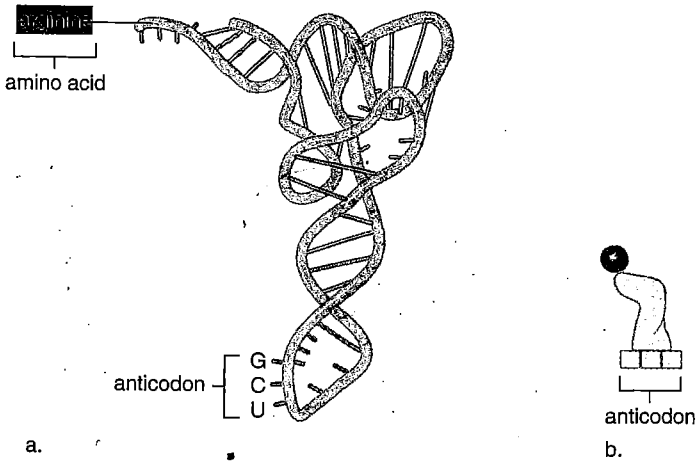


Figure 25.10 Transfer RNA: amino acid carrier.
a. A tRNA is a polynucleotide that folds into a bootlike shape because of complementary base pairing. At one end of the molecule is its specific anticodon—in this case GCU; at the other end an amino acid attaches that corresponds to this anticodon—in this case arginine. **b.** tRNA will be represented like this in the illustrations that follow.

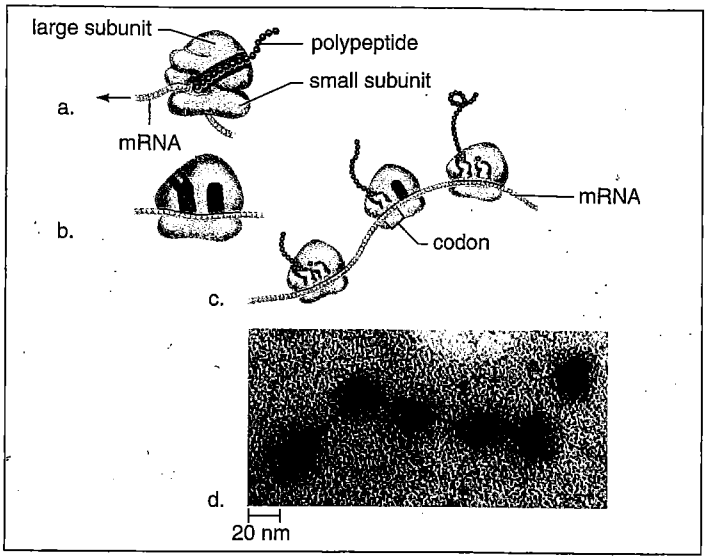


Figure 25.11 Polyribosome structure and function.
a. Side view of a ribosome shows positioning of mRNA and growing protein. **b.** Frontal view of a ribosome. **c.** Several ribosomes, collectively called a polyribosome, move along an mRNA at one time. Therefore, several proteins can be made at the same time. **d.** Electron micrograph of a polyribosome.

Translation

Translation is the second step by which gene expression leads to protein synthesis. During translation, the sequence of codons in mRNA specifies the order of amino acids in a protein. Translation requires several enzymes and two other types of RNA: transfer RNA and ribosomal RNA.

Transfer RNA

Transfer RNA (tRNA) molecules bring amino acids to the ribosomes. Each is a single-stranded nucleic acid that doubles back on itself to create regions where complementary base pairing results in a bootlike shape (Fig. 25.10). There is at least one tRNA molecule for each of the twenty amino acids found in proteins. The amino acid binds to one end of the molecule. The opposite end of the molecule contains an **anticodon,** a group of three bases that is complementary to a specific codon of mRNA. The entire complex is designated as tRNA–amino acid. One area of active research is to determine how the correct amino acid becomes attached to the correct tRNA molecule.

When a tRNA–amino acid complex comes to the ribosome, its anticodon pairs with an mRNA codon. Let us consider an example: if the codon is ACC, what is the anticodon, and what amino acid will be attached to the tRNA molecule? From Figure 25.6, we can determine this:

Codon	Anticodon	Amino Acid
ACC	UGG	Threonine

The order of the codons of the mRNA determines the order that tRNA–amino acids come to a ribosome, and therefore the final sequence of amino acids in a protein.

