Gene to Protein Outline – Chapter 17

- How does DNA code for traits?
- What is a gene?
- Transcription
- Translation
- Mutations

The Flow of Genetic Information

- The information content of DNA is in the form of specific sequences of nucleotides along the DNA strands
- The DNA inherited by an organism leads to specific traits by dictating the synthesis of proteins
- The process by which DNA directs protein synthesis, gene expression includes two stages, called transcription and translation

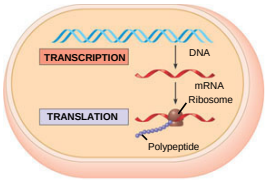
Evidence from a series of studies

- In 1909, British physician Archibald Garrod suggested genes dictate phenotypes through enzymes that catalyze chemical reactions in the cell
- Using bread mold, Beadle and Tatum developed the “one gene–one enzyme hypothesis”
- As researchers learned more about proteins they made minor revision to the one gene–one enzyme hypothesis
- The current wisdom is that genes code for polypeptide chains or for RNA molecules

Basic Principles of Transcription and Translation

- Transcription
  - The synthesis of RNA under the direction of DNA
  - Produces messenger RNA (mRNA)
- Translation
  - Is the actual synthesis of a polypeptide, which occurs under the direction of mRNA
  - Occurs on ribosomes

- In prokaryotes
  - Transcription and translation occur together

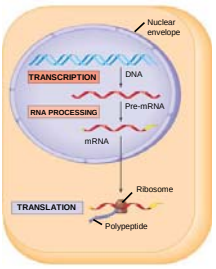


(a) Prokaryotic cell. In a cell lacking a nucleus, mRNA produced by transcription is immediately translated without additional processing.

Figure 17.3a

Transcription

- In eukaryotes
  - RNA transcripts are modified before becoming true mRNA



(b) Eukaryotic cell. The nucleus provides a separate compartment for transcription. The original RNA transcript, called pre-mRNA, is processed in various ways before leaving the nucleus as mRNA.

Figure 17.3b

The Genetic Code

- Cells are governed by a cellular chain of command
  - DNA → RNA → protein
- How many bases correspond to an amino acid?
- Three
  - Genetic information is encoded as a sequence of nonoverlapping base triplets, or codons

- During transcription
  - The gene determines the sequence of bases along the length of an mRNA molecule

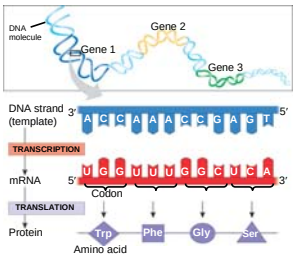


Figure 17.4

Cracking the Code

- A codon in messenger RNA
  - Is either translated into an amino acid or serves as a translational stop signal

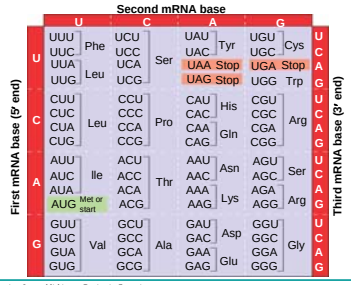


Figure 17.5

- Codons must be read in the correct reading frame
  - For the specified polypeptide to be produced
- The genetic code is nearly universal
  - Shared by organisms from the simplest bacteria to the most complex animals

- In laboratory experiments
  - Genes can be transcribed and translated after being transplanted from one species to another

This transgenic goat produces a human milk protein

Molecular Components of Transcription

- RNA synthesis
  - Is catalyzed by RNA polymerase, which pries the DNA strands apart and hooks together the RNA nucleotides
  - Follows the same base-pairing rules as DNA, except that in RNA, uracil substitutes for thymine

