Chapter 3

Nucleic Acids and Genetics

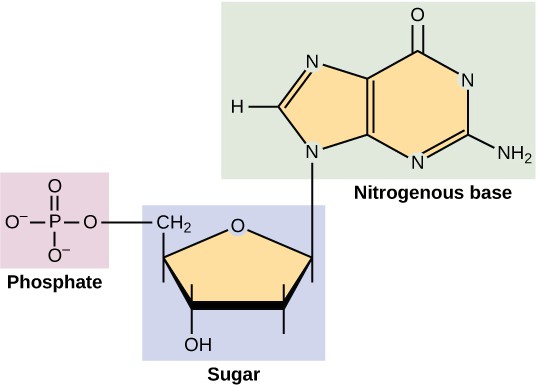
#### Nucleic Acids

Nucleic acids are key macromolecules in the continuity of life. They carry the genetic blueprint of a cell and carry instructions for the functioning of the cell.

The two main types of **nucleic acids** are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**. DNA is the genetic material found in all living organisms, ranging from single-celled bacteria to multicellular mammals.

The other type of nucleic acid, RNA, is mostly involved in protein synthesis. The DNA molecules never leave the nucleus, but instead use an RNA intermediary to communicate with the rest of the cell. Other types of RNA are also involved in protein synthesis and its regulation.

DNA and RNA are made up of monomers known as **nucleotides**. The nucleotides combine with each other to form a polynucleotide, DNA or RNA. Each nucleotide is made up of three components: a nitrogenous base, a pentose (five-carbon) sugar, and a phosphate group (Figure 3.1). Each nitrogenous base in a nucleotide is attached to a sugar molecule, which is attached to a phosphate group.

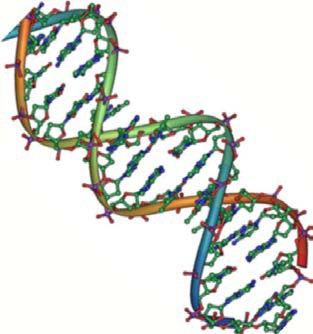


**Figure 3.1** A nucleotide is made up of three components: a nitrogenous base, a pentose sugar, and a phosphate group.

#### DNA Double-Helical Structure

DNA has a double-helical structure (Figure 3.2). It is composed of two strands, or polymers, of nucleotides. The strands are formed with bonds between phosphate and sugar groups of adjacent nucleotides. The strands are bonded to each other at their bases with hydrogen bonds, and the strands coil about each other along their length, hence the “double helix” description, which means a double spiral.

62



**Figure 3.2** The double-helix model shows DNA as two parallel strands of intertwining molecules. (credit: Jerome Walker, Dennis Myts)

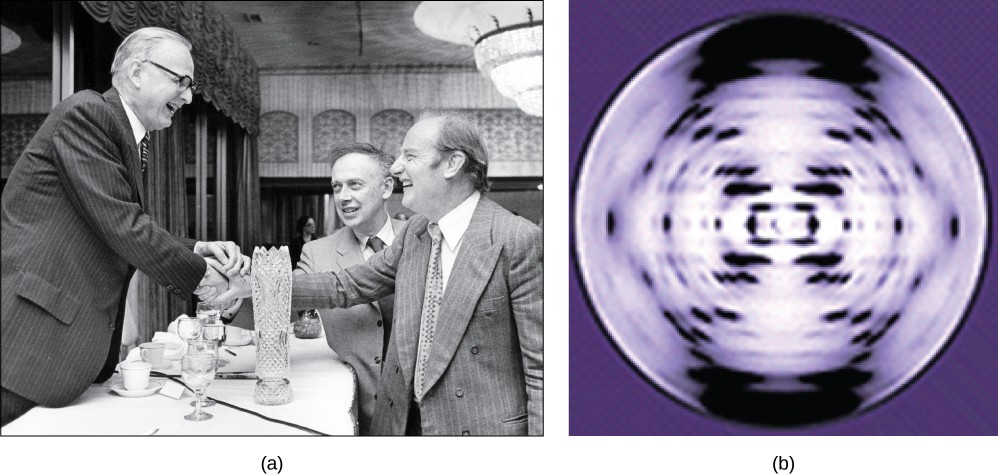
The alternating sugar and phosphate groups lie on the outside of each strand, forming the backbone of the DNA. The nitrogenous bases are stacked in the interior, like the steps of a staircase, and these bases

## The Structure of DNA

By the end of this section, you will be able to:

* Describe the structure of DNA
* Describe how eukaryotic and prokaryotic DNA is arranged in the cell

