals can differ by more than 3 million base pairs
 - Combinations of **single-nucleotide polymorphisms** account for all human genetic variation
 - Some chromosomes are gene-rich and some are gene-poor
 - Currently we know locations of over 1,400 disease-producing mutations
 - Opens possibilities of genomic medicine

The Genetic Code

- Body can make millions of different proteins (the **proteome**), from just 20 amino acids, and encoded by genes made of just **four nucleotides** (A, T, C, G)
- **Genetic code**—a system that enables these four nucleotides to code for amino acid sequences of all proteins
- **Minimum code to symbolize 20 amino acids is three nucleotides per amino acid**

The Genetic Code

- **Base triplet**—a sequence of three DNA nucleotides that stands for one amino acid
 - **Codon**—the 3-base sequence in mRNA
 - **64 possible codons** available to represent the 20 amino acids
 - 61 code for amino acids; 3 are stop codons
 - **Stop codons**—**UAG**, **UGA**, and **UAA**: signal “end of message,” like a period at the end of a sentence
 - **Start codon**—**AUG** codes for methionine, and begins the amino acid sequence of the protein

Genomic Medicine

- **Application of knowledge of the genome to the prediction, diagnosis, and treatment of disease**
 - Relevant to many disorders (e.g., cancer, Alzheimer disease, schizophrenia, obesity, AIDS, tuberculosis)
- **Allows for early detection of diseases, more effective clinical intervention**
- **Expands potential for gene-substitution therapy**

Protein Synthesis

- **All body cells, except sex cells and some immune cells, contain identical genes**
- **Different genes are activated in different cells**
- **Any given cell uses one-third to two-thirds of its genes**
 - Rest remain dormant and may be functional in other types of cells

Protein Synthesis

- When a gene is activated, **messenger RNA (mRNA)** is made
 - **mRNA**—complementary to gene
 - Migrates from the nucleus to cytoplasm where it codes for amino acids
- Process of protein synthesis
 - **DNA** → **mRNA** → **protein**
 - In **transcription**, DNA codes for mRNA
 - Occurs within nucleus
 - In **translation**, mRNA codes for protein
 - Usually occurs in cytoplasm

Simple Gene Expression

DNA



The sequence of nucleotide bases in DNA carries genetic information in units that are called genes.

Transcription

- **Transcription**—copying genetic instructions from DNA to mRNA
- **RNA polymerase**—enzyme that binds to DNA and assembles mRNA
 - Certain DNA base sequences signal start (e.g., TATATA)
 - RNA polymerase opens up the DNA helix and reads bases from one strand of DNA
 - Makes corresponding mRNA
 - Where it finds C on the DNA, it adds G to the mRNA
 - Where it finds G on the DNA, it adds C to the mRNA
 - Where it finds T on the DNA, it adds A to the mRNA
 - **But** where it finds A on the DNA, it adds U to the mRNA

Transcription

- **RNA polymerase rewinds the DNA helix behind it**
 - Gene can be transcribed by several polymerase molecules
 - **Terminator:** base sequence at the end of a gene signaling stop
- **Pre-mRNA—immature RNA produced by transcription**
 - **Exons**—“sense” portions of the pre-mRNA that will be exported from the nucleus and translated into protein
 - **Introns**—“nonsense” portions of the pre-mRNA that must be removed before translation
- **Enzymes within the nucleus remove introns from the RNA and splice exons together**
- **Alternative splicing**—variations in the way exons are spliced allow for a variety of proteins to be produced from one gene

Alternative Splicing of mRNA

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

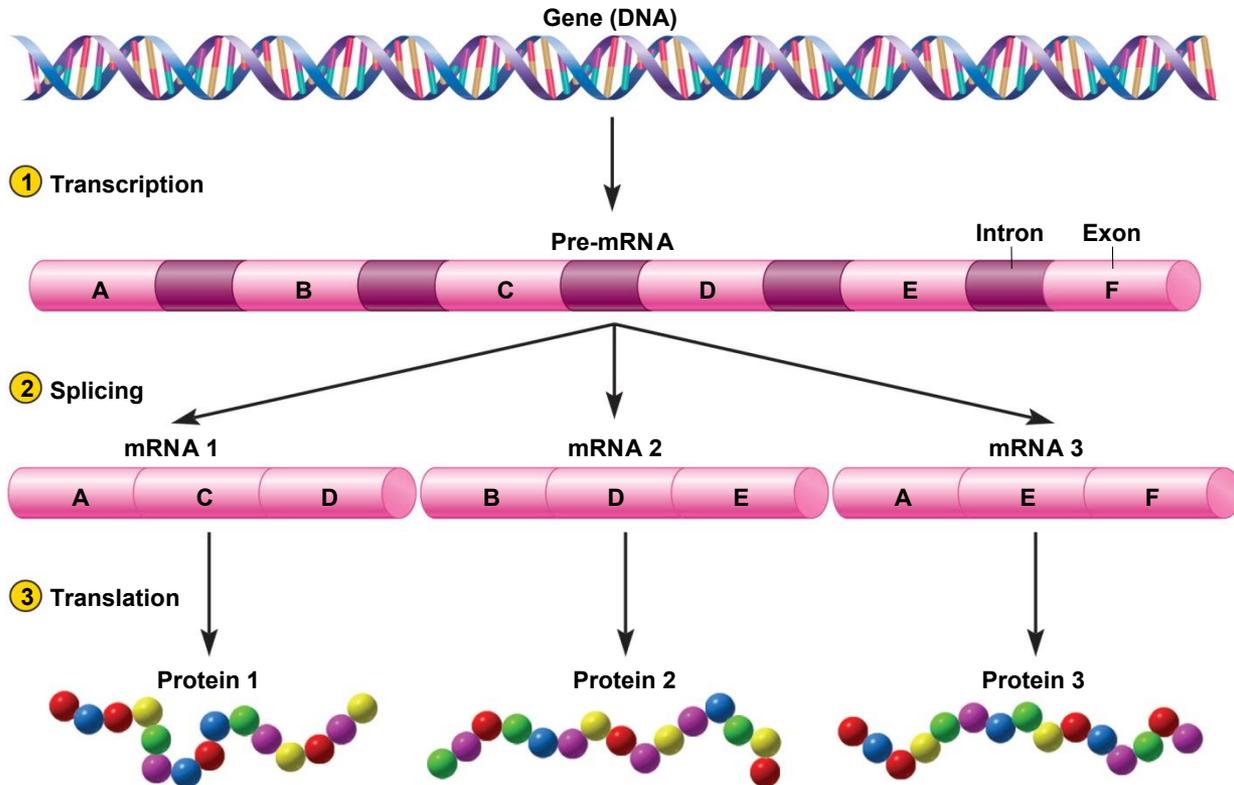


Figure 4.6

- One gene can code for more than one protein
- Exons can be spliced together into a variety of different mRNAs

Stages of Transcription



Play



Pause



Audio



Text

A structural gene is made up of a sequence of bases in a DNA molecule consisting of a coding region with an upstream promoter and a terminator downstream of the coding region.

Translation

- **Translation**—process that converts the language of nucleotides into the language of amino acids
- **Three main participants in translation**
 - **mRNA** carries code from nucleus to cytoplasm
 - Has protein cap that is recognition site for ribosome
 - **Transfer RNA (tRNA)** delivers a single amino acid to the ribosome for it to be added to growing protein chain
 - Contains an **anticodon**—series of 3 nucleotides that are complementary to codon of mRNA
 - **Ribosomes**—organelles that read the message
 - Found free in cytosol, on rough ER, and on nuclear envelope
 - Consist of large and small subunits, where each subunit is made of several enzymes and ribosomal RNA (rRNA) molecules

Translation

- **mRNA** molecule begins with **leader sequence**
 - Acts as binding site for small ribosomal subunit
 - Large subunit attaches to small subunit
 - Ribosome pulls mRNA molecule through it like a ribbon, reading the bases as it goes
 - When start **codon (AUG)** is reached, protein synthesis begins
 - All proteins begin with **methionine** when first synthesized

Transfer RNA

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

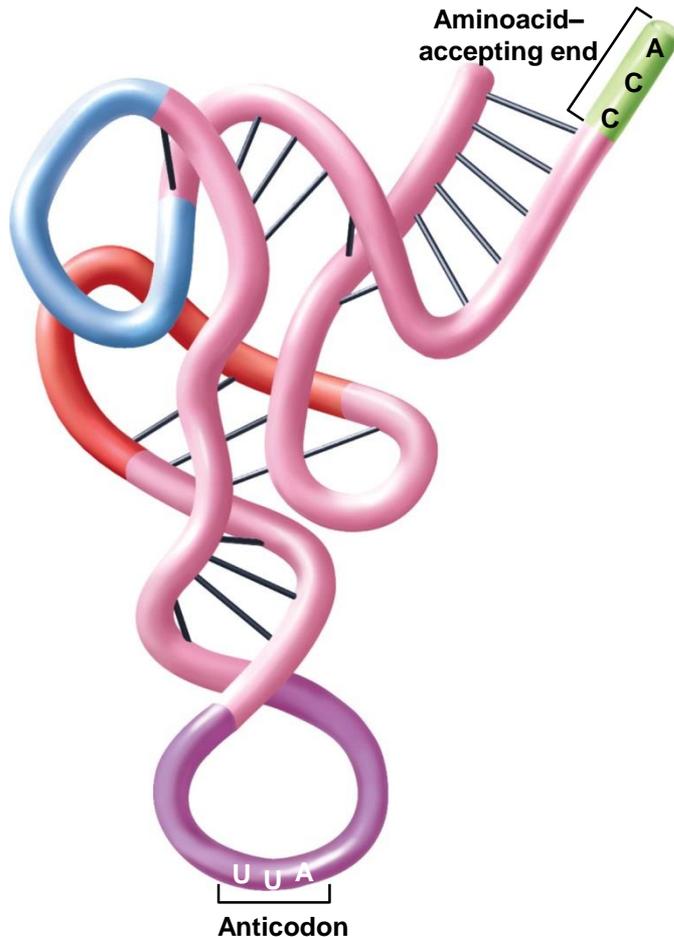


Figure 4.7

- **Transfer RNA (tRNA)**
 - Small RNA molecule
 - Coils on itself to form an angular L shape
 - One end includes three nucleotides called an **anticodon**
 - Other end has binding site specific for one amino acid
 - tRNA picks up free amino acid in cytosol
 - Cost of binding an amino acid to the tRNA is one ATP

Translation

- **Three steps to translation: Initiation, Elongation, Termination**
- **Initiation**
 - Leader sequence in mRNA binds to small ribosomal subunit
 - Initiator tRNA (bearing methionine) pairs with start codon
 - Large ribosomal subunit joins the complex and the now fully formed ribosome begins reading bases

Translation

- **Elongation**

- Next tRNA (with its amino acid) binds to ribosome while its anticodon pairs with next codon of mRNA
- Peptide bond forms between methionine and second amino acid
- Ribosome slides to read next codon and releases initiator tRNA (empty)
- Next tRNA with appropriate anticodon brings its amino acid to ribosome
- Another peptide bond forms (between 2nd and 3rd amino acids)
- Process continually repeats, extending peptide to a protein

- **Termination**

- When ribosome reaches stop codon a release factor binds to it
- Finished protein breaks away from ribosome
- Ribosome dissociates into two subunits

