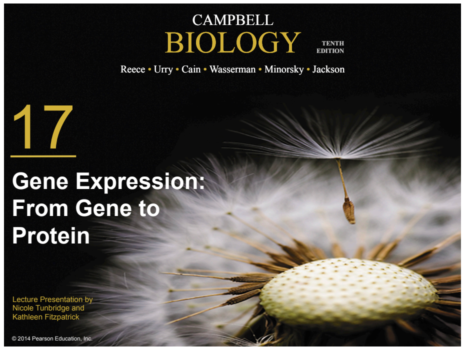


The Flow of Genetic Information

- The information content of genes is in the specific sequences of nucleotides
- The DNA inherited by an organism leads to specific traits by dictating the synthesis of proteins
- Proteins are the links between genotype and phenotype
- **Gene expression**, the process by which DNA directs protein synthesis, includes two stages: transcription and translation

Figure 17.1

Figure 17.1a

An albino racoon

Concept 17.1: Genes specify proteins via transcription and translation

- How was the fundamental relationship between genes and proteins discovered?

Evidence from the Study of Metabolic Defects

- In 1902, British physician Archibald Garrod first suggested that genes dictate phenotypes through enzymes that catalyze specific chemical reactions
- He thought symptoms of an inherited disease reflect an inability to synthesize a certain enzyme
- Cells synthesize and degrade molecules in a series of steps, a metabolic pathway

Nutritional Mutants in Neurospora: Scientific Inquiry

- George Beadle and Edward Tatum exposed bread mold to X-rays, creating mutants that were unable to survive on minimal media
- Using crosses, they and their coworkers identified three classes of arginine-deficient mutants, each lacking a different enzyme necessary for synthesizing arginine
- They developed a one gene–one enzyme hypothesis, which states that each gene dictates production of a specific enzyme

Figure 17.2

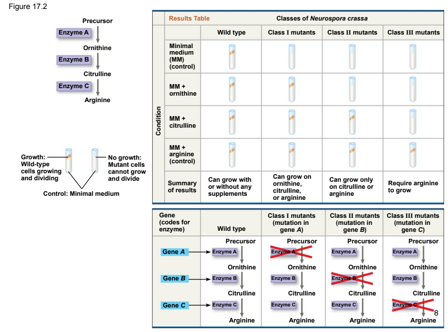


Figure 17.2a

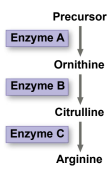


Figure 17.2b

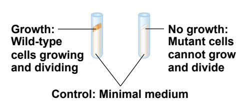


Figure 17.2c

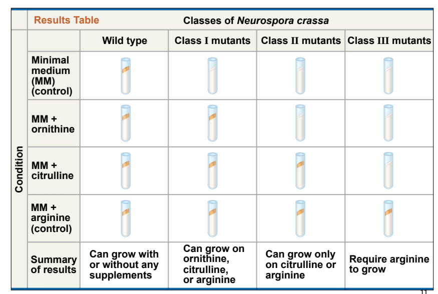
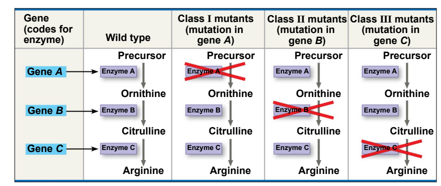


Figure 17.2d



The Products of Gene Expression: A Developing Story

- Some proteins aren't enzymes, so researchers later revised the hypothesis: one gene–one protein
- Many proteins are composed of several polypeptides, each of which has its own gene
- Therefore, Beadle and Tatum's hypothesis is now restated as the one gene–one polypeptide hypothesis
- It is common to refer to gene products as proteins rather than polypeptides

Basic Principles of Transcription and Translation

- RNA is the bridge between genes and the proteins for which they code
- **Transcription** is the synthesis of RNA using information in DNA
- Transcription produces **messenger RNA (mRNA)**
- **Translation** is the synthesis of a polypeptide, using information in the mRNA
- **Ribosomes** are the sites of translation

- In prokaryotes, translation of mRNA can begin before transcription has finished
- In a eukaryotic cell, the nuclear envelope separates transcription from translation
- Eukaryotic RNA transcripts are modified through RNA processing to yield the finished mRNA

Figure 17.3

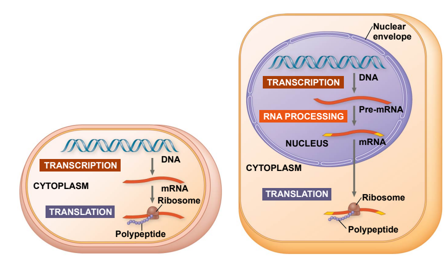
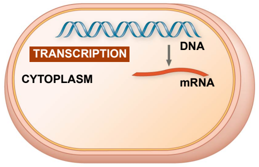
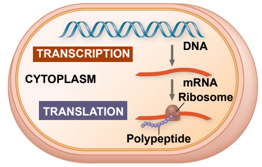