Ribosomal RNA

Ribosomal RNA (rRNA) is called structural RNA because it is found in the **ribosomes,** small structural bodies. In eukaryotic cells, ribosomal RNA is produced in a nucleolus within the nucleus. There it joins with proteins manufactured in the cytoplasm to form two ribosomal subunits, one large and one small. Each subunit contains an rRNA molecule and many different types of proteins. The subunits leave the nucleus and join together in the cytoplasm to form a ribosome just as protein synthesis begins.

A ribosome has a binding site for mRNA as well as binding sites for two tRNA molecules at a time. These binding sites facilitate complementary base pairing between tRNA anticodons and mRNA codons. As the ribosome moves down the mRNA molecule, new tRNAs arrive, and a polypeptide forms and grows longer. Translation terminates once the polypeptide is fully formed; the ribosome dissociates into its two subunits and falls off the mRNA molecule.

As soon as the initial portion of mRNA has been translated by one ribosome, and the ribosome has begun to move down the mRNA, another ribosome attaches to the same mRNA. Therefore, several ribosomes are often attached to and translating the same mRNA. The entire complex is called a **polyribosome** (Fig. 25.11.)

During translation, the sequence of bases in mRNA determines the order that tRNA amino acids come to a ribosome and therefore the order of amino acids in a particular polypeptide.

Translation Requires Three Steps

During translation, the codons of an mRNA base-pair with the anticodons of tRNA molecules. Each tRNA carries a specific amino acid. The order of the codons determines the order of the tRNA molecules and therefore the sequence of amino acids in a polypeptide. The process of translation must be extremely orderly so that the amino acids of a polypeptide are sequenced correctly.

Protein synthesis involves three steps:

1. Chain initiation—The steps necessary to begin the process of translation.
2. Chain elongation—The steps necessary to bring about polypeptide synthesis.
3. Chain termination—The steps necessary to end the process of translation.

It should be kept in mind that enzymes are required for each of the steps to occur, and that energy is needed for the first two steps also.

Chain Initiation

During chain initiation, a small ribosomal subunit, the mRNA, an initiator tRNA, and a large ribosomal subunit all come together. First, a small ribosomal subunit attaches to the mRNA in the vicinity of the start codon (AUG). The anticodon of a tRNA, called the initiator RNA, pairs with this codon. Then a large ribosomal subunit joins to the small subunit (Fig. 25.12*a*).

Notice that a ribosome has two binding sites for tRNAs. They are called binding sites because this is where a tRNA is located when its anticodon binds to a codon of mRNA. The initiator tRNA is always at the first binding site because its anticodon binds to the codon AUG.

When chain initiation occurs, the first tRNA has come to a ribosome.

Chain Elongation

During chain elongation, the tRNA at the first binding site usually bears an attached peptide. Why? Because the initiator tRNA passes its amino acid to a tRNA–amino acid complex that has come to the second binding site. Then the ribosome moves forward—the tRNA at the second binding site is now at the first binding site (Fig. 25.12*b*). This sequence of events is called translocation.