Protein Synthesis

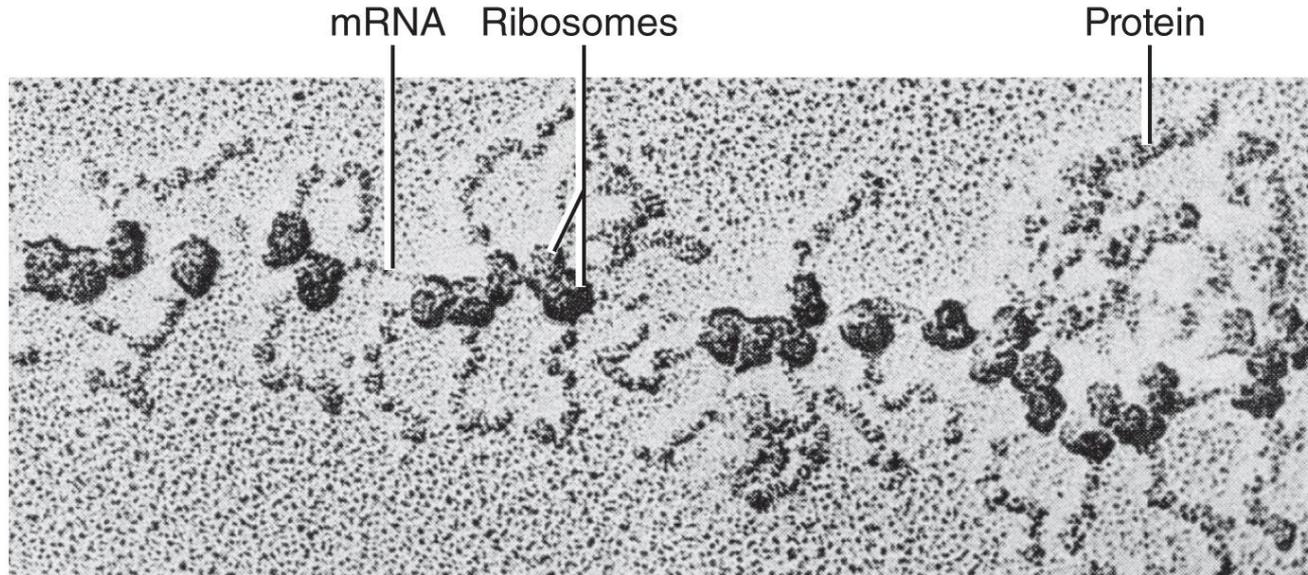


▶ Play
⏸ Pause
🔊 Audio
📄 Text

Translation is initiated by formation of an initiation complex consisting of the smaller ribosomal subunit, the first amino acid-tRNA and messenger RNA.

Translation

Copyright © McGraw-Hill Education. Permission required for reproduction or display.



60 nm

©E. V. Kiseleva, February 5 Letter 257; 251-253, 1989

Figure 4.9

- **Translation can be rapid**
 - **Polyribosome**—one mRNA attached to multiple ribosomes (commonly 10-20 ribosomes at once)
 - Cell may have 300,000 identical mRNA molecules undergoing simultaneous translation
 - Cell can produce over 100,000 protein molecules per second

Translation

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

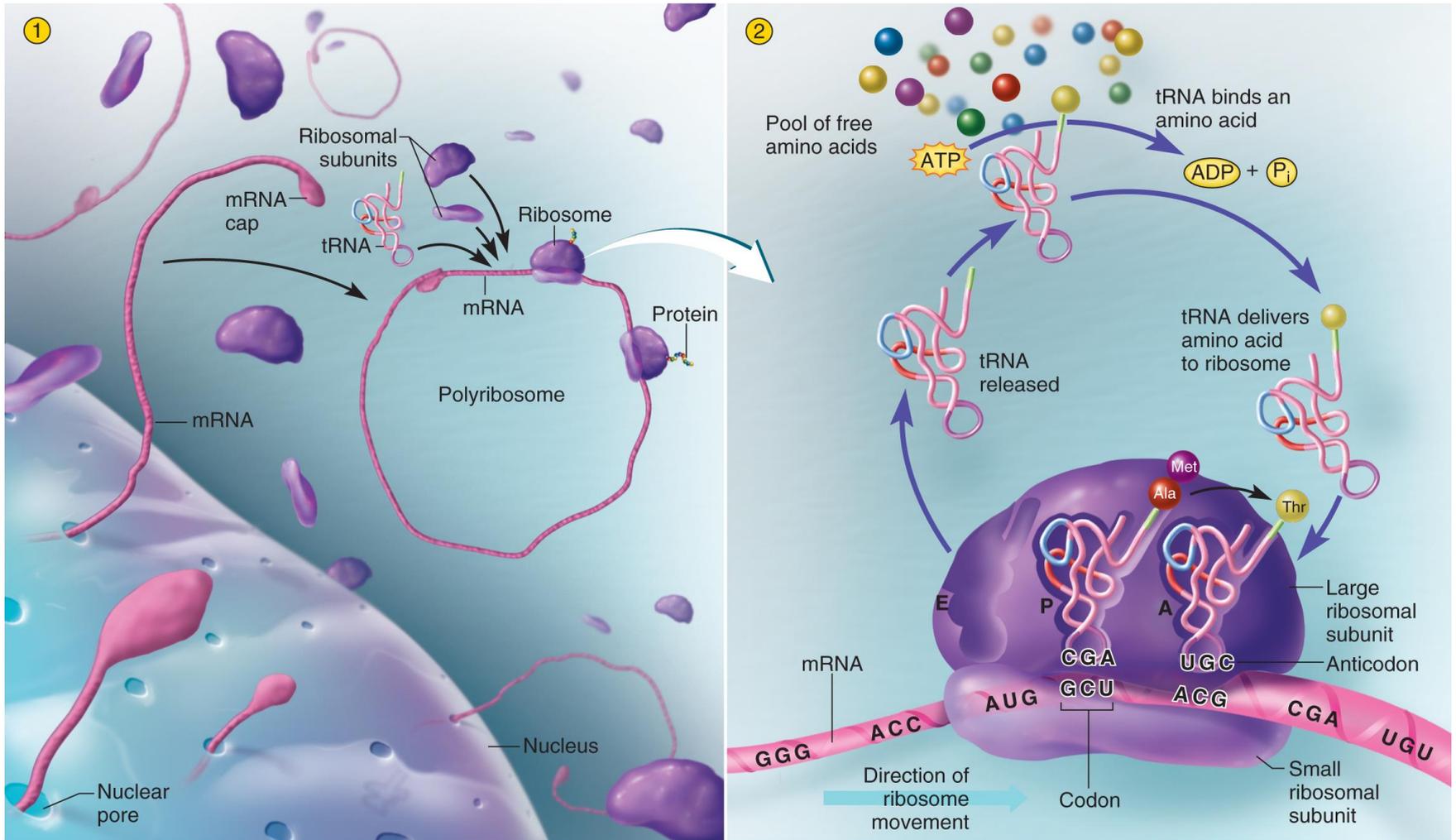


Figure 4.8 (top)

Translation

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

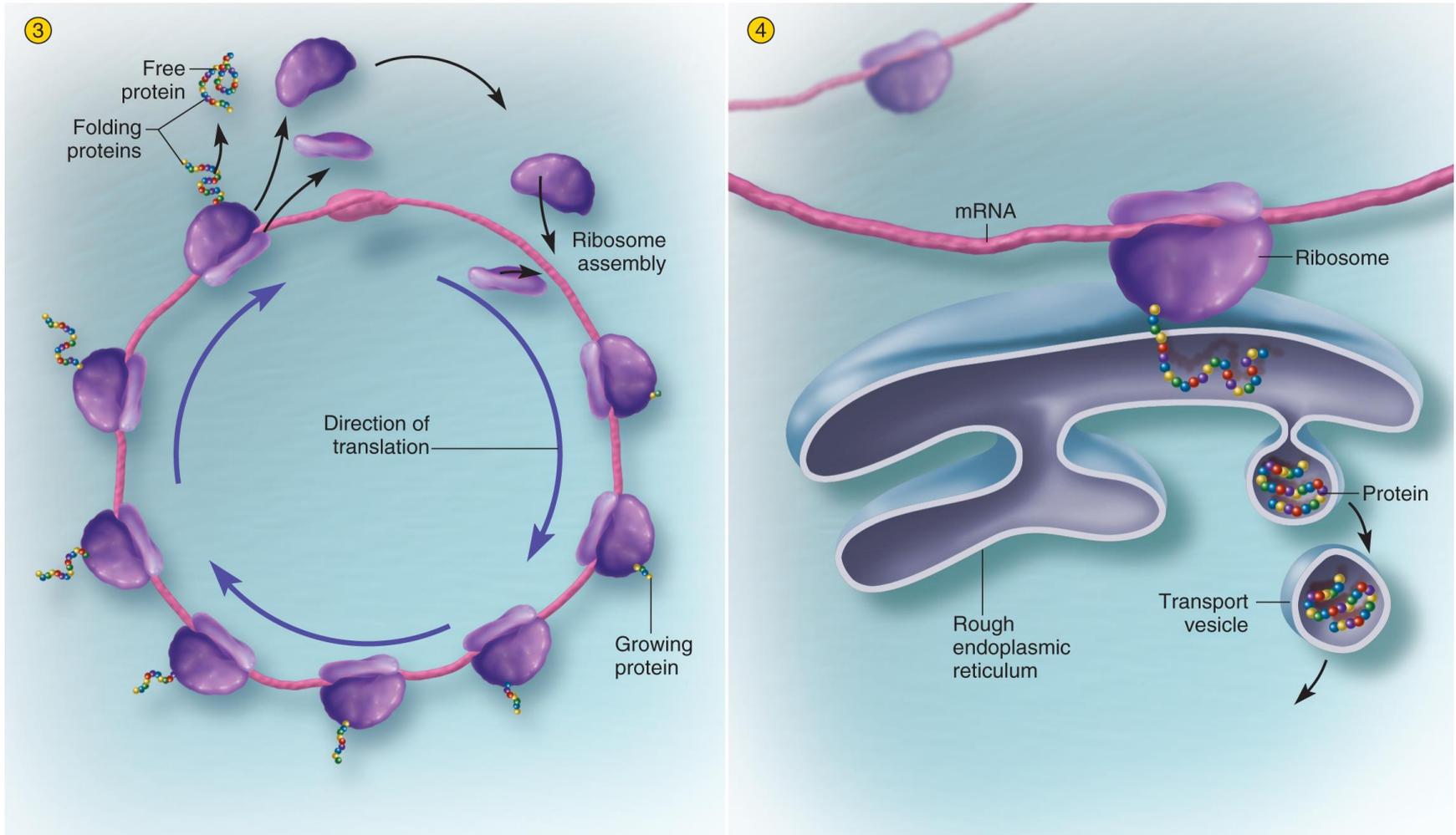


Figure 4.8 (bottom)

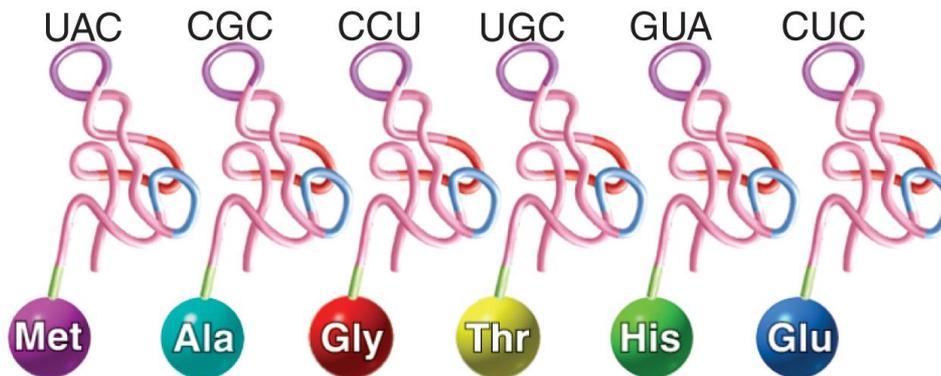
Translation

- **After translation, some proteins are packaged and some are exported**
- **Proteins headed for lysosomes or for secretion are made on ribosomes on the rough ER**
 - Newly made protein is threaded into rough ER where it is modified and packaged into a transport vesicle