Figure 17.3a-1



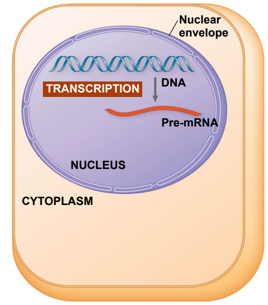
(a) Bacterial cell

Figure 17.3a-2



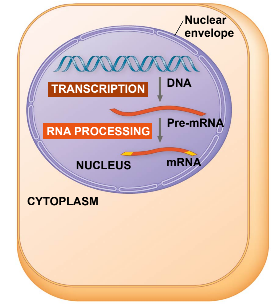
(a) Bacterial cell

Figure 17.3b-1



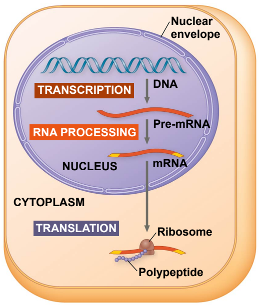
(b) Eukaryotic cell

Figure 17.3b-2



(b) Eukaryotic cell

Figure 17.3b-3



(b) Eukaryotic cell

- A **primary transcript** is the initial RNA transcript from any gene prior to processing
- The *central dogma* is the concept that cells are governed by a cellular chain of command: DNA → RNA → protein

Figure 17.UN01

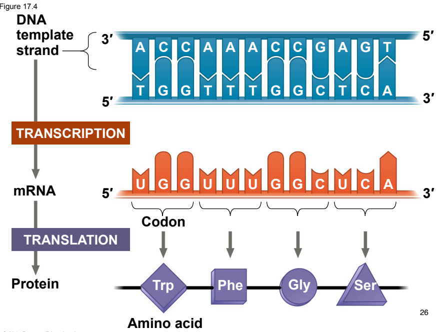
The Genetic Code

- How are the instructions for assembling amino acids into proteins encoded into DNA?
- There are 20 amino acids, but there are only four nucleotide bases in DNA
- How many nucleotides correspond to an amino acid?

Codons: Triplets of Nucleotides

- The flow of information from gene to protein is based on a **triplet code**: a series of nonoverlapping, three-nucleotide words
- The words of a gene are transcribed into complementary nonoverlapping three-nucleotide words of mRNA
- These words are then translated into a chain of amino acids, forming a polypeptide

Figure 17.4



- During transcription, one of the two DNA strands, called the **template strand**, provides a template for ordering the sequence of complementary nucleotides in an RNA transcript
- The template strand is always the same strand for a given gene

- During translation, the mRNA base triplets, called **codons**, are read in the 5′ → 3′ direction
- Each codon specifies the amino acid (one of 20) to be placed at the corresponding position along a polypeptide

Cracking the Code

- All 64 codons were deciphered by the mid-1960s
- Of the 64 triplets, 61 code for amino acids; 3 triplets are "stop" signals to end translation
- The genetic code is redundant (more than one codon may specify a particular amino acid) but not ambiguous; no codon specifies more than one amino acid
- Codons must be read in the correct **reading frame** (correct groupings) in order for the specified polypeptide to be produced

Figure 17.5

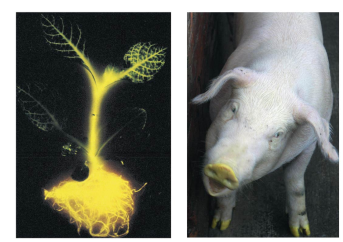
Second mRNA base

First mRNA base (5′ end of codon)	U	C	A	G	Third mRNA base (3′ end of codon)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
U	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
U	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
U	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
C	CUC Leu	CCC Pro	CAC His	CGC Arg	C
C	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
C	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
A	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
A	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
A	AUG Met or start	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
G	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
G	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
G	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

Evolution of the Genetic Code

- The genetic code is nearly universal, shared by the simplest bacteria to the most complex animals
- Genes can be transcribed and translated after being transplanted from one species to another

Figure 17.6



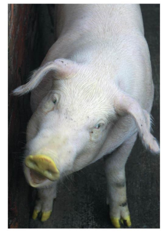
(a) Tobacco plant expressing a firefly gene

(b) Pig expressing a jellyfish gene

Figure 17.6a

(a) Tobacco plant expressing a firefly gene

Figure 17.6b



(b) Pig expressing a jellyfish gene

Concept 17.2: Transcription is the DNA-directed synthesis of RNA: *A closer look*

- Transcription is the first stage of gene expression

Molecular Components of Transcription

- RNA synthesis is catalyzed by **RNA polymerase**, which pries the DNA strands apart and joins together the RNA nucleotides
- The RNA is complementary to the DNA template strand
- RNA polymerase does not need any primer
- RNA synthesis follows the same base-pairing rules as DNA, except that uracil substitutes for thymine

Figure 17.7-1

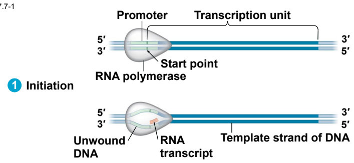


Figure 17.7-2

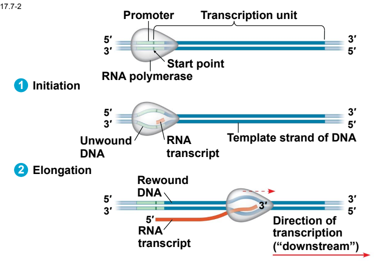
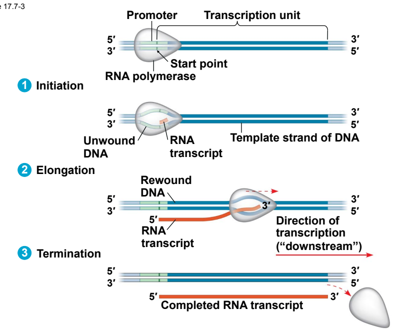
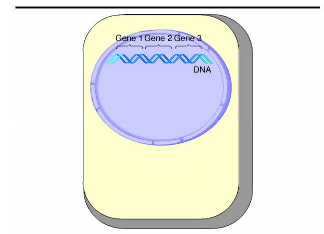