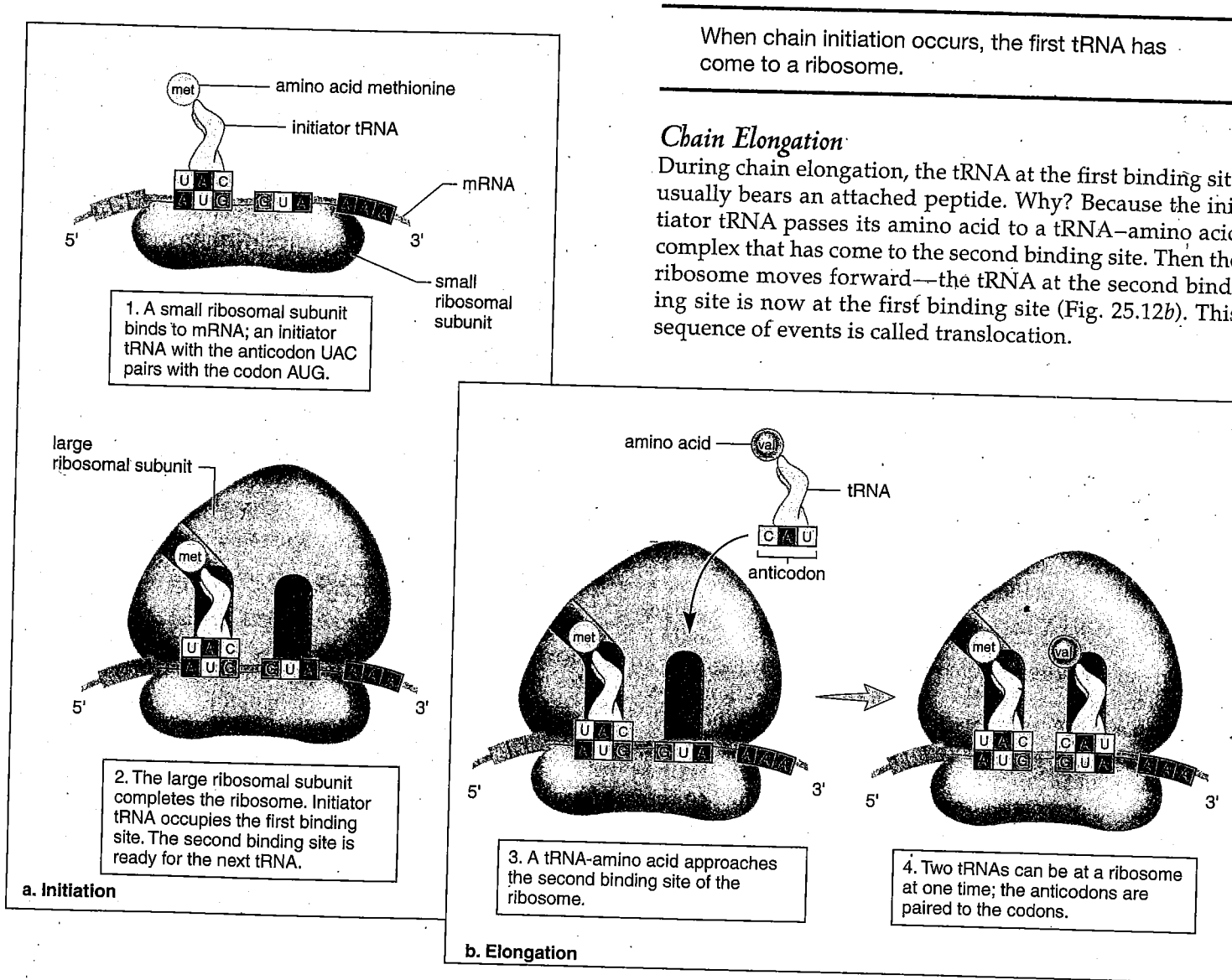


Figure 25.12 Protein synthesis.

Translocation occurs again and again during chain elongation. Each time, the growing polypeptide is transferred and attached by peptide bond formation to the newly arrived amino acid. Bringing about this transfer requires energy and a ribozyme, which is a part of the larger ribosomal subunit. After translocation occurs, the outgoing tRNA molecule will pick up another amino acid before returning to the ribosome.

The complete cycle—complementary base pairing of new tRNA, transfer of peptide chain and translocation—is repeated at a rapid rate (about 15 times each second in *Escherichia coli*).

During chain elongation, amino acids are added one at a time to the growing polypeptide.

Chain Termination

Chain termination occurs when protein synthesis comes to an end. Termination occurs at a stop codon—that is, a codon which does not code for an amino acid (Fig. 25.12*c*). The polypeptide is enzymatically cleaved from the last tRNA by a release factor.

Now the tRNA and polypeptide leave the ribosome, which dissociates into its two subunits (see also Fig. 25.11).

During chain termination, the ribosome separates into its two subunits and the polypeptide is released.

A newly synthesized polypeptide may function alone, or it may become a part of a protein that has more than one polypeptide. Proteins play a role in the anatomy and physiology of cells, as discussed earlier in this text. The plasma membrane of all cells contains proteins that carry out various functions, and many proteins are enzymes that participate in cellular metabolism. The tissues of multicellular animals are distinguished by the uniqueness of their proteins. Properly functioning proteins are of paramount importance to the cell and to the organism. Organisms inherit genes that code for their own particular mix of proteins in their cells. If an organism inherits a mutated gene, the result can be a genetic disorder or a propensity toward cancer, in which proteins are not fulfilling their usual functions. This topic is explored later in this chapter.