Review of Peptide Formation

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

Figure 4.10



- 1 DNA double helix
- 2 Seven base triplets on the template strand of DNA
- 3 The corresponding codons of mRNA transcribed from the DNA triplets
- 4 The anticodons of tRNA that bind to the mRNA codons
- 5 The amino acids carried by those six tRNA molecules
- 6 The amino acids linked into a peptide chain

Protein Processing and Secretion

- Protein synthesis is not finished when the amino acid sequence (**primary structure**) has been assembled
- To work, protein must fold into precise **secondary** and **tertiary structures**
- **Chaperone proteins**
 - Older proteins that pick up new proteins and guide their folding into the proper shapes
 - Help prevent improper association between different proteins
 - Some also called **stress proteins** or **heat-shock proteins**
 - Chaperones produced in response to heat or stress
 - Help damaged proteins fold back into correct functional shapes

Protein Processing and Secretion

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

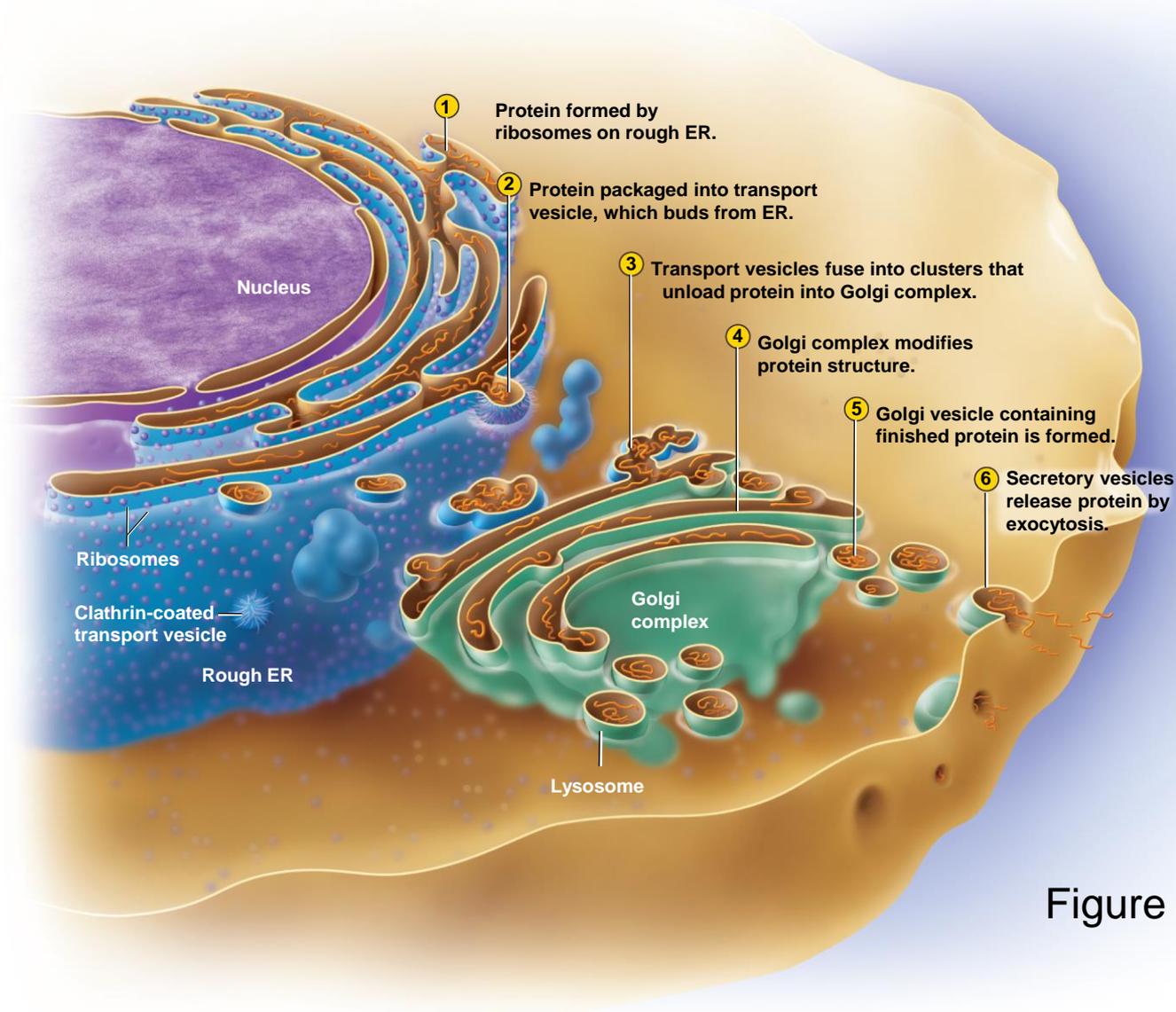


Figure 4.11

Protein Processing and Secretion

- **Proteins to be used in the cytosol are likely to be made on free ribosomes in the cytosol**
- **Proteins destined for packaging into lysosomes or secretion from the cell are assembled on rough ER and sent to Golgi complex for packaging**
 - Entire polyribosome migrated to the rough ER and docks on its surface
 - Assembled amino acid chain completed on rough ER
 - Sent to Golgi for final modification

Protein Processing and Secretion

- **Proteins assembled on ER surface, threads itself through a pore in the ER membrane into cisterna**
- ER modifies protein by **posttranslational modification**
 - Removing some amino acid segments; folding the protein; stabilizing protein with disulfide bridges; adding carbohydrates
- **When rough ER is finished with protein**
 - Pinches off bubble-like **transport vesicle** coated with **clathrin**
 - Clathrin helps select the proteins to be transported in vesicles and helps mold forming vesicle
 - Vesicles detach from ER and carry protein to the nearest cisterna of Golgi complex

Protein Processing and Secretion

- **Vesicles fuse and unload proteins into Golgi cisterna**
- **Golgi complex further modifies the protein**
 - Often adds carbohydrate chains and assembles glycoproteins
 - Golgi cisterna farthest from ER buds off new coated Golgi vesicles containing finished protein
- **Some Golgi vesicles become lysosomes**
- Other Golgi vesicles become secretory vesicles and migrate to plasma membrane, fuse to it, and release their cell product by **exocytosis**

Gene Regulation

- **Genes can be turned on and off**
 - Cells can turn some genes permanently off
 - Example: liver cells turn off hemoglobin genes
 - Cells can turn genes on only when needed
 - The level of gene expression can vary from day to day or hour to hour
 - This can be controlled by chemical messengers such as hormones
 - Example: mammary gland cells turn on gene for casein protein only when breast milk is produced

Gene Regulation

- **Steps leading to casein synthesis and secretion**
 1. **Hormone** prolactin binds to **receptors** on membrane of mammary cell
 2. Receptors trigger activation of a regulatory protein (**transcription activator**) in cytoplasm
 3. Regulatory protein moves into the nucleus and binds to the DNA near the **casein gene**
 4. The binding enables RNA polymerase to bind to the gene and **transcribe** it, producing the mRNA for casein
 5. The casein mRNA moves to the cytoplasm, and ribosomes on rough ER **translate** it
 6. The Golgi complex **packages** casein into secretory vesicles
 7. The secretory vesicles release the casein by **exocytosis**, and it becomes part of the milk

Gene Regulation

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

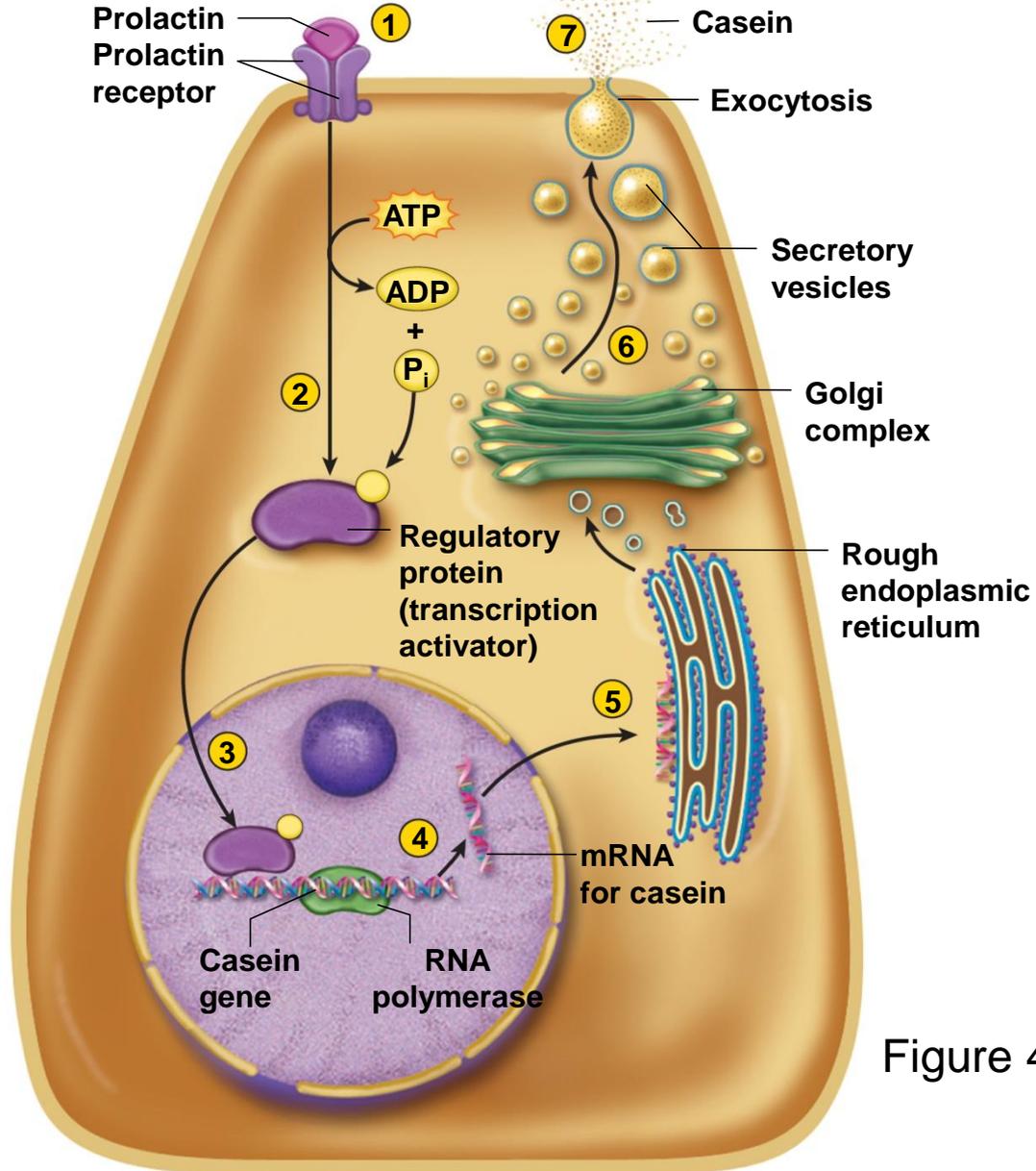
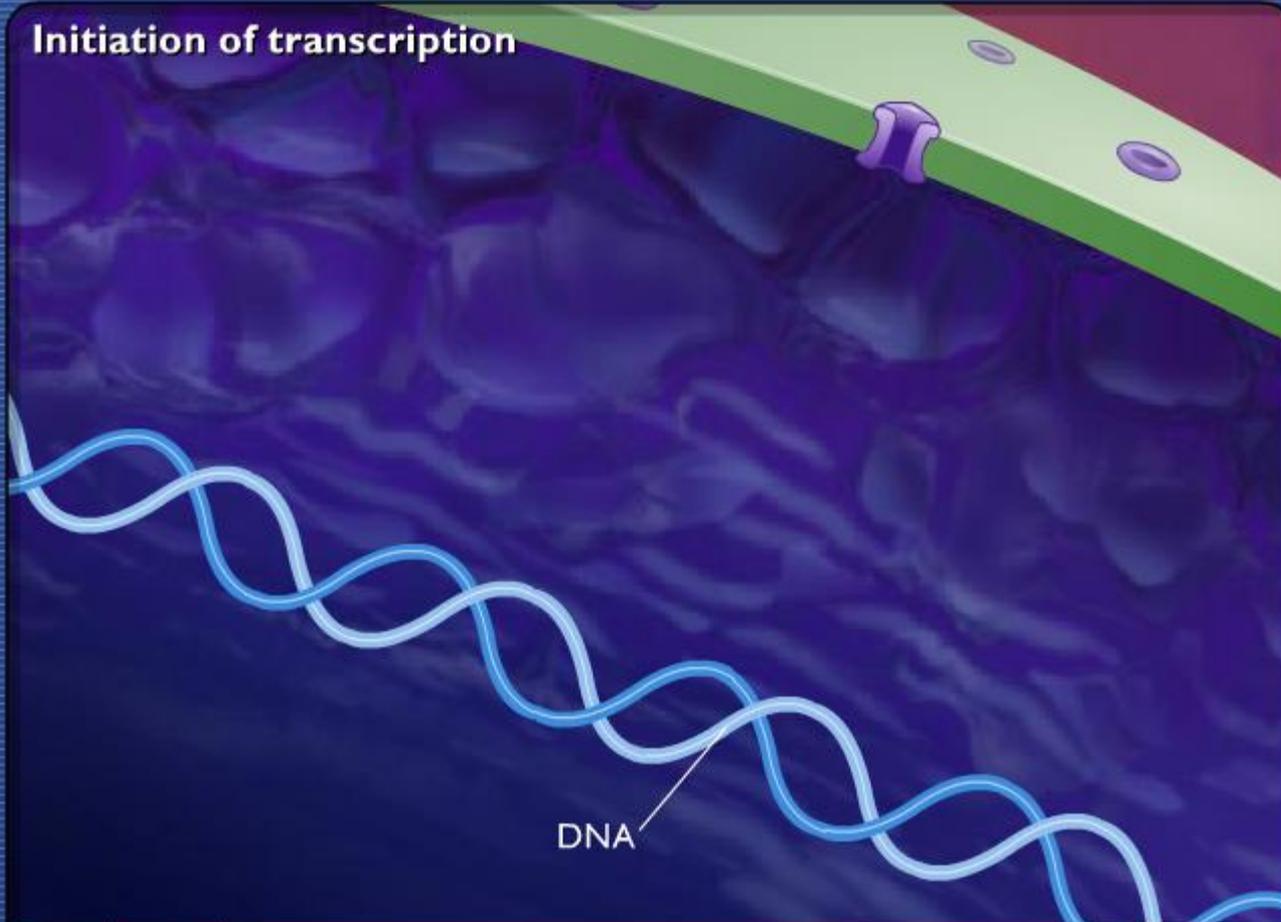