Figure 17.7-3



Animation: Transcription



- The DNA sequence where RNA polymerase attaches is called the **promoter**; in bacteria, the sequence signaling the end of transcription is called the **terminator**
- The stretch of DNA that is transcribed is called a **transcription unit**

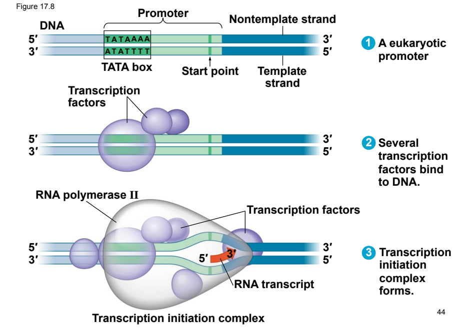
Synthesis of an RNA Transcript

- The three stages of transcription
  - Initiation
  - Elongation
  - Termination

RNA Polymerase Binding and Initiation of Transcription

- Promoters signal the transcriptional **start point** and usually extend several dozen nucleotide pairs upstream of the start point
- **Transcription factors** mediate the binding of RNA polymerase and the initiation of transcription
- The completed assembly of transcription factors and RNA polymerase II bound to a promoter is called a **transcription initiation complex**
- A promoter called a **TATA box** is crucial in forming the initiation complex in eukaryotes

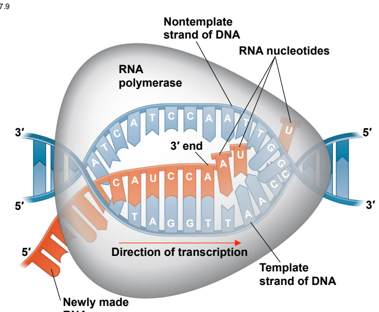
Figure 17.8



Elongation of the RNA Strand

- As RNA polymerase moves along the DNA, it untwists the double helix, 10 to 20 bases at a time
- Transcription progresses at a rate of 40 nucleotides per second in eukaryotes
- A gene can be transcribed simultaneously by several RNA polymerases
- Nucleotides are added to the 3′ end of the growing RNA molecule

Figure 17.9



Termination of Transcription

- The mechanisms of termination are different in bacteria and eukaryotes
- In bacteria, the polymerase stops transcription at the end of the terminator and the mRNA can be translated without further modification
- In eukaryotes, RNA polymerase II transcribes the polyadenylation signal sequence; the RNA transcript is released 10–35 nucleotides past this polyadenylation sequence

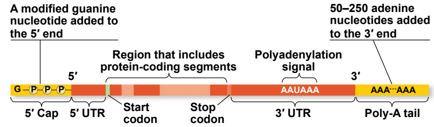
Concept 17.3: Eukaryotic cells modify RNA after transcription

- Enzymes in the eukaryotic nucleus modify pre-mRNA (**RNA processing**) before the genetic messages are dispatched to the cytoplasm
- During RNA processing, both ends of the primary transcript are usually altered
- Also, usually certain interior sections of the molecule are cut out, and the remaining parts spliced together

Alteration of mRNA Ends

- Each end of a pre-mRNA molecule is modified in a particular way
  - The 5′ end receives a modified nucleotide **5′ cap**
  - The 3′ end gets a **poly-A tail**
- These modifications share several functions
  - They seem to facilitate the export of mRNA to the cytoplasm
  - They protect mRNA from hydrolytic enzymes
  - They help ribosomes attach to the 5′ end

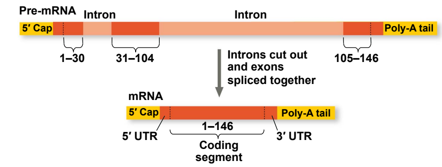
Figure 17.10



Split Genes and RNA Splicing

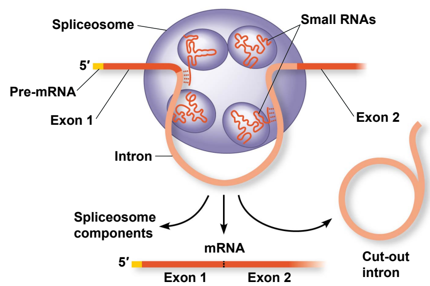
- Most eukaryotic genes and their RNA transcripts have long noncoding stretches of nucleotides that lie between coding regions
- These noncoding regions are called intervening sequences, or **introns**
- The other regions are called **exons** because they are eventually expressed, usually translated into amino acid sequences
- **RNA splicing** removes introns and joins exons, creating an mRNA molecule with a continuous coding sequence