Synthesis of an RNA Transcript

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

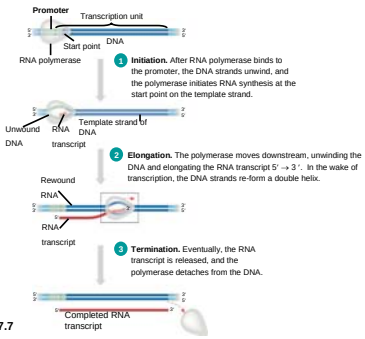
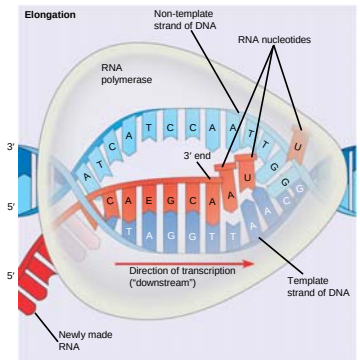


Figure 17.7



RNA Polymerase Binding and Initiation of Transcription

- Promoters signal the initiation of RNA synthesis
- Transcription factors
  - Help eukaryotic RNA polymerase recognize promoter sequences

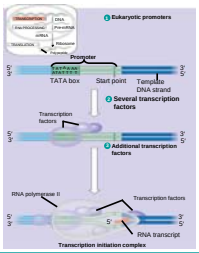


Figure 17.8

Elongation of the RNA Strand

- As RNA polymerase moves along the DNA
  - It continues to untwist the double helix, exposing about 10 to 20 DNA bases at a time for pairing with RNA nucleotides

Eukaryotic cells modify RNA after transcription

- Enzymes in the eukaryotic nucleus
  - Modify pre-mRNA in specific ways before the genetic messages are dispatched to the cytoplasm
  - This modification does not occur in prokaryotes

Alteration of mRNA Ends

- Each end of a pre-mRNA molecule is modified in a particular way
  - The 5′ end receives a modified nucleotide cap
  - The 3′ end gets a poly-A tail

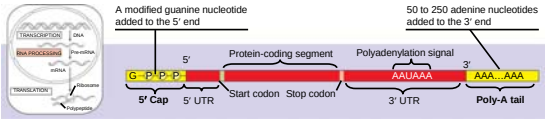


Figure 17.9

Split Genes and RNA Splicing

- RNA splicing
  - Removes introns and joins exons

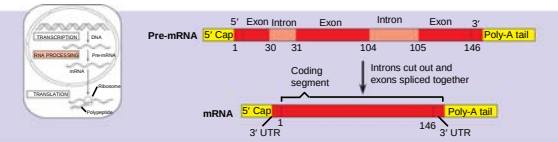


Figure 17.10

- Is carried out by spliceosomes in some cases

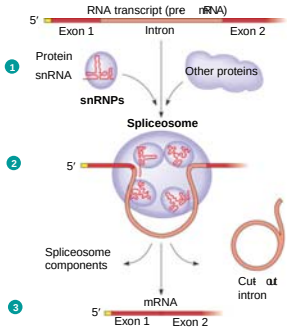


Figure 17.11

Ribozymes

- Ribozymes
  - Are catalytic RNA molecules that function as enzymes and can splice RNA
- The presence of introns
  - Allows for alternative RNA splicing

- Proteins often have a modular architecture
  - Consisting of discrete structural and functional regions called domains
- In many cases
  - Different exons code for the different domains in a protein

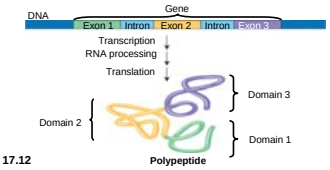


Figure 17.12

Translation

- Translation is the RNA-directed synthesis of a polypeptide
- A cell translates an mRNA message into protein
  - With the help of transfer RNA (tRNA)

Translation: the basic concept

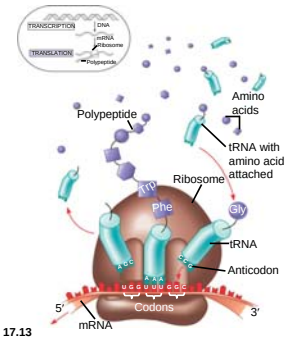
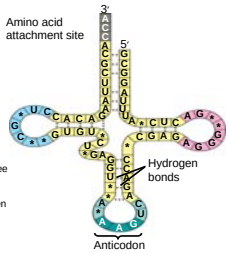