Figure 4.12

Control of Gene Expression in Eukaryotes

Initiation of transcription



DNA

▶ Play
⏸ Pause
🔊 Audio
📄 Text

Most of the control of gene expression in eukaryotes is achieved by regulating the frequency of transcription initiation.

Synthesizing Compounds Other Than Proteins

- **Cells synthesize glycogen, fat, steroids, phospholipids, pigments, and other compounds**
 - No genes for these products, but their synthesis is under indirect genetic control
 - They are produced by enzymatic reactions, and enzymes are proteins encoded by genes
- **Example: production of testosterone (a steroid)**
 - A cell of the testes takes in cholesterol
 - Enzymatically converts it to testosterone
 - Only occurs when genes for enzyme are active
- **Genes may greatly affect such complex outcomes as behavior, aggression, and sex drive**

DNA Replication and the Cell Cycle

- **Expected Learning Outcomes**
 - Describe how DNA is replicated.
 - Discuss the consequences of replication errors.
 - Describe the life history of a cell, including the events of mitosis.
 - Explain how the timing of cell division is regulated.

DNA Replication and the Cell Cycle

- Before a cell divides, it must **duplicate its DNA** so it can give a complete copy of all its genes to each daughter cell
- **Since DNA controls all cellular function, this replication process must be very exact**
- **Law of complementary base pairing**—we can predict the base sequence of one DNA strand if we know the sequence of the other

DNA Replication

Four steps of DNA replication: unwinding, unzipping, building new DNA strands, repackaging

1. DNA unwinds from histones

2. **DNA helicase** unzips a segment of the double helix exposing its nitrogenous bases

– **Replication fork**—the point of DNA opening

DNA Replication

3. **DNA polymerase** builds new DNA strands
 - Polymerase reads exposed bases and matches complementary free nucleotides
 - Separate polymerase molecules work on each strand proceeding in opposite directions
 - The polymerase moving toward the replication fork makes a long, continuous, new strand of DNA
 - The polymerase moving away from the replication fork makes short segments of DNA; **DNA ligase** joins them together
 - Ultimately, two daughter DNA molecules are made from the original parental DNA
 - **Semiconservative replication**—each daughter DNA consists of one old and one new helix

DNA Replication

4. Newly made DNA is repackaged

- With thousands of polymerase molecules working simultaneously on the DNA, all 46 chromosomes are replicated in 6 to 8 hours
- Millions of histones are made in the cytoplasm while DNA is replicated and they are transported into the nucleus soon after DNA replication ends
- Each new DNA helix wraps around the histones to make new nucleosomes

DNA Replication

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

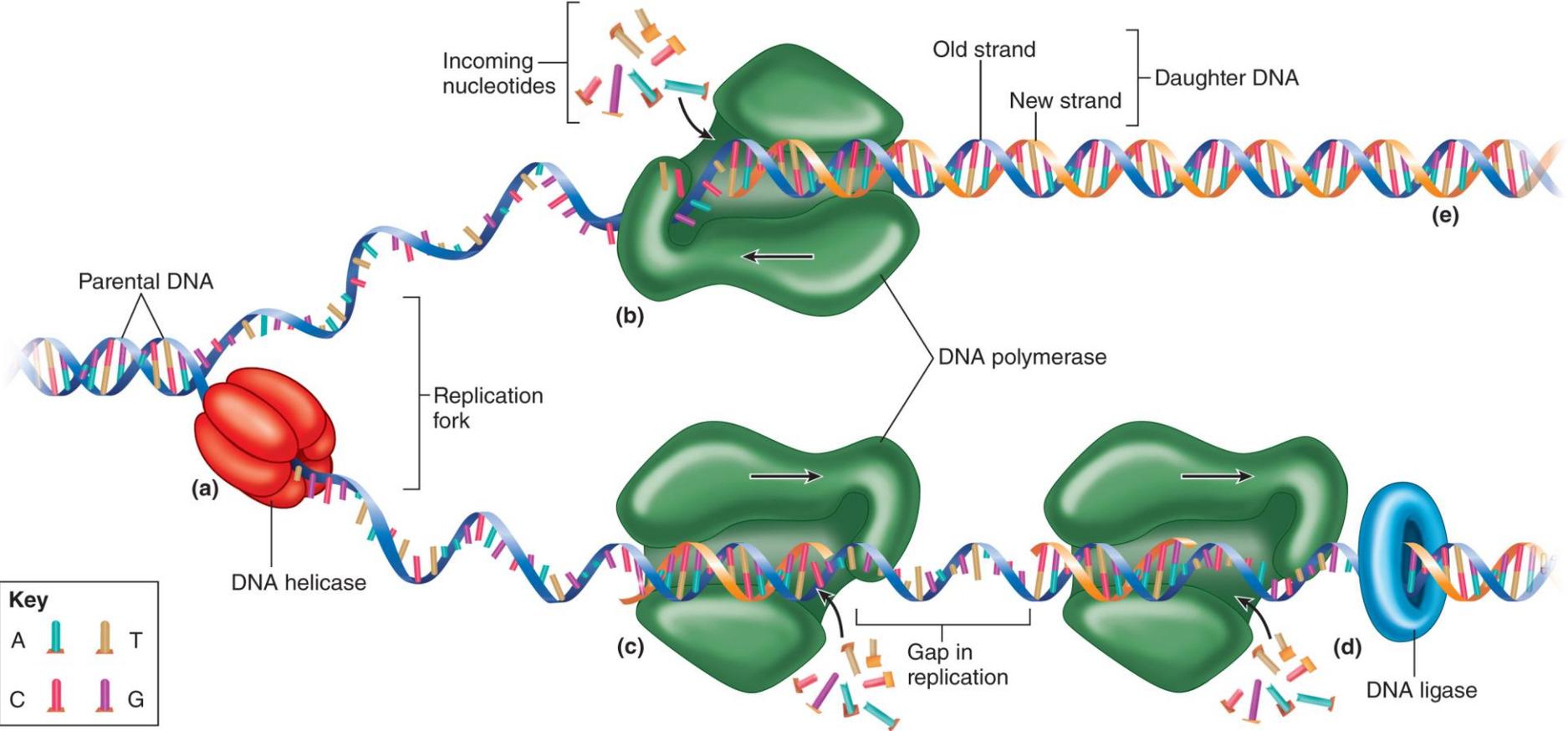


Figure 4.14



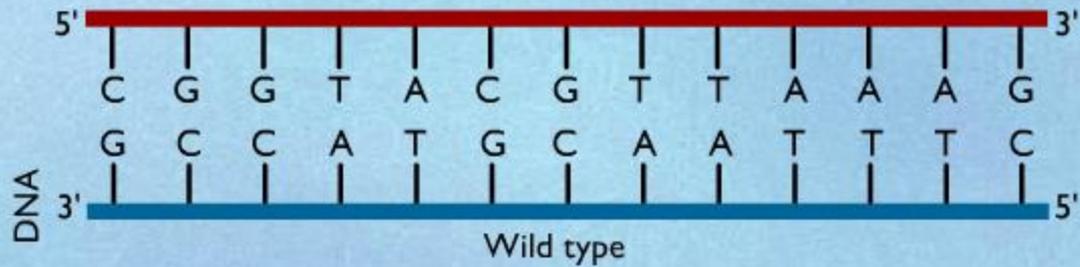
▶ Play
⏸ Pause
◀ Audio
📄 Text

DNA replication begins at a specific point in the DNA molecule called the origin of replication site.

Errors and Mutations

- **DNA polymerase** does make mistakes
 - Multiple modes for correction of replication errors
 - Double checks the new base pair and tends to replace incorrect, biochemically unstable pairs with more stable, correct pairs
 - Result is only one error per 1 billion bases replicated
- **Mutations**—changes in DNA structure due to replication errors or environmental factors (radiation, viruses, chemicals)
 - Some mutations cause no ill effects, others kill the cell, turn it cancerous, or cause genetic defects in future generations

Addition and Deletion Mutations

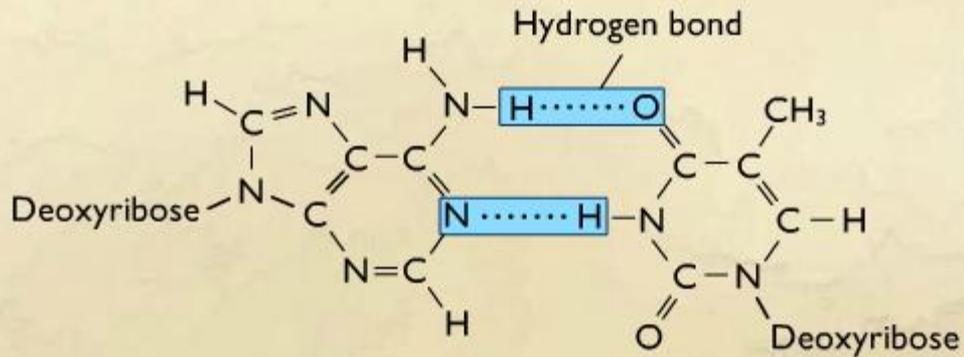


Play
 Pause

 Audio
 Text

The nucleotide sequence in DNA determines the nucleotide sequence in messenger RNA and, consequently, the sequence of amino acids in a protein.