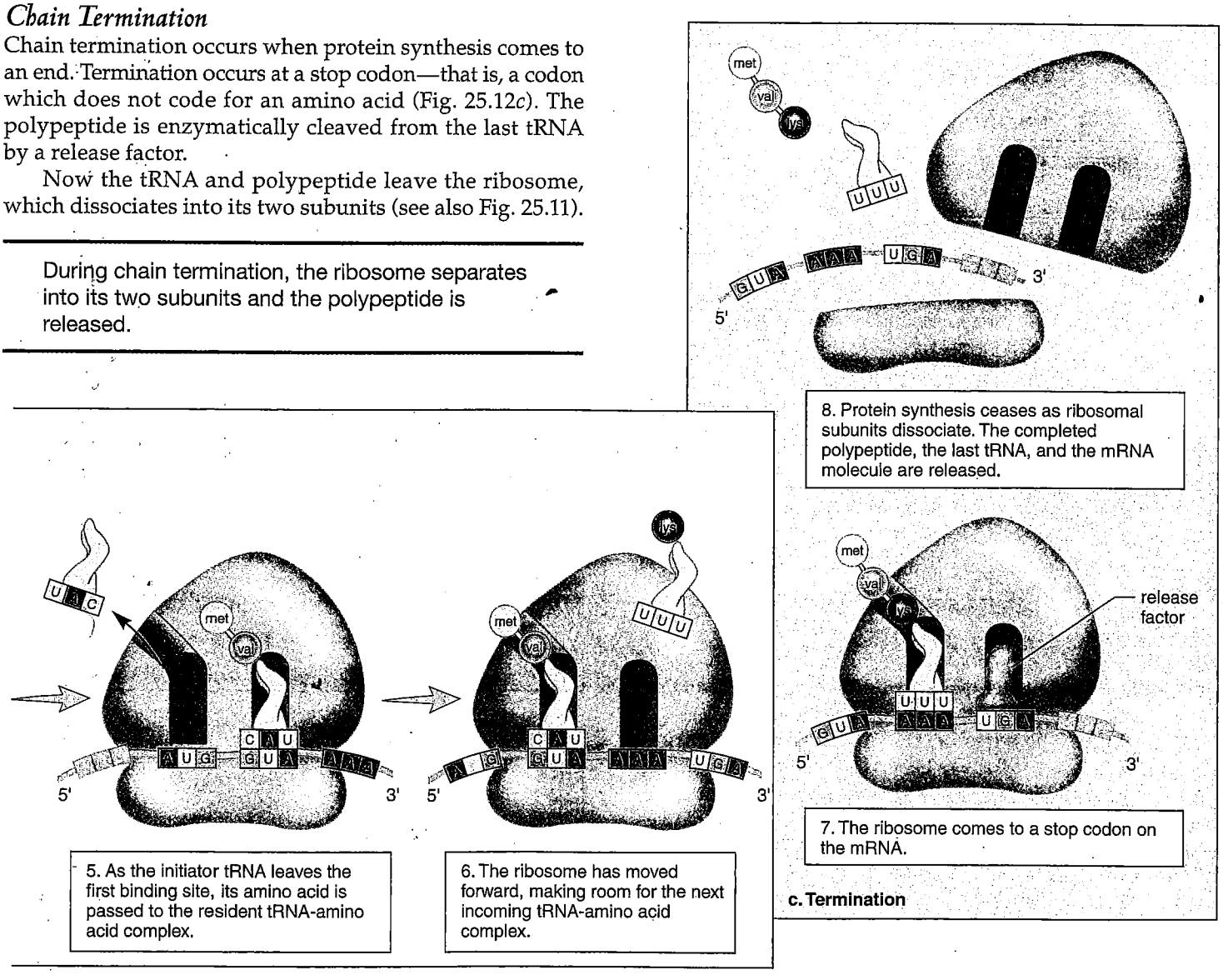


Figure 25.12 **Protein synthesis—*continued.***

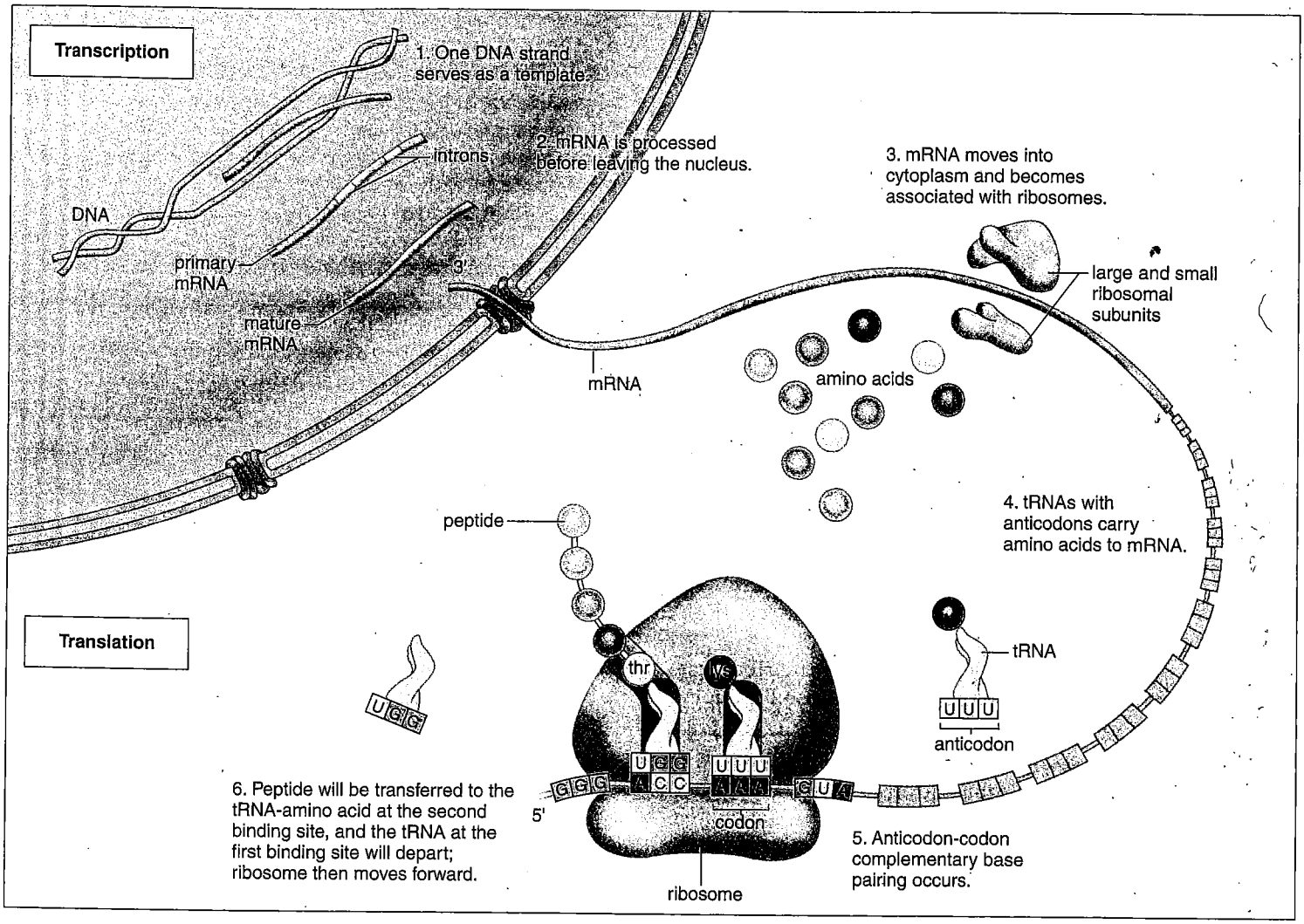


Figure 25.13 Gene expression.
Gene expression leads to the formation of a product, most often a protein. The two steps required for gene expression are transcription, which occurs in the nucleus, and translation, which occurs in the cytoplasm at the ribosomes.

Review of Gene Expression

DNA in the nucleus contains a *triplet code*. Each group of three bases stands for a specific amino acid (Figure 25.13 and Table 25.2). During transcription, a segment of a DNA strand serves as a template for the formation of messenger RNA (mRNA). The bases in mRNA are complementary to those in DNA; every three bases is a *codon* for a certain amino acid. mRNA is processed before it leaves the nucleus, during which time the introns are removed. mRNA carries a sequence of codons to the *ribosomes*, which are composed of rRNA and proteins. A transfer RNA (tRNA) bond to a particular amino acid has an *anticodon* that pairs complementarily to a codon in mRNA. During translation, tRNAs and their attached amino acids arrive at the ribosomes, where the linear sequence of codons of mRNA determines the order in which amino acids become incorporated into a protein.

Table 25.2 Participants in Gene Expression

Name of Molecule	Special Significance	Definition
DNA	Genetic information	Sequence of DNA bases
mRNA	Codons	Sequence of three RNA bases complementary to DNA
tRNA	Anticodon	Sequence of three RNA bases complementary to codon
rRNA	Ribosome	Site of protein synthesis
Amino acid	Building block for protein	Transported to ribosome by tRNA
Protein	Enzyme, structural protein, or secretory product	Amino acids joined in a predetermined order

25.4 Gene Mutations

Early geneticists understood that genes undergo mutations, but they didn't know what causes mutations. It is apparent today that a *gene mutation* is a change in the sequence of bases within a gene.