Figure 17.13

- Molecules of tRNA are not all identical
  - Each carries a specific amino acid on one end
  - Each has an anticodon on the other end

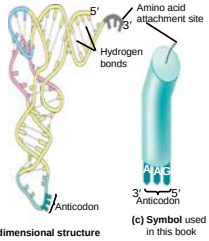
The Structure and Function of Transfer RNA

- A tRNA molecule
  - Consists of a single RNA strand that is only about 80 nucleotides long
  - Is roughly L-shaped



(a) Two-dimensional structure. The four base-paired regions and three loops are characteristic of all tRNAs, as is the base sequence of the amino acid attachment site at the 3′ end. The anticodon triplet is unique to each tRNA type. (The asterisks mark bases that have been chemically modified, a characteristic of tRNA.)

Figure 17.14a



(b) Three-dimensional structure

(c) Symbol used in this book

Figure 17.14b

- A specific enzyme called an aminoacyl-tRNA synthetase
  - Joins each amino acid to the correct tRNA

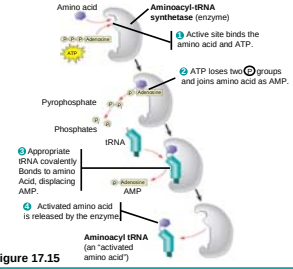
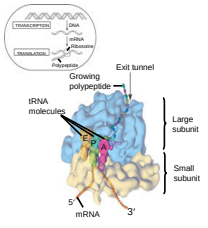


Figure 17.15

Ribosomes

- Ribosomes
  - Facilitate the specific coupling of tRNA anticodons with mRNA codons during protein synthesis

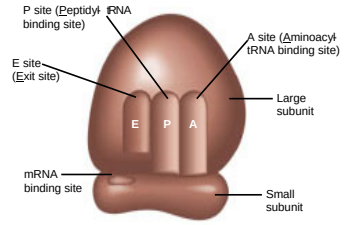
- The ribosomal subunits
  - Are constructed of proteins and RNA molecules named ribosomal RNA or rRNA



(a) Computer model of functioning ribosome. This is a model of a bacterial ribosome, showing its overall shape. The eukaryotic ribosome is roughly similar. A ribosomal subunit is an aggregate of ribosomal RNA molecules and proteins.

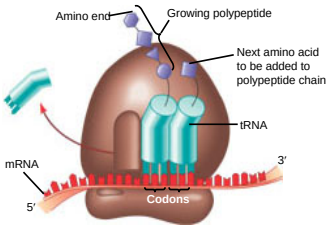
Figure 17.16a

- The ribosome has three binding sites for tRNA
  - The P site
  - The A site
  - The E site



(b) Schematic model showing binding sites. A ribosome has an mRNA binding site and three tRNA binding sites, known as the A, P, and E sites. This schematic ribosome will appear in later diagrams.

Figure 17.16b



(c) Schematic model with mRNA and tRNA. A tRNA fits into a binding site when its anticodon base pairs with an mRNA codon. The P site holds the tRNA attached to the growing polypeptide. The A site holds the tRNA carrying the next amino acid to be added to the polypeptide chain. Discharged tRNA leaves via the E site.

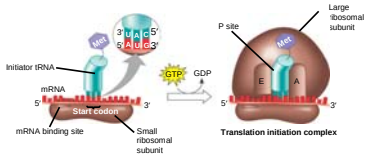
Figure 17.16c

Building a Polypeptide

- We can divide translation into three stages
  - Initiation
  - Elongation
  - Termination

Ribosome Association and Initiation of Translation

- The initiation stage of translation
  - Brings together mRNA, tRNA bearing the first amino acid of the polypeptide, and two subunits of a ribosome



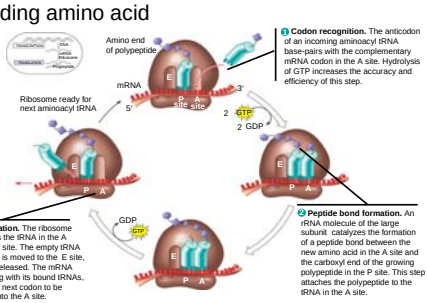
❶ A small ribosomal subunit binds to a molecule of mRNA. In a prokaryotic cell, the mRNA binding site on this subunit recognizes a specific nucleotide sequence on the mRNA just upstream of the start codon. An initiator tRNA, with the anticodon UAC, base-pairs with the start codon, AUG. This tRNA carries the amino acid methionine (Met).