Mutation by Base Substitution



A mutation occurs by base substitution when an incorrect base is incorporated into DNA. Some base substitutions occur because purines and pyrimidines exist in two structural forms.

The Cell Cycle

- **Cell cycle**—cell's life from one division to the next
 - Includes interphase and mitotic phase
 - **Interphase** includes three subphases
 - G_1 , S, G_2
 - **Mitotic phase** includes multiple subphases
 - Prophase, Metaphase, Anaphase, Telophase

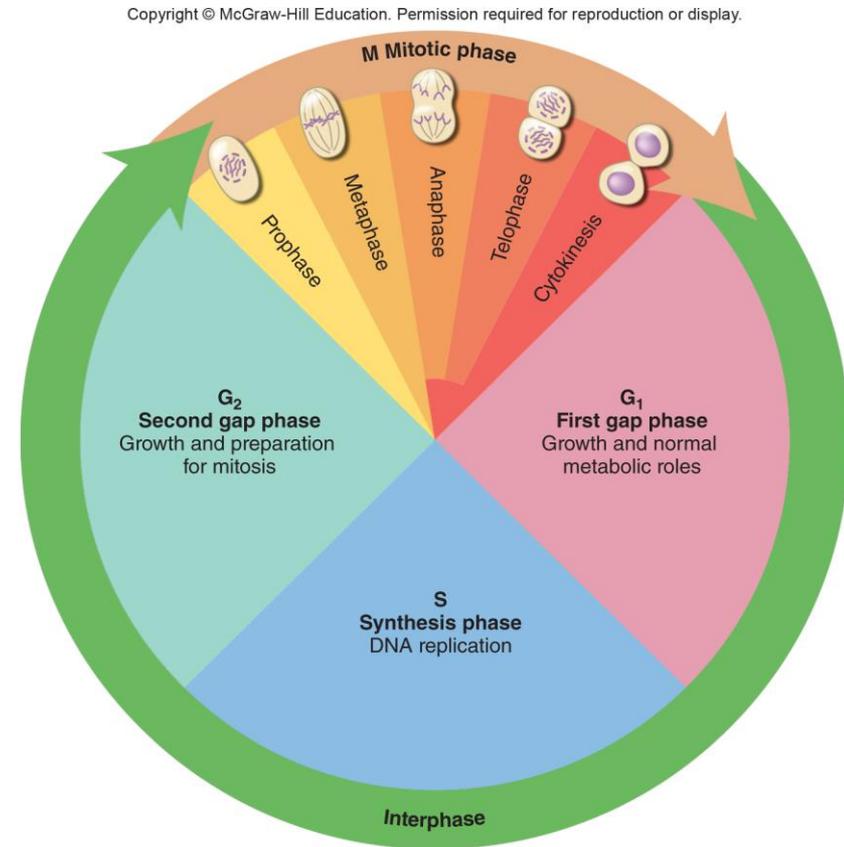
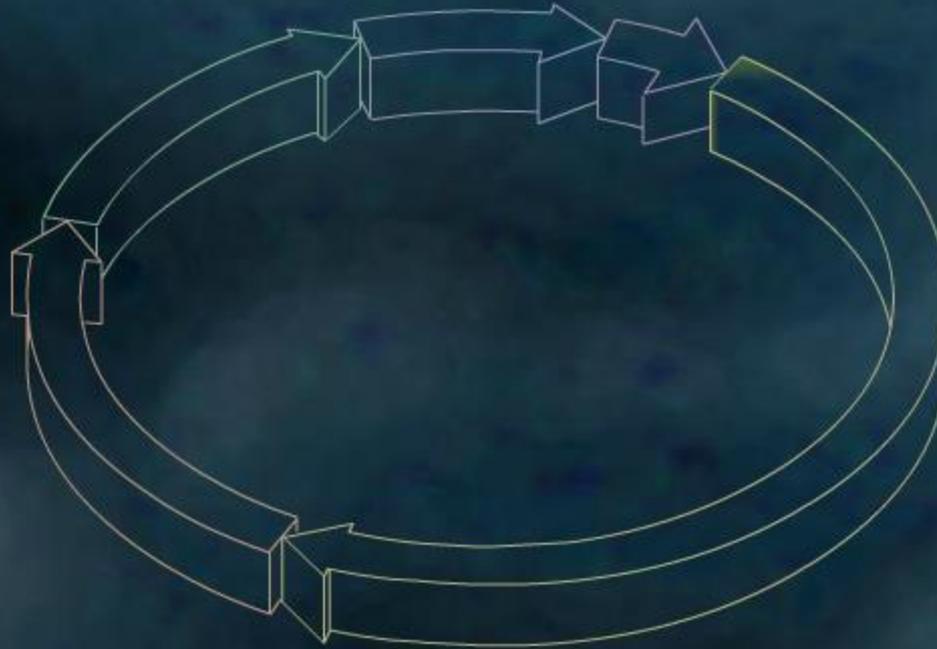


Figure 4.15

The Cell Cycle

- **G₁ phase**—the first gap phase
 - Interval between cell birth (from division) and DNA replication
 - Cell carries out normal tasks and accumulates materials for next phase
- **S phase**—synthesis phase
 - Cell replicates all nuclear DNA and duplicates centrioles
- **G₂ phase**—second gap phase
 - Interval between DNA replication and cell division
 - Cell repairs DNA replication errors, grows and synthesizes enzymes that control cell division
- **M phase**—mitotic phase
 - Cell replicates its nucleus
 - Pinches in two to form new daughter cells
- **G₀ (G zero) phase**—describes cells that have left the cycle and cease dividing for a long time (or permanently)
- **Cell cycle duration varies between cell types**

Control of the Cell Cycle



The process of cell growth and division in eukaryotes is called the cell cycle. This cycle is divided into phases based on what is happening in the cell at a given time. A cell grows during the G₁ phase.

Mitosis

- **Mitosis is cell division resulting in two genetically identical daughter cells**
- **Functions of mitosis**
 - Development of the individual from one fertilized egg to roughly 50 trillion cells
 - Growth of all tissues and organs after birth
 - Replacement of cells that die
 - Repair of damaged tissues
- **Four phases of mitosis**
 - Prophase, metaphase, anaphase, telophase

Mitosis

- **Prophase**

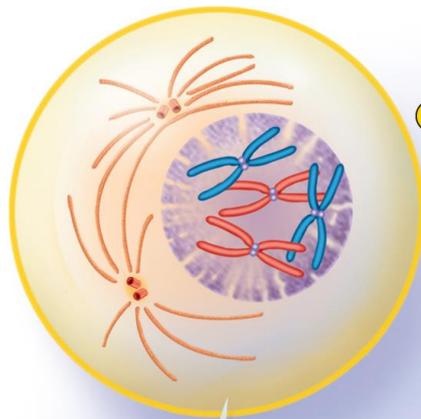
- Genetic material condenses into compact chromosomes
 - Easier to distribute to daughter cells than chromatin
- 46 chromosomes
 - Two **chromatids** per chromosome
- Nuclear envelope disintegrates
- Centrioles sprout **spindle fibers** (long microtubules)
 - Spindle fibers push centriole pairs apart
 - Some spindle fibers attach to kinetochores of centromeres of chromosomes

- **Metaphase**

- Chromosomes are aligned on **cell equator**
- Spindle fibers complete mitotic **spindle** (lemon-shaped)
- Shorter microtubules from centrioles complete an **aster** which anchors itself to inside of cell membrane

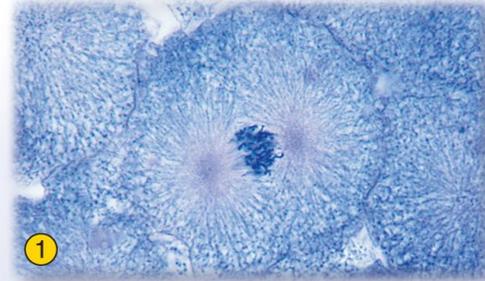
Mitosis

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

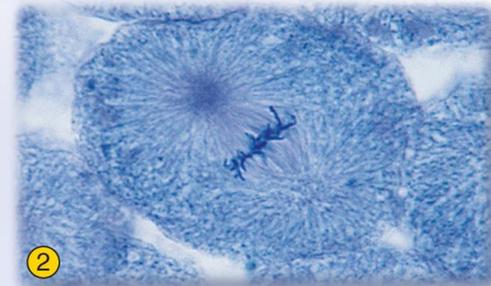


1 Prophase

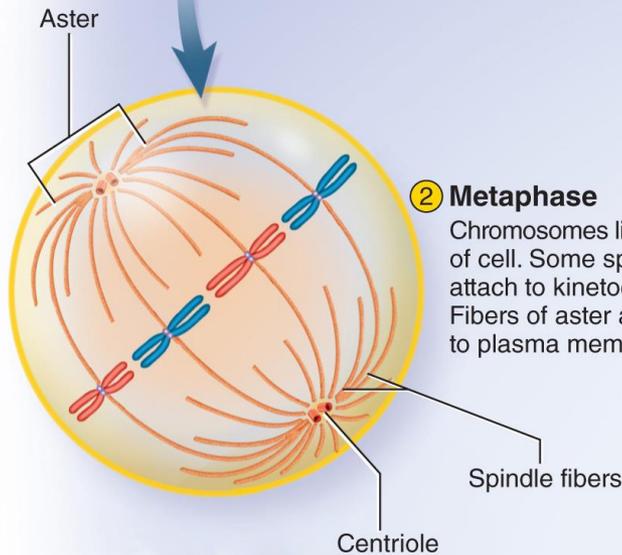
Chromosomes condense and nuclear envelope breaks down. Spindle fibers grow from centrioles. Centrioles migrate to opposite poles of cell.



1



2



2 Metaphase

Chromosomes lie along midline of cell. Some spindle fibers attach to kinetochores. Fibers of aster attach to plasma membrane.

(both): ©Ed Reschke

Figure 4.16 parts 1 & 2

Mitosis

- **Anaphase**

- Enzyme cleaves two sister chromatids apart at centromere
- Single-stranded daughter chromosomes migrate to each pole of the cell as motor proteins in kinetochores crawl along spindle fibers

- **Telophase**

- Chromosomes cluster on each side of the cell
- Rough ER makes new nuclear envelope around each cluster
- Chromosomes uncoil to chromatin
- Mitotic spindle disintegrates
- Each nucleus forms nucleoli