Figure 17.11



- In some cases, RNA splicing is carried out by spliceosomes
- **Spliceosomes** consist of a variety of proteins and several small nuclear ribonucleoproteins (snRNPs) that recognize the splice sites
- The RNAs of the spliceosome also catalyze the splicing reaction

Figure 17.12



Ribozymes

- **Ribozymes** are catalytic RNA molecules that function as enzymes and can splice RNA
- The discovery of ribozymes rendered obsolete the belief that all biological catalysts were proteins

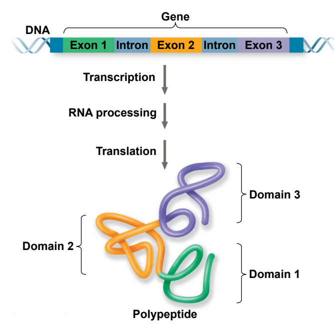
- Three properties of RNA enable it to function as an enzyme
  - It can form a three-dimensional structure because of its ability to base-pair with itself
  - Some bases in RNA contain functional groups that may participate in catalysis
  - RNA may hydrogen-bond with other nucleic acid molecules

The Functional and Evolutionary Importance of Introns

- Some introns contain sequences that may regulate gene expression
- Some genes can encode more than one kind of polypeptide, depending on which segments are treated as exons during splicing
- This is called **alternative RNA splicing**
- Consequently, the number of different proteins an organism can produce is much greater than its number of genes

- Proteins often have a modular architecture consisting of discrete regions called **domains**
- In many cases, different exons code for the different domains in a protein
- Exon shuffling may result in the evolution of new proteins

Figure 17.13



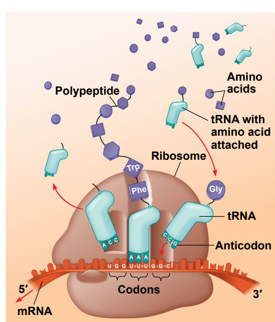
Concept 17.4: Translation is the RNA-directed synthesis of a polypeptide: *A closer look*

- Genetic information flows from mRNA to protein through the process of translation

Molecular Components of Translation

- A cell translates an mRNA message into protein with the help of **transfer RNA (tRNA)**
- tRNAs transfer amino acids to the growing polypeptide in a ribosome
- Translation is a complex process in terms of its biochemistry and mechanics

Figure 17.14



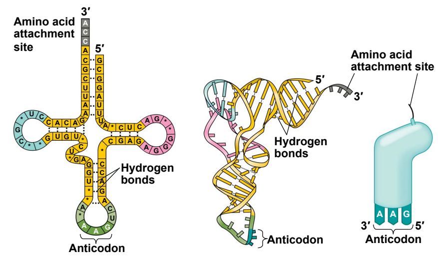
The Structure and Function of Transfer RNA

- Molecules of tRNA are not identical
  - Each carries a specific amino acid on one end
  - Each has an **anticodon** on the other end; the anticodon base-pairs with a complementary codon on mRNA

- A tRNA molecule consists of a single RNA strand that is only about 80 nucleotides long
- Flattened into one plane to reveal its base pairing, a tRNA molecule looks like a cloverleaf

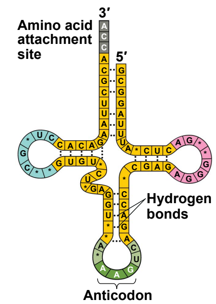
- Because of hydrogen bonds, tRNA actually twists and folds into a three-dimensional molecule
- tRNA is roughly L-shaped

Figure 17.15



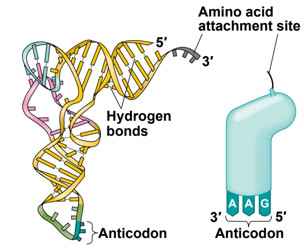
(a) Two-dimensional structure (b) Three-dimensional structure (c) Symbol used in this book

Figure 17.15a



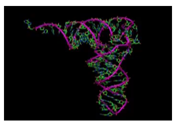
(a) Two-dimensional structure

Figure 17.15b



(b) Three-dimensional structure (c) Symbol used in this book

Video: Stick and Ribbon Rendering of a tRNA



- Accurate translation requires two steps
  - First: a correct match between a tRNA and an amino acid, done by the enzyme **aminoacyl-tRNA synthetase**
  - Second: a correct match between the tRNA anticodon and an mRNA codon
- Flexible pairing at the third base of a codon is called **wobble** and allows some tRNAs to bind to more than one codon

Figure 17.16-1

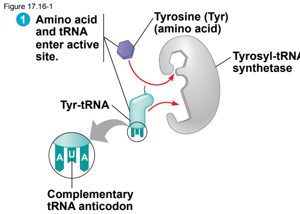


Figure 17.16-2

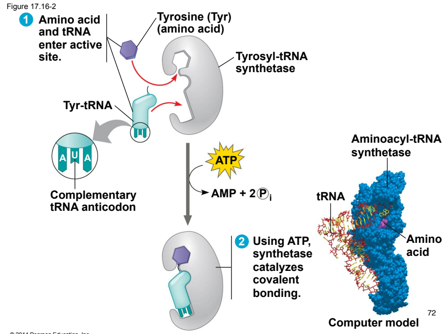
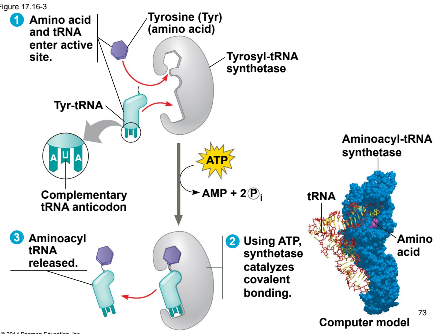