❷ The arrival of a large ribosomal subunit completes the initiation complex. Proteins called initiation factors (not shown) are required to bring all the translation components together. GTP provides the energy for the assembly. The initiator tRNA is in the P site; the A site is available to the tRNA bearing the next amino acid.

Figure 17.17

Elongation of the Polypeptide Chain

- In the elongation stage of translation
  - Amino acids are added one by one to the preceding amino acid



❸ **Codon recognition.** The anticodon of an incoming aminoacyl tRNA base-pairs with the complementary mRNA codon in the A site. Hydrolysis of GTP increases the accuracy and efficiency of this step.

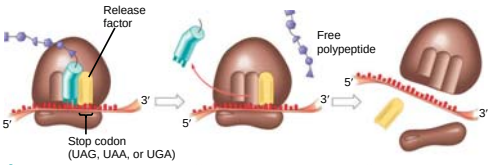
❸ **Translocation.** The ribosome translocates the tRNA in the A site to the P site. The empty tRNA in the P site is moved to the E site, where it is released. The mRNA moves along with its bound tRNAs, bringing the next codon to be translated into the A site.

❷ **Peptide bond formation.** An rRNA molecule of the large subunit catalyzes the formation of a peptide bond between the new amino acid in the A site and the carboxyl end of the growing polypeptide in the P site. This step attaches the polypeptide to the tRNA in the A site.

Figure 17.18

Termination of Translation

- The final stage of translation is termination
  - When the ribosome reaches a stop codon in the mRNA



❶ When a ribosome reaches a stop codon on mRNA, the A site of the ribosome accepts a protein called a release factor instead of tRNA.

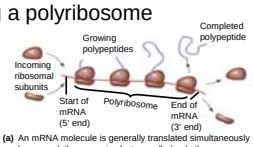
❷ The release factor hydrolyzes the bond between the tRNA in the P site and the last amino acid of the polypeptide chain. The polypeptide is thus freed from the ribosome.

❸ The two ribosomal subunits and the other components of the assembly dissociate.

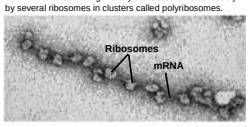
Figure 17.19

Polyribosomes

- A number of ribosomes can translate a single mRNA molecule simultaneously
  - Forming a polyribosome



(a) An mRNA molecule is generally translated simultaneously by several ribosomes in clusters called polyribosomes.



(b) This micrograph shows a large polyribosome in a prokaryotic cell (TEM).

Figure 17.20a, b

Completing and Targeting the Functional Protein

- Polypeptide chains
  - Undergo modifications after the translation process
- *Protein Folding and Post-Translational Modifications*
  - After translation proteins may be modified in ways that affect their three-dimensional shape

Targeting Polypeptides to Specific Locations

- Two populations of ribosomes are evident in cells
  - Free and bound
- Free ribosomes in the cytosol
  - Initiate the synthesis of all proteins

- Proteins destined for the endomembrane system or for secretion
  - Must be transported into the ER
  - Have signal peptides to which a signal-recognition particle (SRP) binds, enabling the translation ribosome to bind to the ER