Mitosis

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

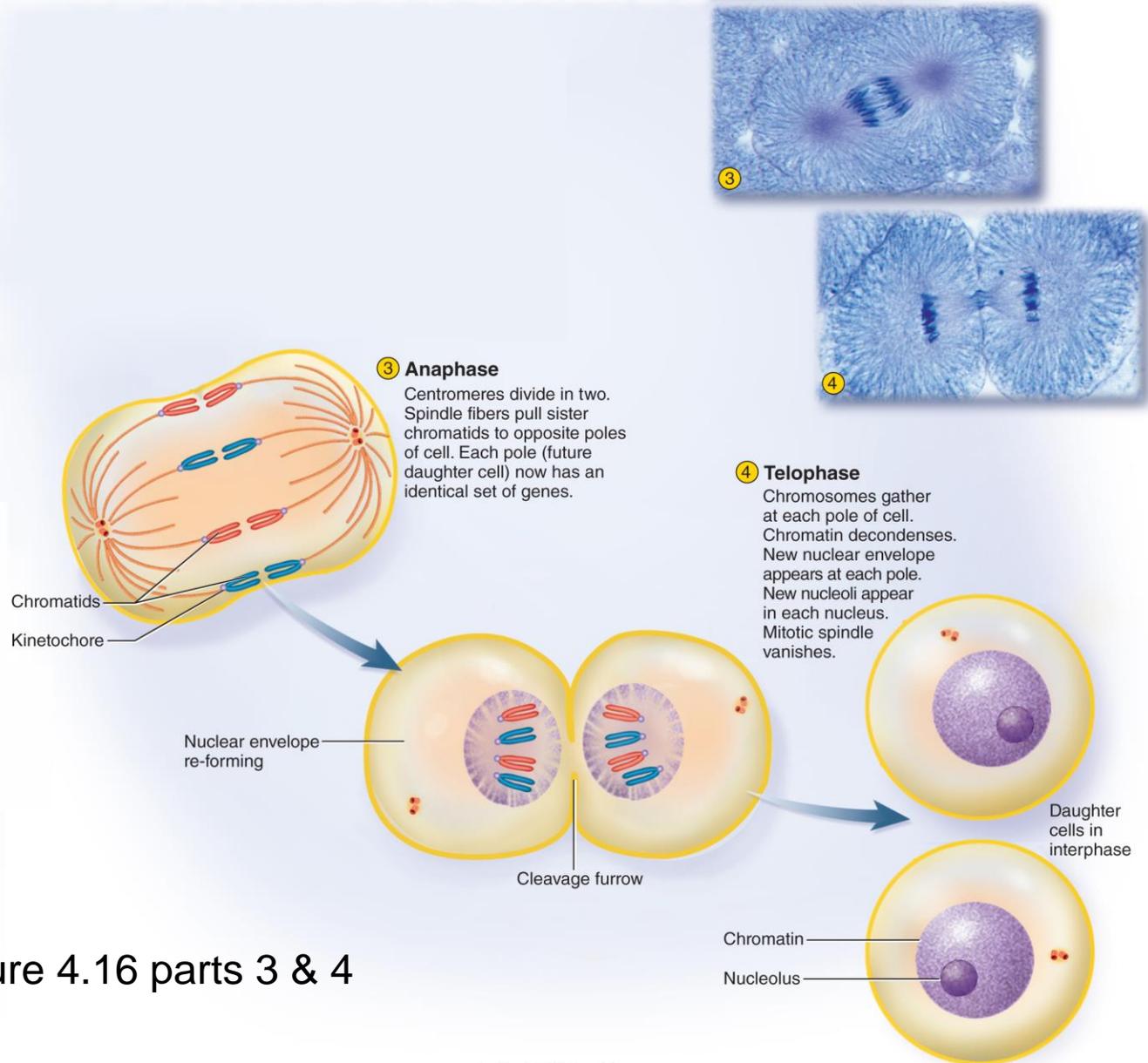
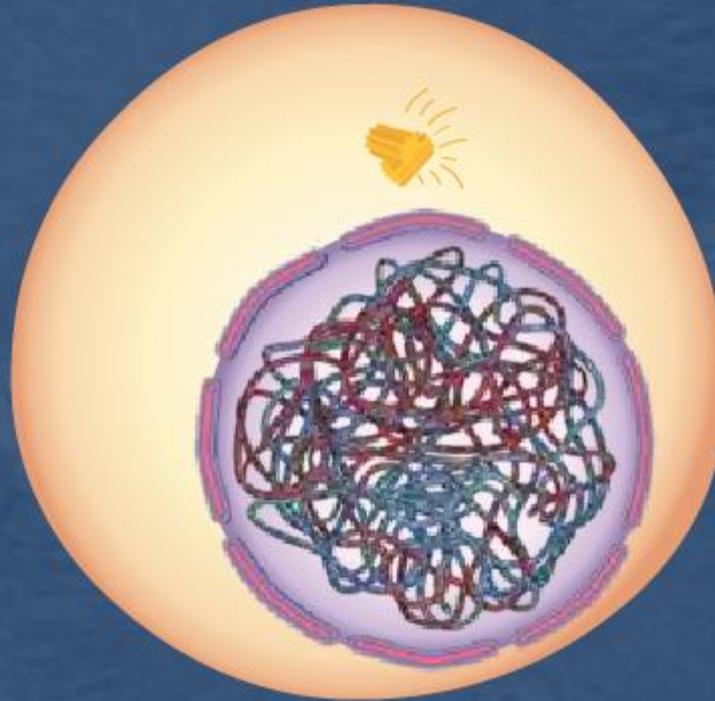


Figure 4.16 parts 3 & 4

Mitosis

- **Cytokinesis**—division of cytoplasm into two cells
 - Telophase is the end of nuclear division but overlaps cytokinesis
- Achieved by **myosin** protein pulling on **actin** in the terminal web of cytoskeleton
- Creates **cleavage furrow** around the equator of cell
- **Cell eventually pinches in two**

INTERPHASE



Play



Pause



Audio



Text

During interphase of the cell cycle, the genetic material of the cell is found in the form of chromatin and located within the nucleus of the cell, which is surrounded by the nuclear envelope.

The Timing of Cell Division

Cells divide when:

- They have enough cytoplasm for two daughter cells
- They have replicated their DNA
- They have adequate supply of nutrients
- They are stimulated by **growth factors** (chemical signals)
- Neighboring cells die, opening up space

Cells stop dividing when:

- They snugly contact neighboring cells
- Nutrients or growth factors are withdrawn
- They undergo **contact inhibition**—the cessation of cell division in response to contact with other cells

Chromosomes and Heredity

- **Expected Learning Outcomes**

- Describe the paired arrangement of chromosomes in the human karyotype.
- Define *allele* and discuss how alleles affect the traits of an individual.
- Discuss the interaction of heredity and environment in producing individual traits.

Chromosomes and Heredity

- **Heredity**—transmission of genetic characteristics from parent to offspring
- **Karyotype**—chart of 46 chromosomes laid out in order by size
- 23 pairs—the two members of each pair are called **homologous chromosomes**
 - 1 chromosome from each pair inherited from each parent
 - 22 pairs called **autosomes**
 - Look alike and carry the same genes
 - 1 pair of **sex chromosomes (X and Y)**
 - Female has homologous pair of X chromosomes
 - Male has one X and one much smaller Y chromosome

Karyotype

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

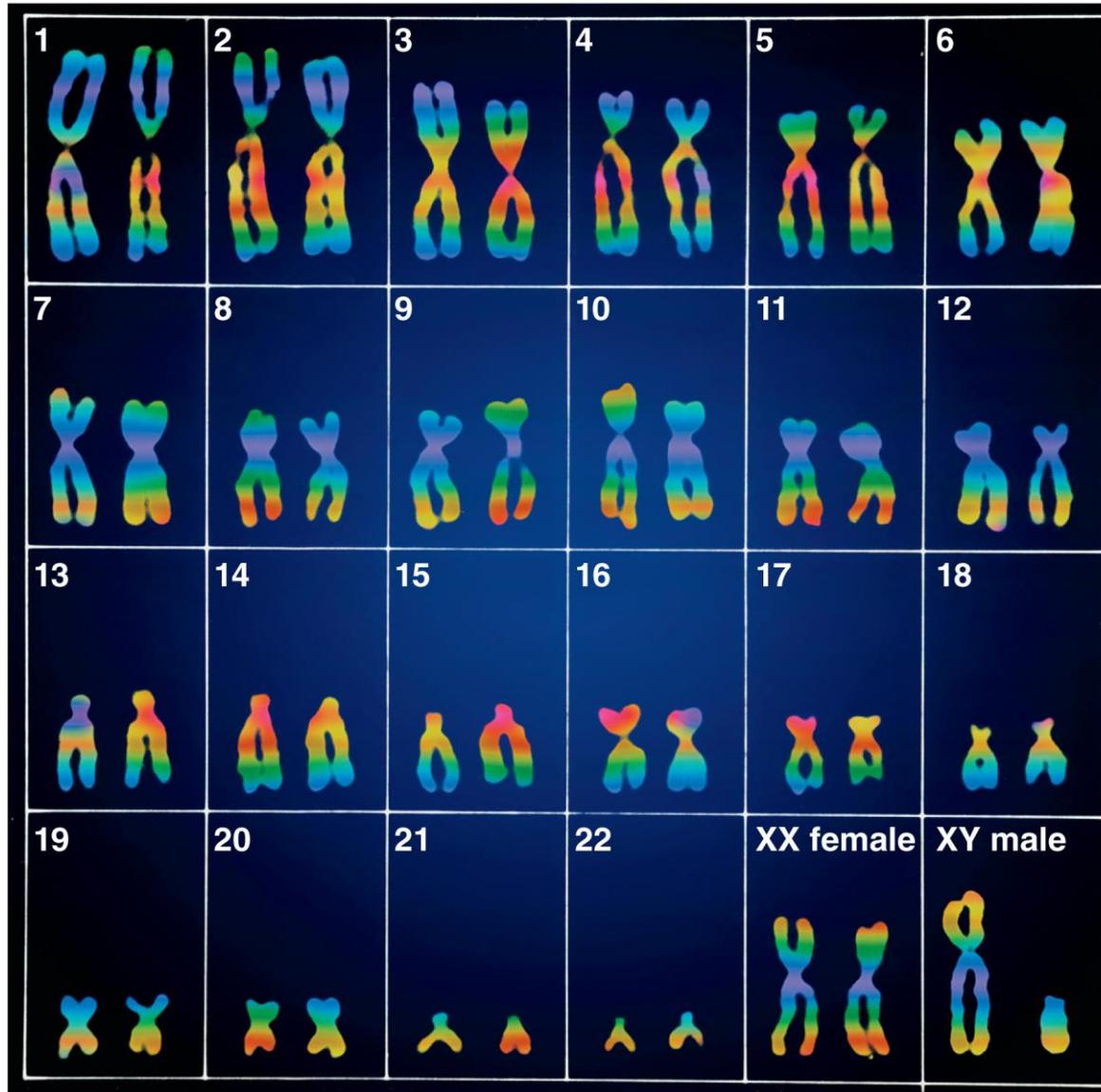


Figure 4.17

The Karyotype

- **Diploid**—describes any cell with 23 pairs of chromosomes (**somatic cells**)
- **Haploid**—describes cells containing half as many chromosomes (23 unpaired) as somatic cells; that is, sperm and egg cells (**germ cells**)
- **Fertilization** restores diploid number to the fertilized egg and the somatic cells arise from it

Genes and Alleles

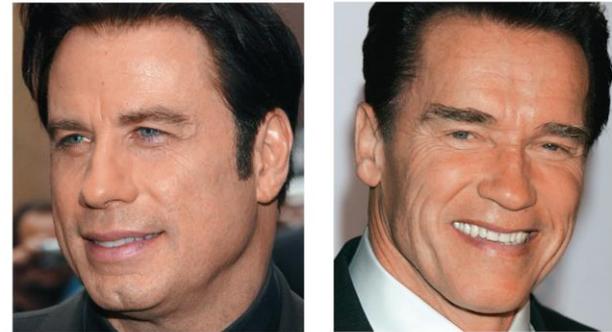
- **Locus**—the location of a particular gene on a chromosome
- **Alleles**—different forms of gene at same locus on two homologous chromosomes
- **Dominant allele** (represented by capital letter)
 - If present, corresponding trait is usually seen in the individual
 - Masks effect of recessive allele
 - Often produces protein responsible for visible trait
- **Recessive allele** (represented by lowercase letter)
 - Corresponding trait only seen when recessive allele present on both homologous chromosomes
 - Often codes for a nonfunctional variant of the protein

Genes and Alleles

- **Genotype**—alleles an individual possesses for a particular trait
 - **Homozygous** individuals—two identical alleles for the trait
 - **Heterozygous** individuals—different alleles for that gene
- **Phenotype**—an observable trait
 - An allele is **expressed** if it shows in the phenotype of an individual
- **Punnet square**—diagram showing possible genotype and phenotype outcomes from parents of known genotype
 - Example: Shows how two parents with dominant trait (cleft chin) can produce child with recessive trait (uncleft chin)

Genetics of Cleft Chin

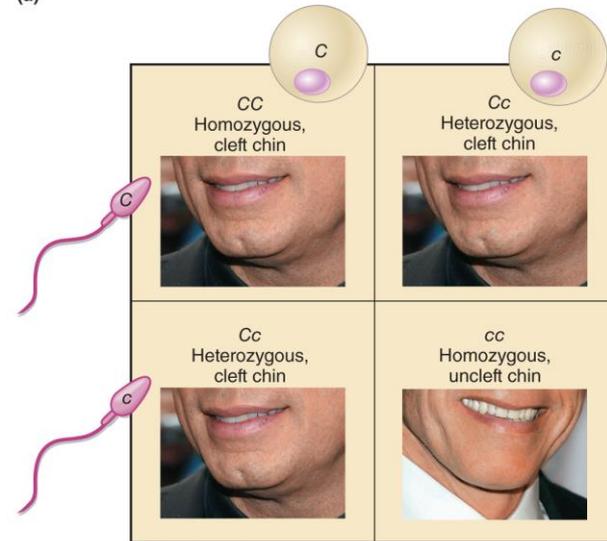
Copyright © McGraw-Hill Education. Permission required for reproduction or display.