Frameshift Mutations

The term *reading frame* applies to the sequence of codons, because they are read from a specific starting point, as in this sentence: THE CAT ATE THE RAT. If the letter C is deleted from this sentence and the reading frame is shifted, we read THE ATA TET HER AT—something that doesn't make sense. *Frameshift mutations* occur most often because one or more nucleotides is either inserted or deleted from DNA. The result of a frameshift mutation can be a completely nonfunctional protein because the sequence of codons is altered.

Point Mutations

Point mutations involve a change in a single nucleotide and therefore a change in a specific codon. When one base is substituted for another, the results can be variable. For example, if UAC is changed to UAU, there is no noticeable effect, because both of these codons code for tyrosine. Therefore, this is called a *silent mutation*. If UAC is changed to UAG, however, the result could very well be drastic, because UAG is a stop codon. If this substitution occurs early in the gene, the resulting protein may be too short and may be unable to function. This is called a *nonsense mutation*. Finally, if UAC is changed to CAC, then histidine is incorporated into the protein instead of tyrosine. A change in one amino acid does not necessarily affect the function of a protein, but in this example the polarities of tyrosine and histidine differ. Therefore, this substitution most likely will affect the final shape of the protein and its function. This is called a *missense mutation*. The occurrence of valine instead of glutamate in the β chain of hemoglobin results in sickle-cell disease (Fig. 25.17). The abnormal hemoglobin stacks up inside of cells, and their sickle shape makes them clog small vessels. Hemorrhaging leads to pain in internal organs and joints.

Cause and Repair of Mutations

Mutations due to DNA replication errors are rare; a frequency of 10^{-8} to 10^{-5} per cell division is often quoted. DNA polymerase, the enzyme that carries out replication, proofreads the new strand against the old strand and detects any mismatched pairs, which are then replaced with the correct nucleotides. In the end, there is usually only one mistake for every one billion nucleotide pairs replicated.

Mutagens, environmental influences that cause mutations, such as radiation (e.g., radioactive elements, X rays, ultraviolet [UV] radiation) and organic chemicals (e.g., chemicals in cigarette smoke and certain pesticides), are another source of mutations in organisms, including humans. If mutagens bring about a mutation in the gametes, the offspring of the individual may be affected. On the other hand, if the mutation occurs in the body cells, cancer may be the result.

A gene mutation is an alteration in the nucleotide sequence of a gene. The usual rate of mutation is low because DNA repair enzymes constantly monitor and repair any irregularities.

Transposons: Jumping Genes

Transposons are specific DNA sequences that have the remarkable ability to move within and between chromosomes. As discussed in the Science Focus on the next page, their movement to a new location sometimes alters neighboring genes, particularly by increasing or decreasing their expression. This can happen if the transposon is a regulator gene. Although "movable elements" in corn were described 40 years ago, their significance was only realized recently. So-called *jumping genes* have now been discovered in bacteria, fruit flies, and humans, and it is likely that all organisms have such elements.