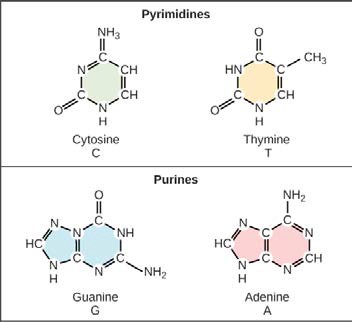
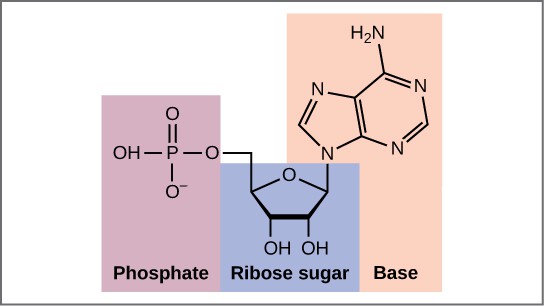
In the 1950s, Francis Crick and James Watson worked together at the University of Cambridge, England, to determine the structure of DNA. Other scientists, such as Linus Pauling and Maurice Wilkins, were also actively exploring this field. Pauling had discovered the secondary structure of proteins using X-ray crystallography. X-ray crystallography is a method for investigating molecular structure by observing the patterns formed by X-rays shot through a crystal of the substance. The patterns give important information about the structure of the molecule of interest. In Wilkins’ lab, researcher Rosalind Franklin was using X-ray crystallography to understand the structure of DNA. Watson and Crick were able to piece together the puzzle of the DNA molecule using Franklin's data (Figure 3.3). Watson and Crick also had key pieces of information available from other researchers such as Chargaff’s rules. Chargaff had shown that of the four kinds of monomers (nucleotides) present in a DNA molecule, two types were always present in equal amounts and the remaining two types were also always present in equal amounts. This meant they were always paired in some way. In 1962, James Watson, Francis Crick, and Maurice Wilkins were awarded the Nobel Prize in Medicine for their work in determining the structure of DNA.



**Figure 3.3** Pioneering scientists (a) James Watson and Francis Crick are pictured here with American geneticist Maclyn McCarty. Scientist Rosalind Franklin discovered (b) the X-ray diffraction pattern of DNA, which helped to elucidate its double helix structure. (credit a: modification of work by Marjorie McCarty; b: modification of work by NIH) 63

Now let’s consider the structure of the two types of nucleic acids, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). The building blocks of DNA are nucleotides, which are made up of three parts: a **deoxyribose** (5-carbon sugar), a **phosphate group**, and a **nitrogenous base** (Figure 3.4). There are four types of nitrogenous bases in DNA. Adenine (A) and guanine (G) are double-ringed purines, and cytosine (C) and thymine (T) are smaller, single-ringed pyrimidines. The nucleotide is named according to the nitrogenous base it contains.

64



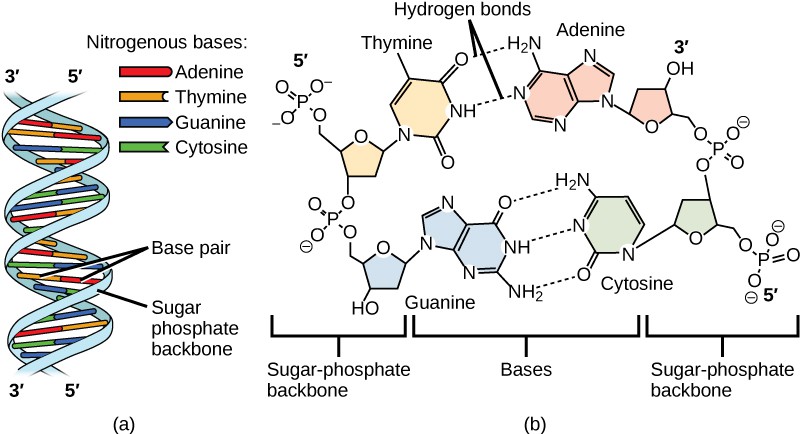
(a)

(b)

**Figure 3.4** (a) Each DNA nucleotide is made up of a sugar, a phosphate group, and a base. (b) Cytosine and thymine are pyrimidines. Guanine and adenine are purines.

The phosphate group of one nucleotide bonds covalently with the sugar molecule of the next nucleotide, and so on, forming a long polymer of nucleotide monomers. The sugar–phosphate groups line up in a “backbone” for each single strand of DNA, and the nucleotide bases stick out from this backbone. The carbon atoms of the five-carbon sugar are numbered clockwise from the oxygen as 1', 2', 3', 4', and 5' (1' is read as “one prime”). The phosphate group is attached to the 5' carbon of one nucleotide and the 3' carbon of the next nucleotide. In its natural state, each DNA molecule is actually composed of two single strands held together along their length with hydrogen bonds between the bases.

Watson and Crick proposed that the DNA is made up of two strands that are twisted around each other to form a right-handed helix, called a **double helix**. Base-pairing takes place between a purine and pyrimidine: namely, A pairs with T, and G pairs with C. In other words, adenine and thymine are complementary base pairs, and cytosine and guanine are also complementary base pairs. This is the basis for Chargaff’s rule; because of their complementarity, there is as much adenine as thymine in a DNA molecule and as much guanine as cytosine. Adenine and thymine are connected by two hydrogen bonds, and cytosine and guanine are connected by three hydrogen bonds. The two strands are anti-parallel in nature; that is, one strand will have the 3' carbon of the sugar in the “upward” position, whereas the other strand will have the 5' carbon in the upward position. The diameter of the DNA double helix is uniform throughout because a purine (two rings) always pairs with a pyrimidine (one ring) and their combined lengths are always equal. (Figure 3.5).

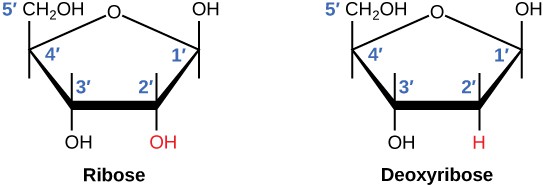


**Figure 3.5** DNA (a) forms a double stranded helix, and (b) adenine pairs with thymine and cytosine pairs with guanine. (credit a: modification of work by Jerome Walker, Dennis Myts)

#### The Structure of RNA

There is a second nucleic acid in all cells called ribonucleic acid, or RNA. Like DNA, RNA is a polymer of nucleotides. Each of the nucleotides in RNA is made up of a nitrogenous base, a five-carbon sugar, and a phosphate group. In the case of RNA, the five-carbon sugar is ribose, not deoxyribose. Ribose has a hydroxyl group at the 2' carbon, unlike deoxyribose, which has only a hydrogen atom (Figure 3.6).