Figure 17.16-3



Ribosomes

- Ribosomes facilitate specific coupling of tRNA anticodons with mRNA codons in protein synthesis
- The two ribosomal subunits (large and small) are made of proteins and **ribosomal RNA (rRNA)**
- Bacterial and eukaryotic ribosomes are somewhat similar but have significant differences: some antibiotic drugs specifically target bacterial ribosomes without harming eukaryotic ribosomes

Figure 17.17

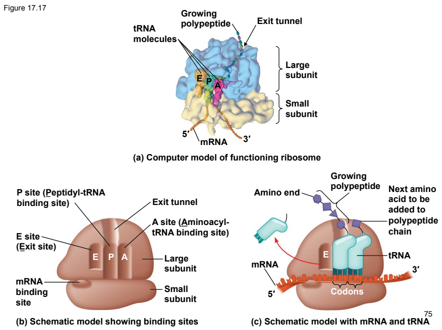
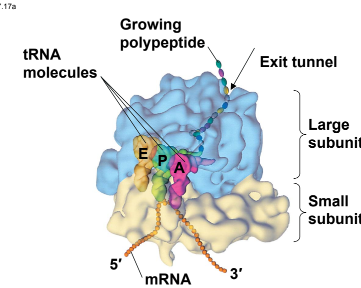
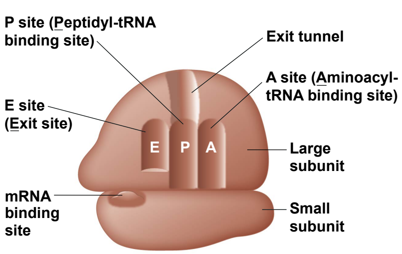


Figure 17.17a



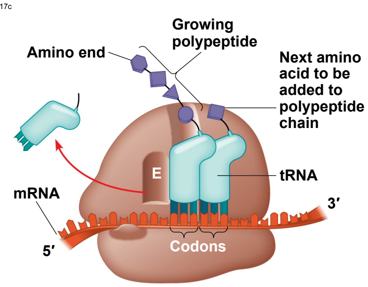
(a) Computer model of functioning ribosome

Figure 17.17b



(b) Schematic model showing binding sites

Figure 17.17c



(c) Schematic model with mRNA and tRNA

- A ribosome has three binding sites for tRNA
  - The **P site** holds the tRNA that carries the growing polypeptide chain
  - The **A site** holds the tRNA that carries the next amino acid to be added to the chain
  - The **E site** is the exit site, where discharged tRNAs leave the ribosome

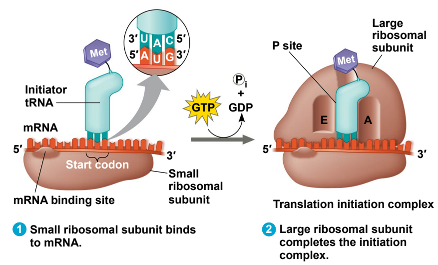
Building a Polypeptide

- The three stages of translation
  - Initiation
  - Elongation
  - Termination
- All three stages require protein “factors” that aid in the translation process
- Energy is required for some steps also

Ribosome Association and Initiation of Translation

- Initiation brings together mRNA, a tRNA with the first amino acid, and the two ribosomal subunits
- First, a small ribosomal subunit binds with mRNA and a special initiator tRNA
- Then the small subunit moves along the mRNA until it reaches the start codon (AUG)
- Proteins called initiation factors bring in the large subunit that completes the translation initiation complex

Figure 17.18



Elongation of the Polypeptide Chain

- During elongation, amino acids are added one by one to the C-terminus of the growing chain
- Each addition involves proteins called elongation factors and occurs in three steps: codon recognition, peptide bond formation, and translocation
- Energy expenditure occurs in the first and third steps
- Translation proceeds along the mRNA in a 5′ → 3′ direction

Figure 17.19-1

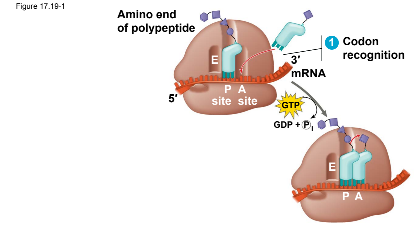


Figure 17.19-2

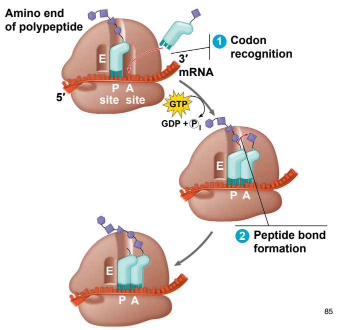
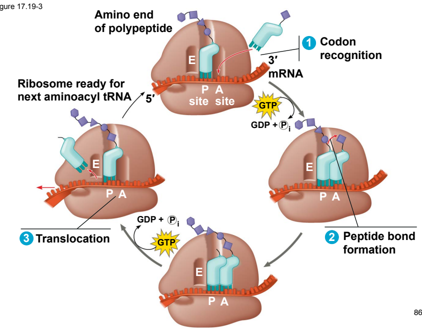