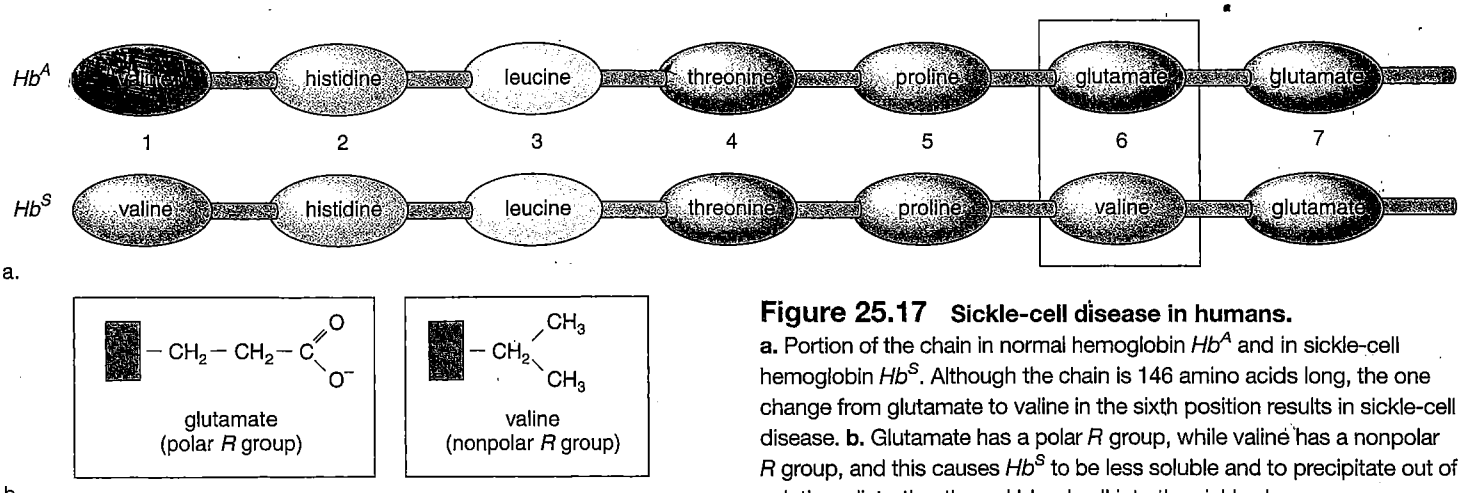
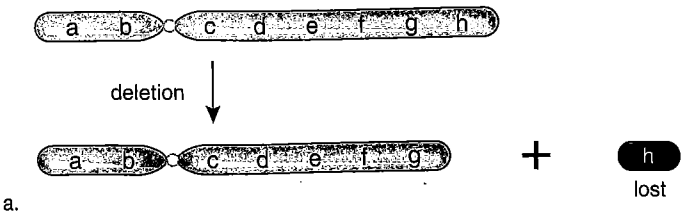


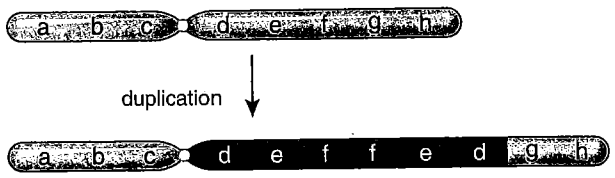
Figure 25.17 Sickle-cell disease in humans.
a. Portion of the chain in normal hemoglobin Hb^A and in sickle-cell hemoglobin Hb^S. Although the chain is 146 amino acids long, the one change from glutamate to valine in the sixth position results in sickle-cell disease. **b.** Glutamate has a polar *R* group, while valine has a nonpolar *R* group, and this causes Hb^S to be less soluble and to precipitate out of solution, distorting the red blood cell into the sickle shape.



a.

b.

Figure 24.5 Deletion.
a. When chromosome 7 loses an end piece, the result is Williams syndrome. **b.** These children, although unrelated, have the same appearance, health, and behavioral problems.



a.

b.

Figure 24.6 Duplication.
a. When a piece of chromosome 15 is duplicated and inverted, (**b**) a syndrome results in which the child has poor muscle tone and autistic characteristics.

24.3 Changes in Chromosome Structure

A mutation is a permanent genetic change. A change in chromosome structure that can be detected microscopically is a **chromosome mutation.** Chromosome mutations occur when chromosomes suffer breaks. Various environmental agents–radiation, certain organic chemicals, or even viruses–can cause chromosomes to break apart. Ordinarily, when breaks occur in chromosomes, the segments reunite to give the same sequence of genes. But their failure to reunite correctly can result in one of several types of mutations: deletion, duplication, translocation, or inversion. Chromosome mutations can occur during meiosis, and if the offspring inherits the abnormal chromosome, a syndrome may very well develop.

Deletions and Duplications

A **deletion** occurs when a single break causes a chromosome to lose an end piece or when two simultaneous breaks lead to the loss of an internal chromosome segment. An individual who inherits a normal chromosome from one parent and a chromosome with a deletion from the other parent no longer has a pair of alleles for each trait, and a syndrome can result.

Williams syndrome occurs when chromosome 7 loses a tiny end piece (Fig. 24.5). Children who have this syndrome look like pixies because they have turned-up noses, wide mouths, a small chin, and large ears. Although their academic skills are poor, they exhibit excellent verbal and musical abilities. The gene that governs the production of the protein elastin is missing, and this affects the health of the cardiovascular system and causes their skin to age prematurely. Such individuals are very friendly but need an ordered life, perhaps because of the loss of a gene for a protein that is normally active in the brain.

Cri du chat (cat's cry) syndrome is seen when chromosome 5 is missing an end piece. The affected individual has a small head, is mentally retarded, and has facial abnormalities. Abnormal development of the glottis and larynx results in the most characteristic symptom–the infant's cry resembles that of a cat.