65

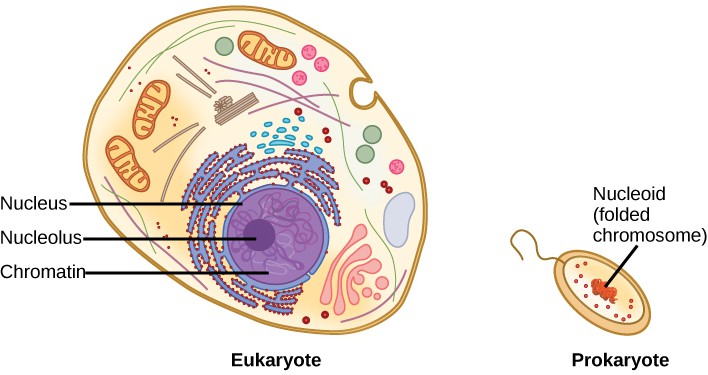


**Figure 3.6** The difference between the ribose found in RNA and the deoxyribose found in DNA is that ribose has a hydroxyl group at the 2' carbon.

RNA nucleotides contain the nitrogenous bases adenine, cytosine, and guanine. However, they do not contain thymine, which is instead replaced by uracil, symbolized by a “U.” RNA exists as a single- stranded molecule rather than a double-stranded helix. Molecular biologists have named several kinds of RNA on the basis of their function. These include messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA)—molecules that are involved in the production of proteins from the DNA code.

#### How DNA Is Arranged in the Cell

DNA is a working molecule; it must be replicated when a cell is ready to divide, and it must be “read” to produce the molecules, such as proteins, to carry out the functions of the cell. For this reason, the DNA is protected and packaged in very specific ways. In addition, DNA molecules can be very long. Stretched end-to-end, the DNA molecules in a single human cell would come to a length of about 2 meters. Thus, the DNA for a cell must be packaged in a very ordered way to fit and function within a structure (the cell) that is not visible to the naked eye. The chromosomes of prokaryotes are much simpler than those of eukaryotes in many of their features (Figure 3.7). Most prokaryotes contain a single, circular chromosome that is found in an area in the cytoplasm called the nucleoid.



**Figure 3.7** A eukaryote contains a well-defined nucleus, whereas in prokaryotes, the chromosome lies in the cytoplasm in an area called the nucleoid.

The size of the genome in one of the most well-studied prokaryotes, *Escherichia coli,* is 4.6 million base pairs, which would extend a distance of about 1.6 mm if stretched out. So how does this fit inside a small bacterial cell? The DNA is twisted beyond the double helix in what is known as supercoiling. Some proteins are known to be involved in the supercoiling; other proteins and enzymes help in maintaining the supercoiled structure.

Eukaryotes, whose chromosomes each consist of a linear DNA molecule, employ a different type of packing strategy to fit their DNA inside the nucleus (Figure 3.8). At the most basic level, DNA is wrapped around proteins known as histones to form structures called nucleosomes. The DNA is wrapped tightly around the histone core. This nucleosome is linked to the next one by a short strand of DNA that is free of histones. This is also known as the “beads on a string” structure; the nucleosomes are the “beads” and the short lengths of DNA between them are the “string.” The nucleosomes, with their DNA coiled around them, stack compactly onto each other to form a 30-nm–wide fiber. This fiber is further coiled into a thicker and more compact structure. At the metaphase stage of mitosis, when the chromosomes are lined up in the center of the cell, the chromosomes are at their most compacted. They are approximately 700 nm in width, and are found in association with scaffold proteins.

66

In interphase, the phase of the cell cycle between mitoses at which the chromosomes are decondensed, eukaryotic chromosomes have two distinct regions that can be distinguished by staining. There is a tightly packaged region that stains darkly, and a less dense region. The darkly staining regions usually contain genes that are not active, and are found in the regions of the centromere and telomeres. The lightly staining regions usually contain genes that are active, with DNA packaged around nucleosomes but not further compacted.

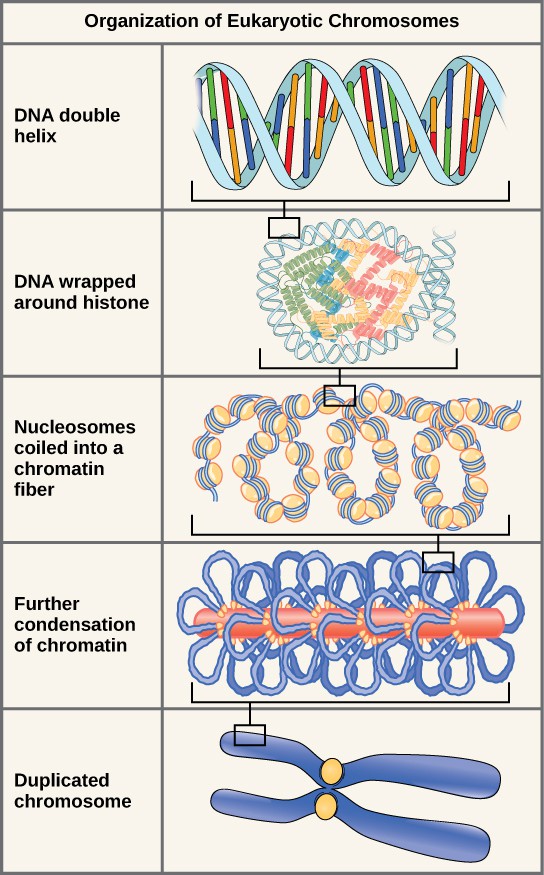


Figure 3.8 Packing of DNA inside of cells

## | DNA Replication

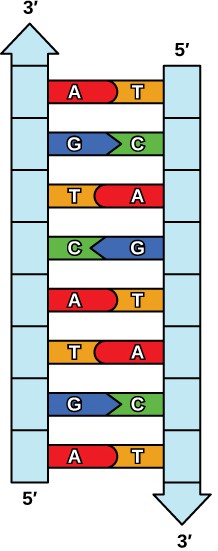
By the end of this section, you will be able to:

* Explain the process of DNA replication
* Explain the importance of telomerase to DNA replication
* Describe mechanisms of DNA repair

When a cell divides, it is important that each daughter cell receives an identical copy of the DNA. This is accomplished by the process of DNA replication. The replication of DNA occurs during the synthesis phase, or S phase, of the cell cycle, before the cell enters mitosis or meiosis.

The elucidation of the structure of the double helix provided a hint as to how DNA is copied. Recall that adenine nucleotides pair with thymine nucleotides, and cytosine with guanine. This means that the two strands are complementary to each other. For example, a strand of DNA with a nucleotide sequence of AGTCATGA will have a complementary strand with the sequence TCAGTACT (Figure 3.9).

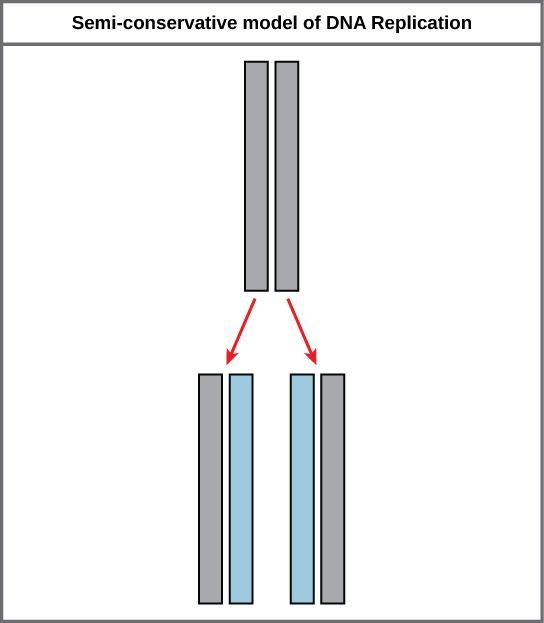
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**Figure 3.9** The two strands of DNA are complementary, meaning the sequence of bases in one strand can be used to create the correct sequence of bases in the other strand.

Because of the complementarity of the two strands, having one strand means that it is possible to recreate the other strand. This model for replication suggests that the two strands of the double helix separate during replication, and each strand serves as a template from which the new complementary strand is copied (Figure 3.10).

68



**Figure 3.10** The semiconservative model of DNA replication is shown. Gray indicates the original DNA strands, and blue indicates newly synthesized DNA.

During DNA replication, each of the two strands that make up the double helix serves as a template from which new strands are copied. The new strand will be complementary to the parental or “old” strand. Each new double strand consists of one parental strand and one new daughter strand. This is known as **semiconservative replication**. When two DNA copies are formed, they have an identical sequence of nucleotide bases and are divided equally into two daughter cells.

#### DNA Replication in Eukaryotes

Because eukaryotic genomes are very complex, DNA replication is a very complicated process that involves several enzymes and other proteins. It occurs in three main stages: initiation, elongation, and termination.

Recall that eukaryotic DNA is bound to proteins known as histones to form structures called nucleosomes. During initiation, the DNA is made accessible to the proteins and enzymes involved in the replication process. How does the replication machinery know where on the DNA double helix to begin? It turns out that there are specific nucleotide sequences called origins of replication at which replication begins. Certain proteins bind to the origin of replication while an enzyme called **helicase** unwinds and opens up the DNA helix. As the DNA opens up, Y-shaped structures called **replication forks** are formed (). Two replication forks are formed at the origin of replication, and these get extended in both directions as replication proceeds. There are multiple origins of replication on the eukaryotic chromosome, such that replication can occur simultaneously from several places in the genome.