Cleft chin
CC, Cc

Uncleft chin
cc

(a)



(b)

a (left): © Brad Barket/Getty Images; (right): © Kurt Krieger/Corbis

- Allele for cleft chin is dominant
- Parents are heterozygous
- Each parent has cleft chin phenotype
- One out of four offspring will have uncleft chin

Figure 4.18 b

Genes and Alleles

- **Parents can be healthy, heterozygous carriers of hereditary diseases**
- **Genetic counselors**—perform genetic testing and advise couples on the probability of transmitting genetic diseases

Multiple Alleles, Codominance, and Incomplete Dominance

- **Gene pool**—genetic makeup of whole population
- **Multiple alleles**—more than two allelic forms of gene
 - Example: three alleles for ABO blood types
 - I^A , I^B , i alleles for ABO blood types
- **Codominance**—both alleles equally dominant
 - Both are phenotypically expressed
 - Example: $I^A I^B$ = type AB blood
- **Incomplete dominance**
 - Heterozygous individual shows phenotype intermediate between traits each allele would have produced alone
 - Example: familial hypercholesterolemia

Polygenic Inheritance and Pleiotropy

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

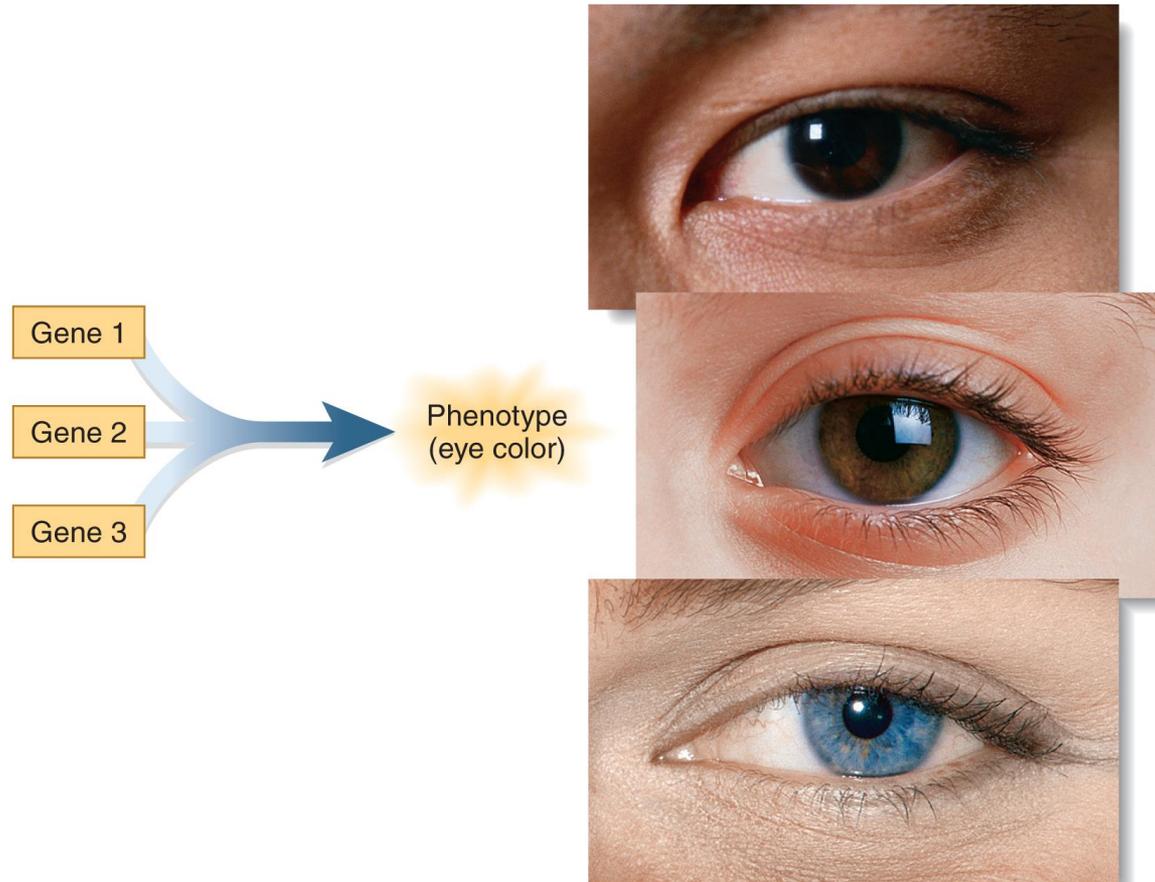


Figure 4.19

(top): © Comstock/Getty Images RF; (middle, bottom): ©Photodisc Red/Getty Images RF

- **Polygenic inheritance**—genes at two or more loci contribute to a single phenotypic trait
 - Examples: eye color, skin color, some forms of cancer

Polygenic Inheritance and Pleiotropy

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

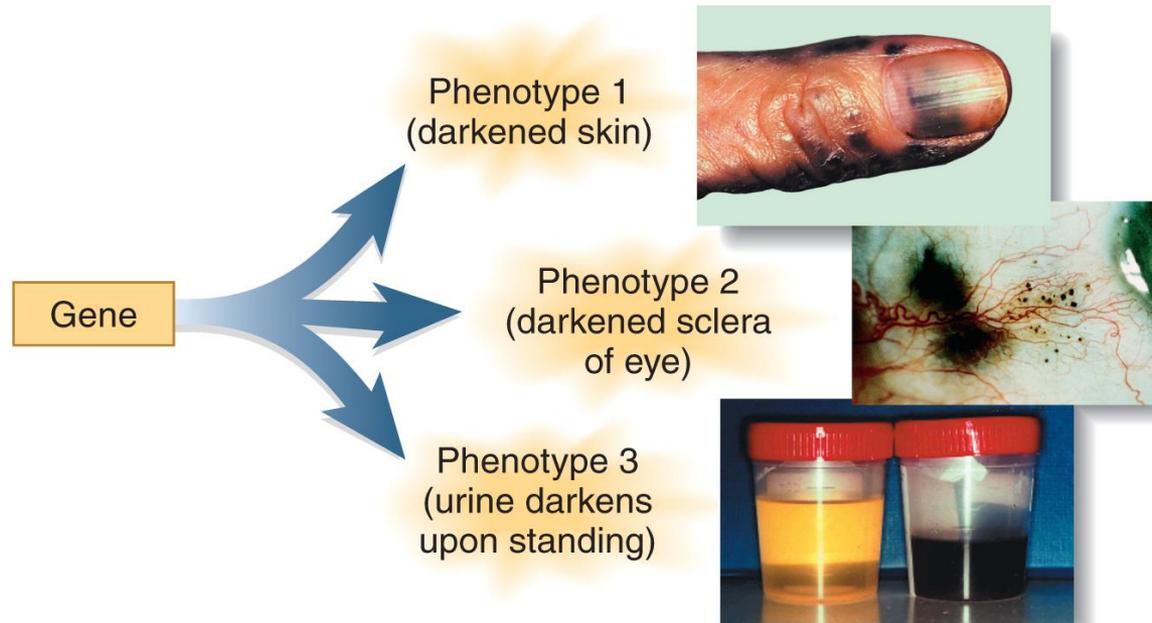


Figure 4.20

(Phenotype 1): From G. Pierrard, A. Nikkels. April 5, 2001, "A Medical Mystery" *The New England Journal of Medicine*, 344: p. 1057. ©2001 Massachusetts Medical Society. All rights reserved; (Phenotype 2): *British Journal of Ophthalmology* 1999; 83:680 ©by BMJ Publishing Group Ltd, <http://www.bjophthalmol.com>; (Phenotype 3): From G. Pierrard, A. Nikkels. April 5, 2001, "A Medical Mystery" *The New England Journal of Medicine*, 344: p. 1057. ©2001 Massachusetts Medical Society. All rights reserved

- **Pleiotropy**—one gene produces multiple phenotypic effects
 - Example: **alkaptonuria**—disorder resulting from mutation on chromosome 3 that blocks the breakdown of tyrosine

Sex Linkage

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.

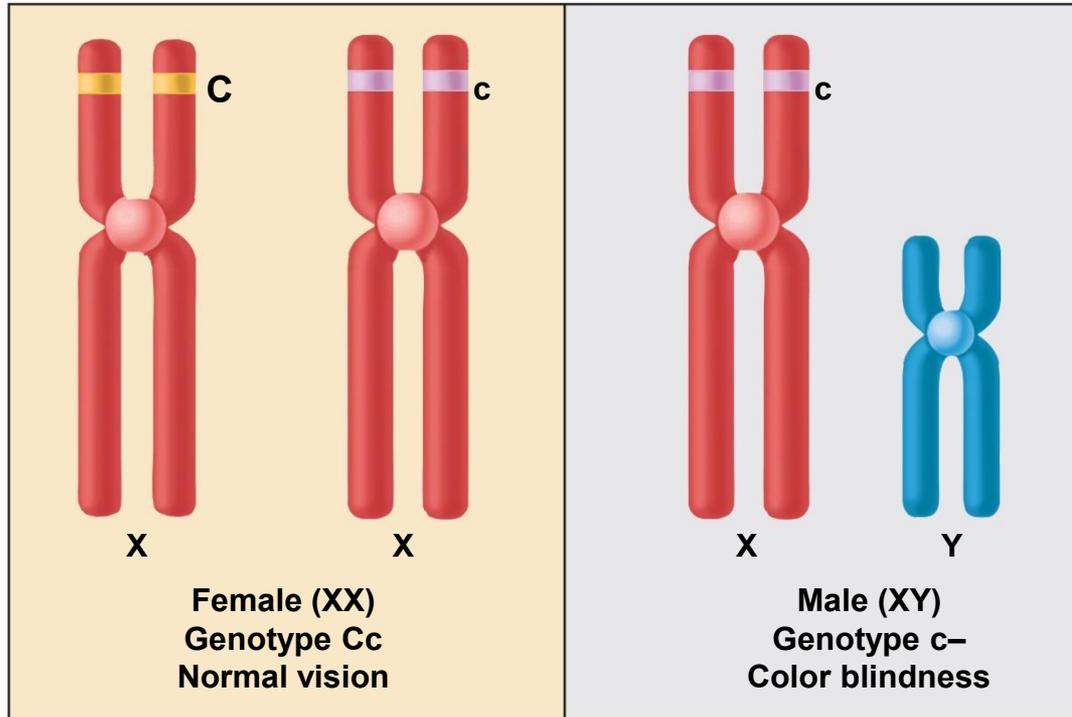


Figure 4.21

- **Sex-linked traits**—carried on X or Y chromosome, and therefore tend to be inherited by one sex more than the other
- **Recessive color blindness allele on X, no gene locus for trait on Y, so color blindness more common in men (mother is carrier in illustrated example)**