Figure 17.19-3



Termination of Translation

- Termination occurs when a stop codon in the mRNA reaches the A site of the ribosome
- The A site accepts a protein called a release factor
- The release factor causes the addition of a water molecule instead of an amino acid
- This reaction releases the polypeptide, and the translation assembly comes apart

Figure 17.20-1

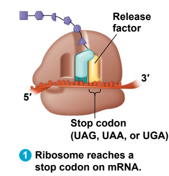


Figure 17.20-2

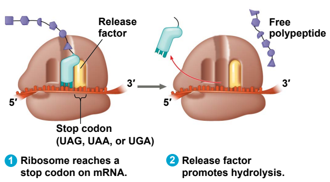
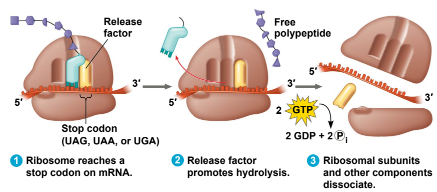


Figure 17.20-3



Completing and Targeting the Functional Protein

- Often translation is not sufficient to make a functional protein
- Polypeptide chains are modified after translation or targeted to specific sites in the cell

Protein Folding and Post-Translational Modifications

- During its synthesis, a polypeptide chain begins to coil and fold spontaneously to form a protein with a specific shape—a three-dimensional molecule with secondary and tertiary structure
- A gene determines primary structure, and primary structure in turn determines shape
- Post-translational modifications may be required before the protein can begin doing its particular job in the cell

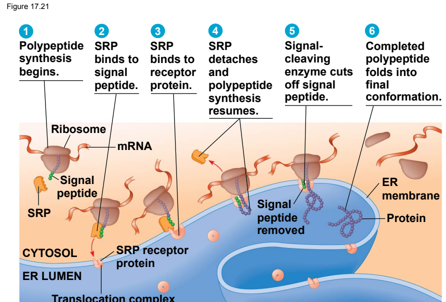
Targeting Polypeptides to Specific Locations

- Two populations of ribosomes are evident in cells: free ribosomes (in the cytosol) and bound ribosomes (attached to the ER)
- Free ribosomes mostly synthesize proteins that function in the cytosol
- Bound ribosomes make proteins of the endomembrane system and proteins that are secreted from the cell
- Ribosomes are identical and can switch from free to bound

- Polypeptide synthesis always begins in the cytosol
- Synthesis finishes in the cytosol unless the polypeptide signals the ribosome to attach to the ER
- Polypeptides destined for the ER or for secretion are marked by a **signal peptide**

- A **signal-recognition particle (SRP)** binds to the signal peptide
- The SRP brings the signal peptide and its ribosome to the ER

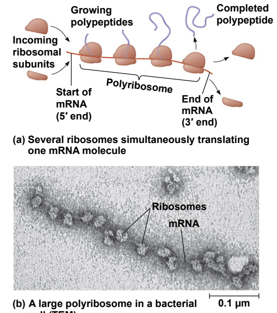
Figure 17.21



Making Multiple Polypeptides in Bacteria and Eukaryotes

- Multiple ribosomes can translate a single mRNA simultaneously, forming a **polyribosome** (or **polysome**)
- Polyribosomes enable a cell to make many copies of a polypeptide very quickly

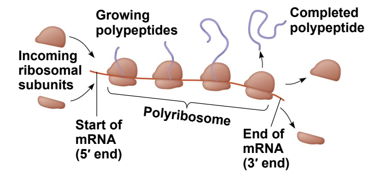
Figure 17.22



(a) Several ribosomes simultaneously translating one mRNA molecule

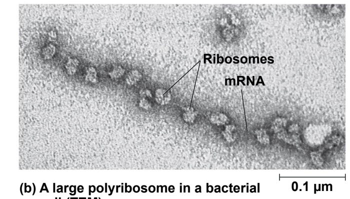
(b) A large polyribosome in a bacterial cell (TEM)

Figure 17.22a



(a) Several ribosomes simultaneously translating one mRNA molecule

Figure 17.22b



(b) A large polyribosome in a bacterial cell (TEM)

- A bacterial cell ensures a streamlined process by coupling transcription and translation
- In this case the newly made protein can quickly diffuse to its site of function

Figure 17.23

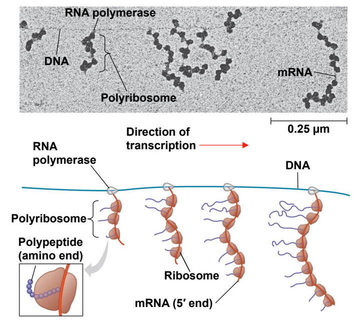
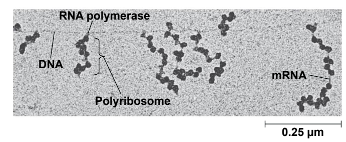


Figure 17.23a



- In eukaryotes, the nuclear envelop separates the processes of transcription and translation
- RNA undergoes processes before leaving the nucleus