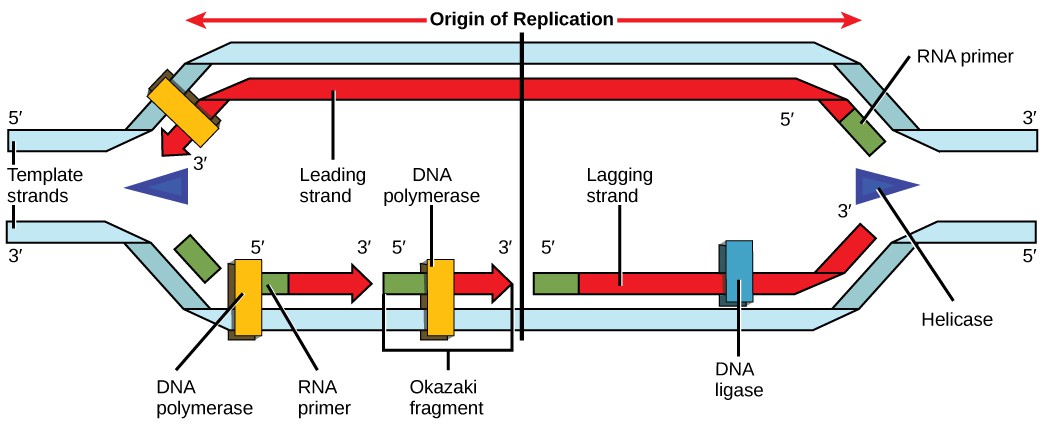
During elongation, an enzyme called **DNA polymerase** adds DNA nucleotides to the 3' end of the template. Because DNA polymerase can only add new nucleotides at the end of a backbone, a **primer** sequence, which provides this starting point, is added with complementary RNA nucleotides. This primer is removed later, and the nucleotides are replaced with DNA nucleotides. One strand, which is complementary to the parental DNA strand, is synthesized continuously toward the replication fork so the polymerase can add nucleotides in this direction. This continuously synthesized strand is known as the **leading strand**. Because DNA polymerase can only synthesize DNA in a 5' to 3' direction, the other new strand is put together in short pieces called **Okazaki fragments**. The Okazaki fragments each require a primer made of RNA to start the synthesis. The strand with the Okazaki fragments is known as the **lagging strand**. As synthesis proceeds, an enzyme removes the RNA primer, which is then replaced with DNA nucleotides, and the gaps between fragments are sealed by an enzyme called **DNA ligase**.

The process of DNA replication can be summarized as follows:

1. DNA unwinds at the origin of replication.

69

1. New bases are added to the complementary parental strands. One new strand is made continuously, while the other strand is made in pieces.
2. Primers are removed, new DNA nucleotides are put in place of the primers and the backbone is sealed by DNA ligase.



**Figure 3.11** A replication fork is formed by the opening of the origin of replication, and helicase separates the DNA strands. An RNA primer is synthesized, and is elongated by the DNA polymerase. On the leading strand, DNA is synthesized continuously, whereas on the lagging strand, DNA is synthesized in short stretches. The DNA fragments are joined by DNA ligase (not shown).

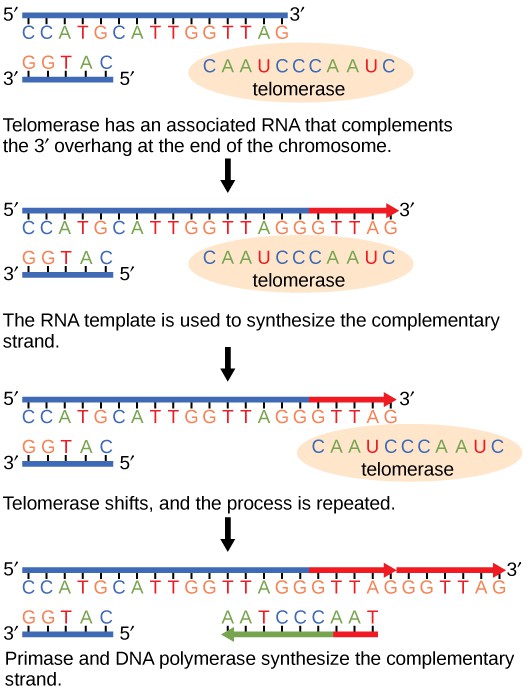
**Figure 9.10** A replication fork is formed by the opening of the origin of replication, and helicase separates the DNA strands. An RNA primer is synthesized, and is elongated by the DNA polymerase. On the leading strand, DNA is synthesized continuously, whereas on the lagging strand, DNA is synthesized in short stretches. The DNA fragments are joined by DNA ligase (not shown).

You isolate a cell strain in which the joining together of Okazaki fragments is impaired and suspect that a mutation has occurred in an enzyme found at the replication fork. Which enzyme is most likely to be mutated?

Telomere Replication

Because eukaryotic chromosomes are linear, DNA replication comes to the end of a line in eukaryotic chromosomes. As you have learned, the DNA polymerase enzyme can add nucleotides in only one direction. In the leading strand, synthesis continues until the end of the chromosome is reached; however, on the lagging strand there is no place for a primer to be made for the DNA fragment to be copied at the end of the chromosome. This presents a problem for the cell because the ends remain unpaired, and over time these ends get progressively shorter as cells continue to divide. The ends of the linear chromosomes are known as **telomeres**, which have repetitive sequences that do not code for a particular gene. As a consequence, it is telomeres that are shortened with each round of DNA replication instead of genes. For example, in humans, a six base-pair sequence, TTAGGG, is repeated 100 to 1000 times. The discovery of the enzyme **telomerase** ([**Figure 3.11**](#_bookmark918)) helped in the understanding of how chromosome ends are maintained. The telomerase attaches to the end of the chromosome, and complementary bases to the RNA template are added on the end of the DNA strand. Once the lagging strand template is sufficiently elongated, DNA polymerase can now add nucleotides that are complementary to the ends of the chromosomes. Thus, the ends of the chromosomes are replicated.

70



**Figure 3.12** The ends of linear chromosomes are maintained by the action of the telomerase enzyme.

Telomerase is typically found to be active in germ cells, adult stem cells, and some cancer cells. For her discovery of telomerase and its action, Elizabeth Blackburn (Figure 3.13) received the Nobel Prize for Medicine and Physiology in 2009.