- The signal mechanism for targeting proteins to the ER

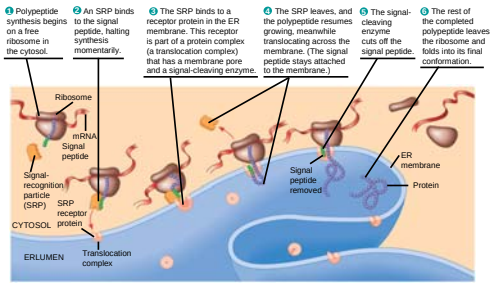


Figure 17.21

- Types of RNA in a Eukaryotic Cell

Type of RNA	Functions
Messenger RNA (mRNA)	Carries information specifying amino acid sequences of proteins from DNA to ribosomes.
Transfer RNA (tRNA)	Serves as adapter molecule in protein synthesis; translates mRNA codons into amino acids.
Ribosomal RNA (rRNA)	Plays catalytic (ribozyme) roles and structural roles in ribosomes
Primary transcript	Serves as a precursor to mRNA, rRNA, or tRNA, before being processed by splicing or cleavage. Some intron RNA acts as a ribozyme, catalyzing its own splicing.
Small nuclear RNA (snRNA)	Plays structural and catalytic roles in spliceosomes, the complexes of protein and RNA that splice pre-mRNA.
SRP RNA	Is a component of the signal-recognition particle (SRP), the protein-RNA complex that recognizes the signal peptides of polypeptides targeted to the ER.
Small nucleolar RNA (snoRNA)	Aids in processing of pre-rRNA transcripts for ribosome subunit formation in the nucleolus.
Small interfering RNA (siRNA) and microRNA (miRNA)	Are involved in regulation of gene expression.

Table 17.1

Comparing prokaryotes and eukaryotes

Prokaryotic cells lack a nuclear envelope

- Allowing translation to begin while transcription is still in progress

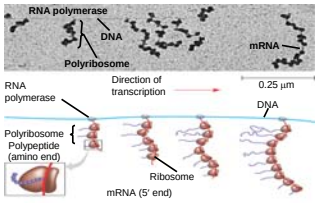


Figure 17.22

- In a eukaryotic cell
  - The nuclear envelope separates transcription from translation
  - Extensive RNA processing occurs in the nucleus

Point mutations can affect protein structure and function

- Mutations are changes in the genetic material of a cell
- Point mutations
  - Are changes in just one base pair of a gene

- The change of a single nucleotide in the DNA's template strand
  - Leads to the production of an abnormal protein

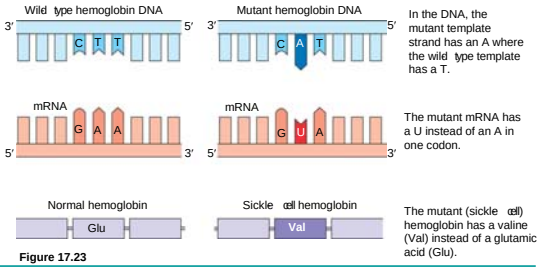


Figure 17.23

Types of Point Mutations

- Point mutations within a gene can be divided into two general categories
  - Base-pair substitutions
  - Base-pair insertions or deletions

Substitutions

- A base-pair substitution
  - Is the replacement of one nucleotide and its partner with another pair of nucleotides
  - Can cause missense or nonsense

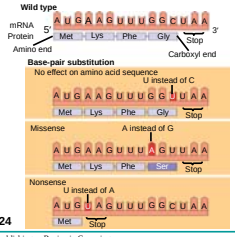


Figure 17.24

Insertions and Deletions

- Insertions and deletions
  - Are additions or losses of nucleotide pairs in a gene
  - May produce frameshift mutations

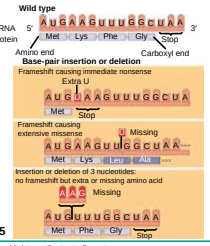


Figure 17.25

Mutagens

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

- A summary of transcription and translation in a eukaryotic cell

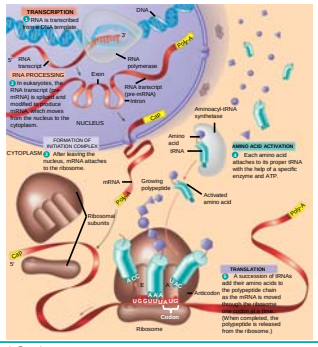


Figure 17.26