Figure 17.24

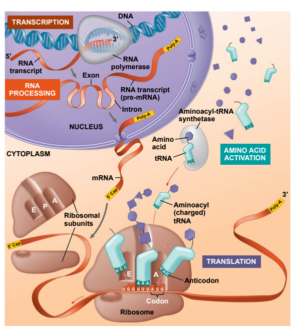


Figure 17.24a

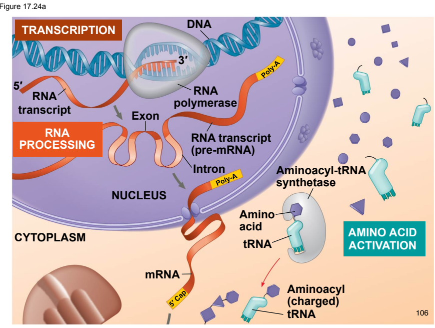
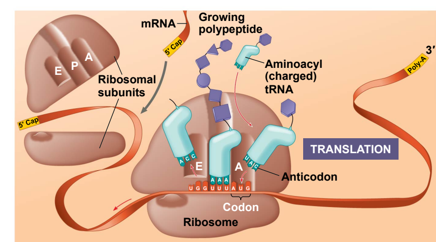
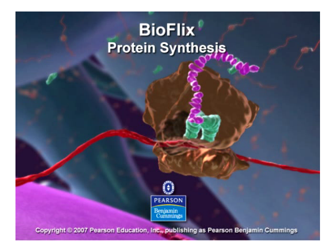


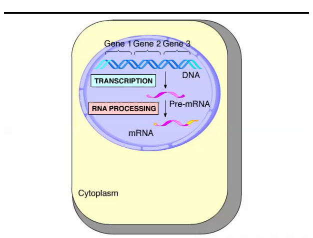
Figure 17.24b



BioFlix: Protein Synthesis



Animation: Translation

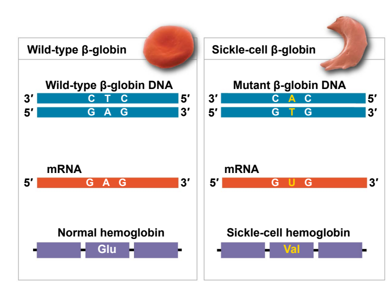


Concept 17.5: Mutations of one or a few nucleotides can affect protein structure and function

- **Mutations** are changes in the genetic material of a cell or virus
- **Point mutations** are chemical changes in just one base pair of a gene
- The change of a single nucleotide in a DNA template strand can lead to the production of an abnormal protein

- If a mutation has an adverse effect on the phenotype of the organism the condition is referred to as a genetic disorder or hereditary disease

Figure 17.25



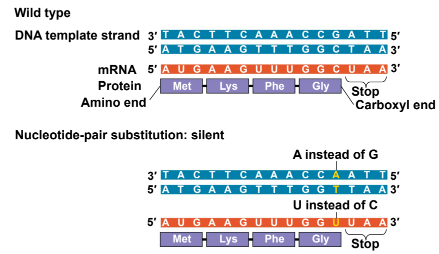
Types of Small-Scale Mutations

- Point mutations within a gene can be divided into two general categories
  - Nucleotide-pair substitutions
  - One or more nucleotide-pair insertions or deletions

Substitutions

- A **nucleotide-pair substitution** replaces one nucleotide and its partner with another pair of nucleotides
- **Silent mutations** have no effect on the amino acid produced by a codon because of redundancy in the genetic code
- **Missense mutations** still code for an amino acid, but not the correct amino acid
- **Nonsense mutations** change an amino acid codon into a stop codon, nearly always leading to a nonfunctional protein

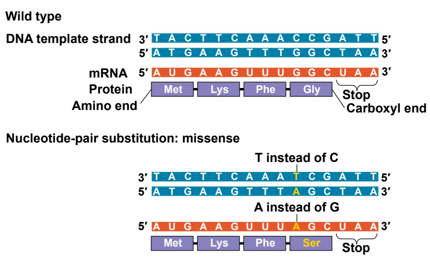
Figure 17.26a



Insertions and Deletions

- **Insertions** and **deletions** are additions or losses of nucleotide pairs in a gene
- These mutations have a disastrous effect on the resulting protein more often than substitutions do
- Insertion or deletion of nucleotides may alter the reading frame, producing a **frameshift mutation**

Figure 17.26b



New Mutations and Mutagens

- Spontaneous mutations can occur during DNA replication, recombination, or repair
- **Mutagens** are physical or chemical agents that can cause mutations

What Is a Gene? *Revisiting the Question*

- The idea of the gene has evolved through the history of genetics
- We have considered a gene as
  - A discrete unit of inheritance
  - A region of specific nucleotide sequence in a chromosome
  - A DNA sequence that codes for a specific polypeptide chain

- A gene can be defined as a region of DNA that can be expressed to produce a final functional product that is either a polypeptide or an RNA molecule