**Figure 3.13** Elizabeth Blackburn, 2009 Nobel Laureate, was the scientist who discovered how telomerase works. (credit: U.S. Embassy, Stockholm, Sweden)

Telomerase is not active in adult somatic cells. Adult somatic cells that undergo cell division continue to have their telomeres shortened. This essentially means that telomere shortening is associated with aging. In 2010, scientists found that telomerase can reverse some age-related conditions in mice, and

[1]

this may have potential in regenerative medicine. Telomerase-deficient mice were used in these

1. Mariella Jaskelioff, et al., “Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice,” *Nature*, 469 (2011):102–7. 71

studies; these mice have tissue atrophy, stem-cell depletion, organ system failure, and impaired tissue injury responses. Telomerase reactivation in these mice caused extension of telomeres, reduced DNA damage, reversed neurodegeneration, and improved functioning of the testes, spleen, and intestines. Thus, telomere reactivation may have potential for treating age-related diseases in humans.

DNA Replication in Prokaryotes

Recall that the prokaryotic chromosome is a circular molecule with a less extensive coiling structure than eukaryotic chromosomes. The eukaryotic chromosome is linear and highly coiled around proteins. While there are many similarities in the DNA replication process, these structural differences necessitate some differences in the DNA replication process in these two life forms.

DNA replication has been extremely well-studied in prokaryotes, primarily because of the small size of the genome and large number of variants available. *Escherichia coli* has 4.6 million base pairs in a single circular chromosome, and all of it gets replicated in approximately 42 minutes, starting from a single origin of replication and proceeding around the chromosome in both directions. This means that approximately 1000 nucleotides are added per second. The process is much more rapid than in eukaryotes. Table 3.2 summarizes the differences between prokaryotic and eukaryotic replications.

##### Differences between Prokaryotic and Eukaryotic Replications

|  |  |  |
| --- | --- | --- |
| **Property** | **Prokaryotes** | **Eukaryotes** |
| Origin of replication | Single | Multiple |
| Rate of replication | 1000 nucleotides/s | 50 to 100 nucleotides/s |
| Chromosome structure | circular | linear |
| Telomerase | Not present | Present |

Table 3.2



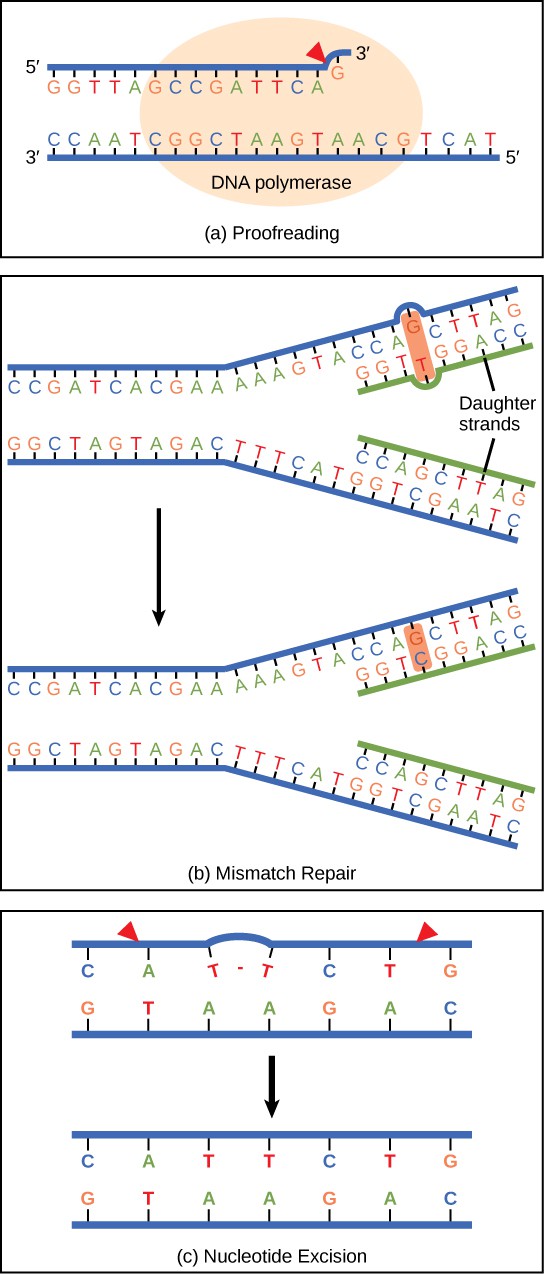


Click through a [**tutorial (http://openstaxcollege.org/l/DNA\_replicatio2)**](http://openstaxcollege.org/l/DNA_replicatio2)on DNA replication.

#### DNA Repair

DNA polymerase can make mistakes while adding nucleotides. It edits the DNA by proofreading every newly added base. Incorrect bases are removed and replaced by the correct base, and then polymerization continues ([**Figure**](#_bookmark923) **3.14a**). Most mistakes are corrected during replication, although when this does not happen, the **mismatch repair** mechanism is employed. Mismatch repair enzymes recognize the wrongly incorporated base and excise it from the DNA, replacing it with the correct base (Figure 3.14**b**). In yet another type of repair, **nucleotide excision repair**, the DNA double strand is unwound and separated, the incorrect bases are removed along with a few bases on the 5' and 3' end, and these are replaced by copying the template with the help of DNA polymerase (Figure 3.14**c**). Nucleotide excision repair is particularly important in correcting thymine dimers, which are primarily caused by ultraviolet light. In a thymine dimer, two thymine nucleotides adjacent to each other on one strand are covalently bonded to each other rather than their complementary bases. If the dimer is not removed and repaired it will lead to a mutation. Individuals with flaws in their nucleotide excision repair genes show extreme sensitivity to sunlight and develop skin cancers early in life.