Penetrance and Environmental Effects

- **Penetrance** of allele—percentage of population exhibiting expected phenotype
 - Example: dominant polydactyly allele only causes extra digits in 80% of those who have it
- **Environmental factors** influence gene expression
 - Example: genes for melanin eye pigment can only be fully expressed if phenylalanine is in diet

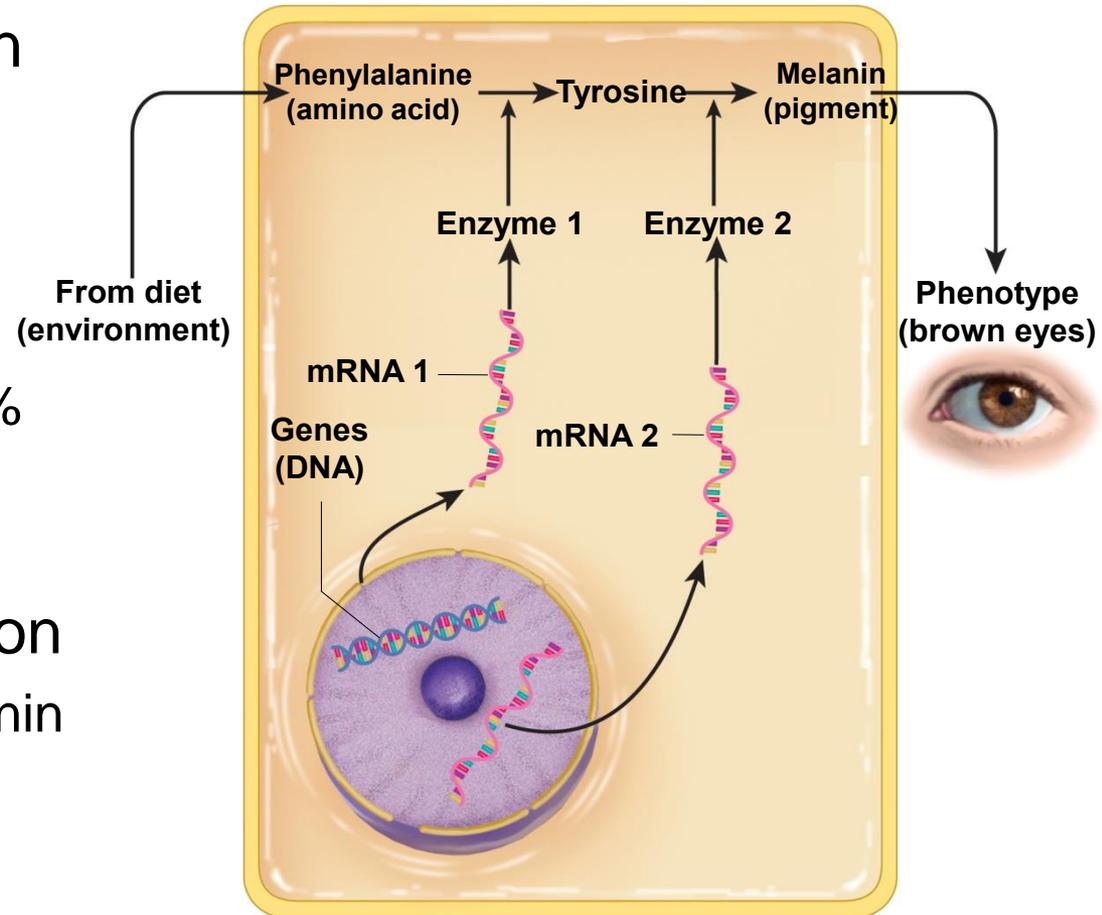


Figure 4.22

Dominant and Recessive Alleles at the Population Level

- **Common misconception that dominant alleles must be more common in the gene pool than recessive alleles**
- **Some recessive alleles, blood type O, are the most common**
- **Some dominant alleles, polydactyly and blood type AB, are rare in the population**

Epigenetics

- **Epigenetics**—field examining nongenetic changes that alter gene expression and can be passed to offspring
 - Gene expression is changed without genetic mutation to base sequence
 - **DNA methylation**—mechanism of epigenetic change in which methyl groups are added to DNA
 - Often silences the gene
 - Inappropriate DNA methylation implicated in some forms of cancer

Cancer

Copyright © McGraw-Hill Education. Permission required for reproduction or display.

- **Malignant tumors cause cancer**

- Fast growing, tend to **metastasize**—to give off cells that spread and seed the growth of tumors elsewhere
- Distinguished from slow growing, encapsulated **benign** tumors

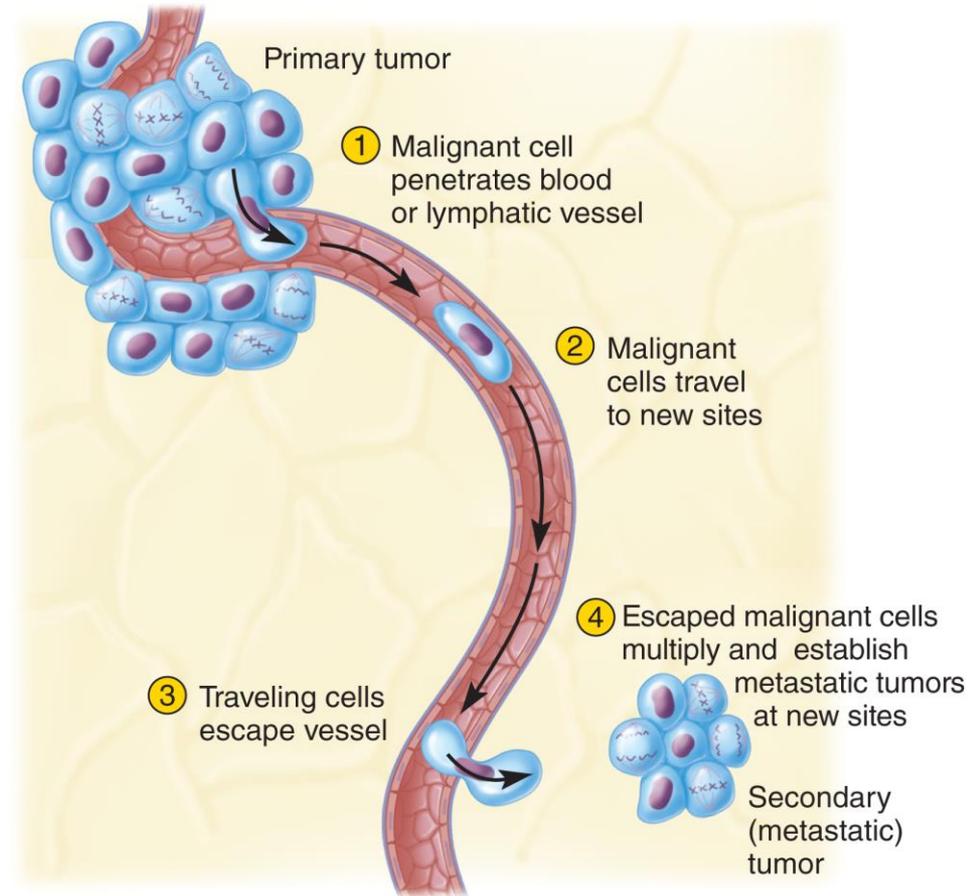


Figure 4.23

Cancer

- **Oncology**—medical specialty dealing with tumors
- **Tumor angiogenesis**—growth of blood vessels by energy-hungry tumors
- **Cancers are named for tissue of origin**
 - **Carcinomas**: in epithelial tissue
 - **Lymphomas**: in lymph nodes
 - **Melanomas**: in pigment cells of epidermis (melanocytes)
 - **Leukemias**: in blood-forming tissues
 - **Sarcomas**: in bone, other connective tissue, or muscle

Cancer

- **Carcinogens**—environmental cancer-causing agents
 - **Radiation**—ultraviolet rays, X-rays
 - **Chemical**—cigarette tar, food preservatives, industrial chemicals
 - **Viruses**—human papillomavirus, hepatitis C, and type 2 herpes simplex
- **Only 5% to 10% of cancers are hereditary**
- **Carcinogens trigger gene mutations**

Cancer

- **Oncogenes**

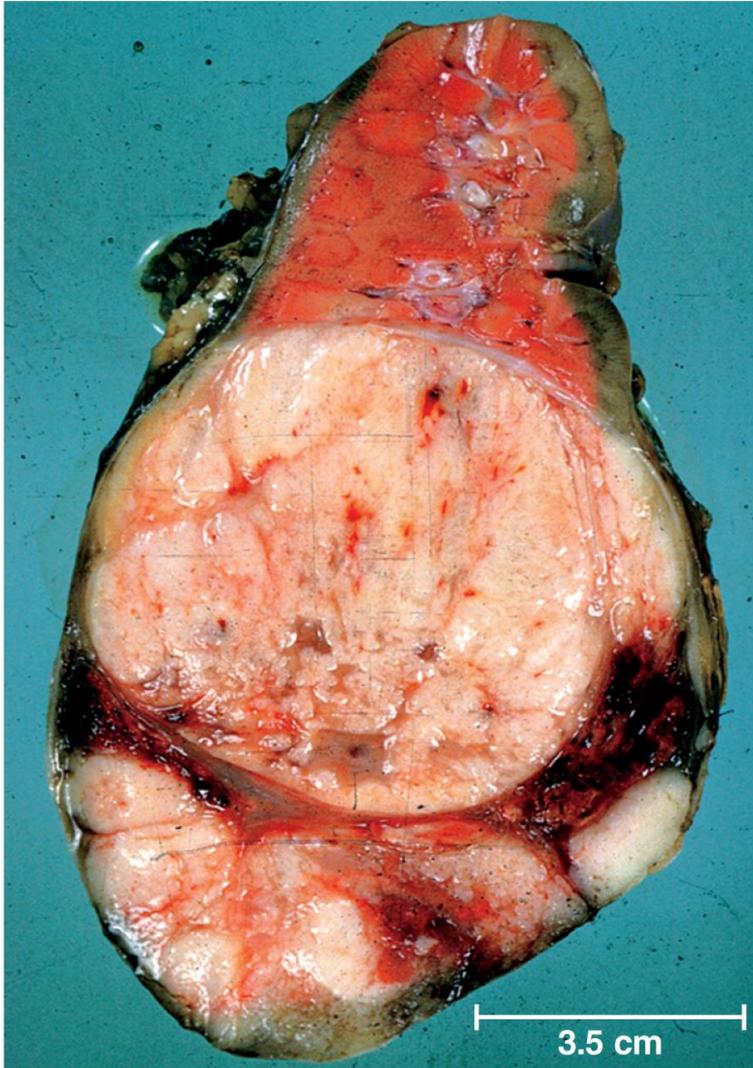
- Cause cell division to accelerate out of control
 - Excessive production of growth factors or growth-factor receptors that stimulate mitosis

- **Tumor-suppressor (TS) genes**

- Healthy tumor suppressor genes inhibit development of cancer
 - Some code for DNA-repair enzymes
- Mutated TS genes or silenced TS genes leave oncogene action unopposed

Cancer

Copyright © McGraw-Hill Education. Permission required for reproduction or display.



- **Wilms tumor**
 - Malignant tumor of the kidney occurring especially in children

Figure 4.24

From the University of Alabama at Birmingham, Department of Pathology PEIR Digital Library ©<http://peir.net>

Lethal Effects of Cancer

- **Replace functional tissue in vital organs**
 - Often invade blood vessels, lung tissue, or brain tissue
- **Steal nutrients from the rest of the body**
 - **Cachexia:** severe wasting away of depleted tissues
- **Weaken one's immunity**
- **Open the door for opportunistic infections**