Figure 17.26

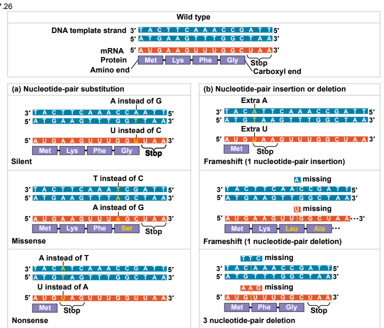


Figure 17.26c

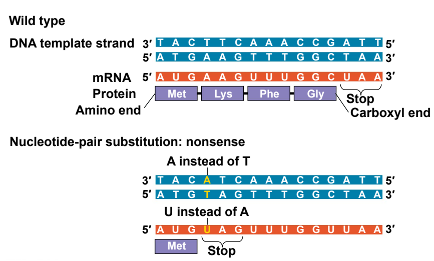


Figure 17.26d

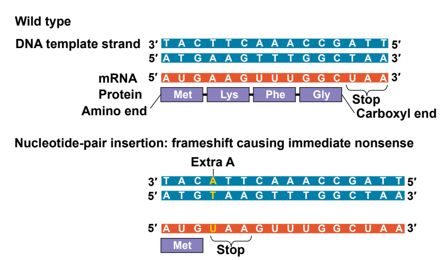


Figure 17.26e

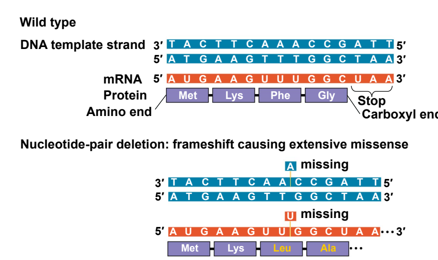


Figure 17.26f

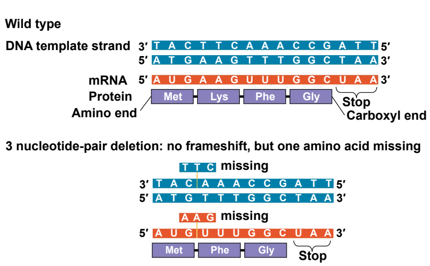


Figure 17.UN02

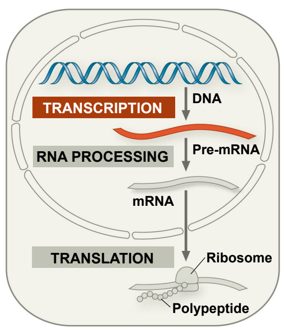


Figure 17.UN03

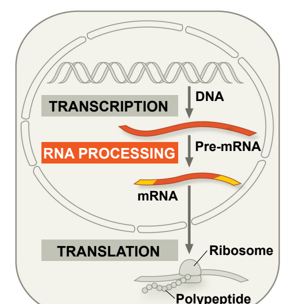


Figure 17.UN04

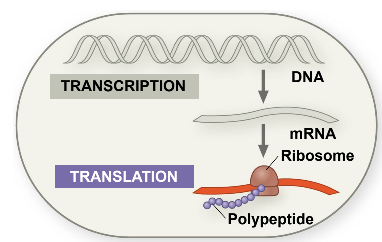
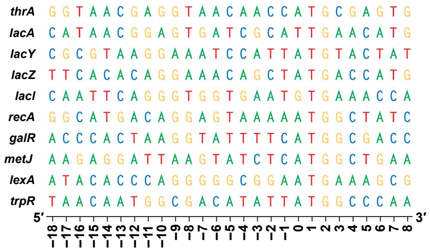
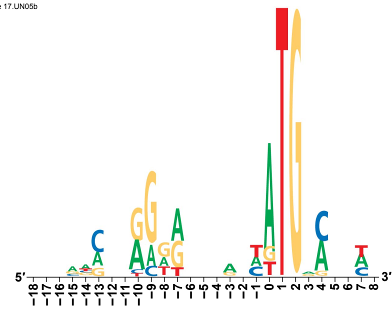


Figure 17.UN05a



Sequence alignment

Figure 17.UN05b



Sequence logo

Figure 17.UN05c

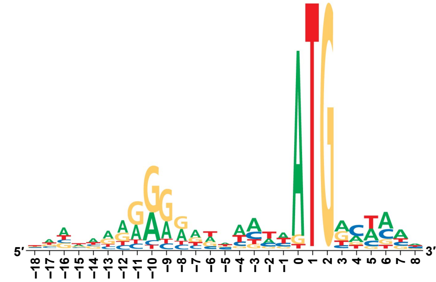


Figure 17.UN06

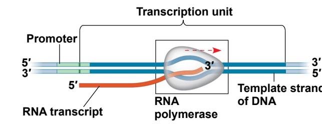


Figure 17.UN07

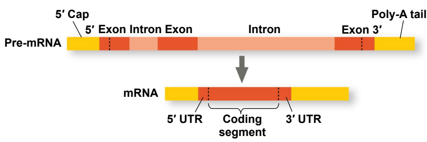


Figure 17.UN08

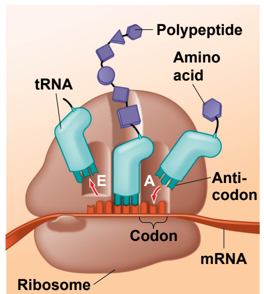


Figure 17.UN09

Type of RNA	Functions
Messenger RNA (mRNA)	
Transfer RNA (tRNA)	
	Plays catalytic (ribozyme) roles and structural roles in ribosomes
Primary transcript	
Small RNAs in the spliceosome	

Figure 17.UN10