72



**Figure 3.14** Proofreading by DNA polymerase (a) corrects errors during replication. In mismatch repair (b), the incorrectly added base is detected after replication. The mismatch repair proteins detect this base and remove it from the newly synthesized strand by nuclease action. The gap is now filled with the correctly paired base. Nucleotide excision (c) repairs thymine dimers. When exposed to UV, thymines lying adjacent to each other can form thymine dimers. In normal cells, they are excised and replaced.

Most mistakes are corrected; if they are not, they may result in a **mutation**—defined as a permanent change in the DNA sequence. Mutations in repair genes may lead to serious consequences like cancer.

73

## | Transcription

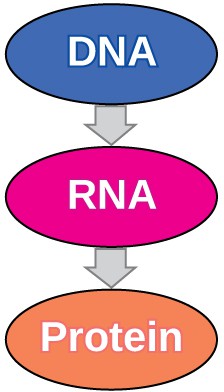
By the end of this section, you will be able to:

* Explain the central dogma
* Explain the main steps of transcription
* Describe how eukaryotic mRNA is processed

In both prokaryotes and eukaryotes, the second function of DNA (the first was replication) is to provide the information needed to construct the proteins necessary so that the cell can perform all of its functions. To do this, the DNA is “read” or transcribed into an **mRNA** molecule. The mRNA then provides the code to form a protein by a process called translation. Through the processes of transcription and translation, a protein is built with a specific sequence of amino acids that was originally encoded in the DNA. This module discusses the details of transcription.

#### The Central Dogma: DNA Encodes RNA; RNA Encodes Protein

The flow of genetic information in cells from DNA to mRNA to protein is described by the central dogma (Figure 3.15), which states that genes specify the sequences of mRNAs, which in turn specify the sequences of proteins.



**Figure 3.15** The central dogma states that DNA encodes RNA, which in turn encodes protein.

The copying of DNA to mRNA is relatively straightforward, with one nucleotide being added to the mRNA strand for every complementary nucleotide read in the DNA strand. The translation to protein is more complex because groups of three mRNA nucleotides correspond to one amino acid of the protein sequence. However, as we shall see in the next module, the translation to protein is still systematic, such that nucleotides 1 to 3 correspond to amino acid 1, nucleotides 4 to 6 correspond to amino acid 2, and so on.

#### Transcription: from DNA to mRNA

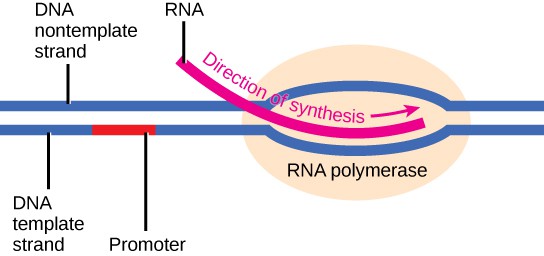
Both prokaryotes and eukaryotes perform fundamentally the same process of transcription, with the important difference of the membrane-bound nucleus in eukaryotes. With the genes bound in the nucleus, transcription occurs in the nucleus of the cell and the mRNA transcript must be transported to the cytoplasm. The prokaryotes, which include bacteria and archaea, lack membrane-bound nuclei and other organelles, and transcription occurs in the cytoplasm of the cell. In both prokaryotes and eukaryotes, transcription occurs in three main stages: initiation, elongation, and termination.

Initiation

Transcription requires the DNA double helix to partially unwind in the region of mRNA synthesis. The region of unwinding is called a **transcription bubble**. The DNA sequence onto which the proteins and enzymes involved in transcription bind to initiate the process is called a **promoter**. In most cases, promoters exist upstream of the genes they regulate. The specific sequence of a promoter is very

74

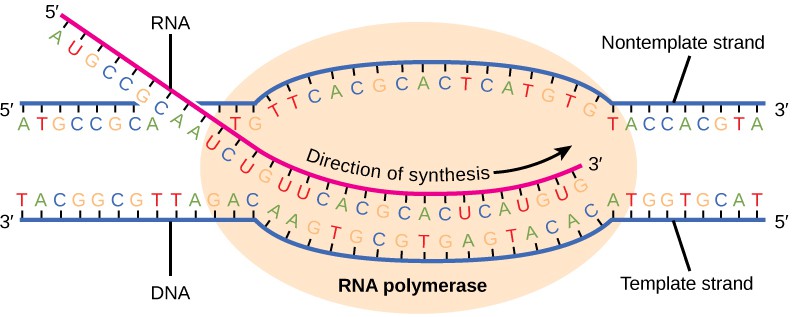
important because it determines whether the corresponding gene is transcribed all of the time, some of the time, or hardly at all (Figure 3.16).



**Figure 3.16** The initiation of transcription begins when DNA is unwound, forming a transcription bubble. Enzymes and other proteins involved in transcription bind at the promoter.

Elongation

Transcription always proceeds from one of the two DNA strands, which is called the **template strand**. The mRNA product is complementary to the template strand and is almost identical to the other DNA strand, called the **nontemplate strand**, with the exception that RNA contains a uracil (U) in place of the thymine (T) found in DNA. During elongation, an enzyme called **RNA polymerase** proceeds along the DNA template adding nucleotides by base pairing with the DNA template in a manner similar to DNA replication, with the difference that an RNA strand is being synthesized that does not remain bound to the DNA template. As elongation proceeds, the DNA is continuously unwound ahead of the core enzyme and rewound behind it (Figure 3.17).