In a **duplication,** a chromosome segment is repeated in the same chromosome or in a nonhomologous chromosome. In any case, the individual has more than two alleles for certain traits. An inverted duplication is known to occur in chromosome 15. Inverted means that the duplicated segment joins in the direction opposite from normal. Children with this syndrome, called inv dup 15 syndrome, have poor muscle tone, mental retardation, seizures, a curved spine, and autistic characteristics, including poor speech, hand flapping, and lack of eye contact (Fig. 24.6).

Translocation

A **translocation** is the exchange of chromosome segments between two, nonhomologous chromosomes. A person who has both of the involved chromosomes has the normal amount of genetic material and is healthy, unless the chromosome exchange breaks an allele into two pieces. The person who inherits only one of the translocated chromosomes will no doubt have only one copy of certain alleles and three copies of certain other alleles. A genetic counselor begins to suspect a translocation has occurred when spontaneous abortions are commonplace and family members suffer from various syndromes. A special microscopic technique allows a technician to determine that a translocation has occurred.

In 5% of cases, a translocation that occurred in a previous generation between chromosomes 21 and 14 is the cause of Down syndrome. The affected person inherits two normal chromosomes 21 and an abnormal chromosome 14 that contains a segment of chromosome 21. In these cases, Down syndrome is not related to the age of the mother, but instead tends to run in the family of either the father or the mother.

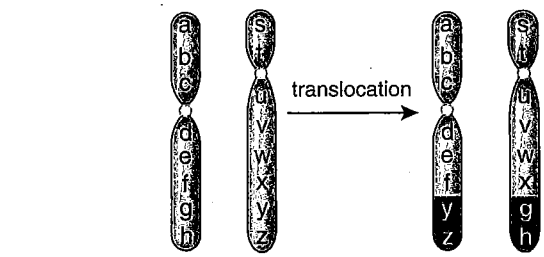
Figure 24.7 shows a father and son who have a translocation between chromosomes 2 and 20. Although they have the normal amount of genetic material, they have the distinctive face, abnormalities of the eyes and internal organs, and severe itching characteristic of Alagille syndrome. People with this syndrome ordinarily have a deletion on chromosome 20; therefore, it can be deduced that the translocation disrupted an allele on chromosome 20 in the father. The symptoms of Alagille syndrome range from mild to severe, so some people may not be aware they have the syndrome. This father did not realize it until he had a child with the syndrome.

Inversion

An **inversion** occurs when a segment of a chromosome is turned 180 degrees. You might think this is not a problem because the same genes are present, but the reverse sequence of alleles can lead to altered gene activity.

Crossing-over between an inverted chromosome and the noninverted homologue can lead to recombinant chromosomes that have both duplicated and deleted segments. This happens because alignment between the two homologues is only possible when the inverted chromosome forms a loop (Fig. 24.8).

Chromosome mutations can lead to various syndromes among offspring when the mutation produces chromosomes that have deleted, duplicated, translocated, and inverted segments.



a.

b.

Figure 24.7 Translocation.
a. When chromosomes 2 and 20 exchange segments, (**b**) Alagille syndrome, with distinctive facial features, sometimes results because the translocation disrupts an allele on chromosome 20.

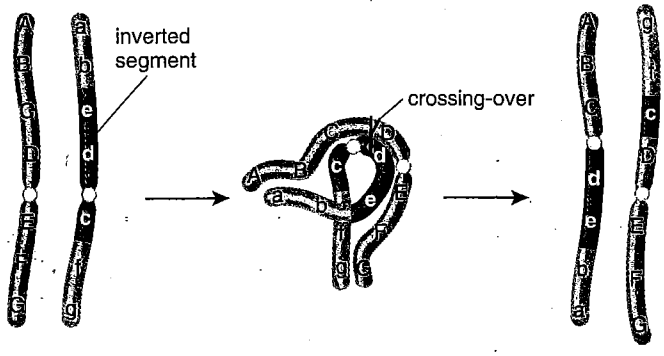


Figure 24.8 Inversion.
(Left) A segment of one homologue is inverted. Notice that in the shaded segment *edc* occurs instead of *cde*. *(Middle)* The two homologues can pair only when the inverted sequence forms an internal loop. After crossing over, a duplication and a deletion can occur. *(Right)* The homologue on the left has *AB* and *ab* sequences and neither *fg* nor *FG* genes. The homologue on the right has *gf* and *FG* sequences and neither *AB* nor *ab* genes.