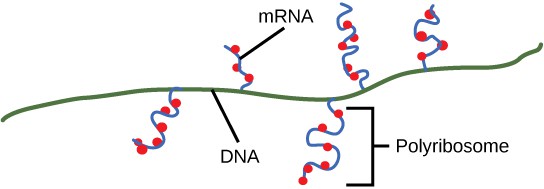
**Figure 3.17** During elongation, RNA polymerase tracks along the DNA template, synthesizes mRNA in the 5' to 3' direction, and unwinds then rewinds the DNA as it is read.

Termination

Once a gene is transcribed, the prokaryotic polymerase needs to be instructed to dissociate from the DNA template and liberate the newly made mRNA. Depending on the gene being transcribed, there are two kinds of termination signals, but both involve repeated nucleotide sequences in the DNA template that result in RNA polymerase stalling, leaving the DNA template, and freeing the mRNA transcript.

On termination, the process of transcription is complete. In a prokaryotic cell, by the time termination occurs, the transcript would already have been used to partially synthesize numerous copies of the encoded protein because these processes can occur concurrently using multiple ribosomes (polyribosomes) (Figure 3.18). In contrast, the presence of a nucleus in eukaryotic cells precludes simultaneous transcription and translation.

75



**Figure 3.18** Multiple polymerases can transcribe a single bacterial gene while numerous ribosomes concurrently translate the mRNA transcripts into polypeptides. In this way, a specific protein can rapidly reach a high concentration in the bacterial cell.

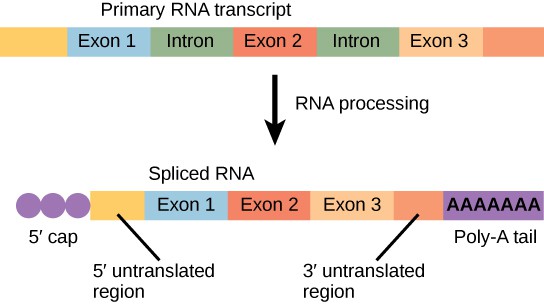
#### Eukaryotic RNA Processing

The newly transcribed eukaryotic mRNAs must undergo several processing steps before they can be transferred from the nucleus to the cytoplasm and translated into a protein. The additional steps involved in eukaryotic mRNA maturation create a molecule that is much more stable than a prokaryotic mRNA. For example, eukaryotic mRNAs last for several hours, whereas the typical prokaryotic mRNA lasts no more than five seconds.

The mRNA transcript is first coated in RNA-stabilizing proteins to prevent it from degrading while it is processed and exported out of the nucleus. This occurs while the pre-mRNA still is being synthesized by adding a special nucleotide “cap” to the 5' end of the growing transcript. In addition to preventing degradation, factors involved in protein synthesis recognize the cap to help initiate translation by ribosomes.

Once elongation is complete, an enzyme then adds a string of approximately 200 adenine residues to the 3' end, called the poly-A tail. This modification further protects the pre-mRNA from degradation and signals to cellular factors that the transcript needs to be exported to the cytoplasm.

Eukaryotic genes are composed of protein-coding sequences called **exons** (*ex-*on signifies that they are *ex*pressed) and *int*ervening sequences called **introns** (*int-*ron denotes their *int*ervening role). Introns are removed from the pre-mRNA during processing. Intron sequences in mRNA do not encode functional proteins. It is essential that all of a pre-mRNA’s introns be completely and precisely removed before protein synthesis so that the exons join together to code for the correct amino acids. If the process errs by even a single nucleotide, the sequence of the rejoined exons would be shifted, and the resulting protein would be nonfunctional. The process of removing introns and reconnecting exons is called **splicing** (Figure 3.19). Introns are removed and degraded while the pre-mRNA is still in the nucleus.



**Figure 3.19** Eukaryotic mRNA contains introns that must be spliced out. A 5' cap and 3' tail are also added.

76

## Translation

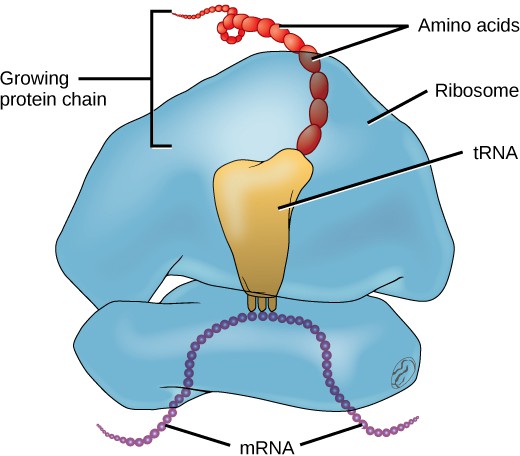
By the end of this section, you will be able to:

* Describe the different steps in protein synthesis
* Discuss the role of ribosomes in protein synthesis
* Describe the genetic code and how the nucleotide sequence determines the amino acid and the protein sequence

The synthesis of proteins is one of a cell’s most energy-consuming metabolic processes. In turn, proteins account for more mass than any other component of living organisms (with the exception of water), and proteins perform a wide variety of the functions of a cell. The process of translation, or protein synthesis, involves decoding an mRNA message into a polypeptide product. Amino acids are covalently strung together in lengths ranging from approximately 50 amino acids to more than 1,000.

#### The Protein Synthesis Machinery

In addition to the mRNA template, many other molecules contribute to the process of translation. The composition of each component may vary across species; for instance, ribosomes may consist of different numbers of ribosomal RNAs ( **rRNA**) and polypeptides depending on the organism. However, the general structures and functions of the protein synthesis machinery are comparable from bacteria to human cells. Translation requires the input of an mRNA template, ribosomes, tRNAs, and various enzymatic factors (Figure 3.20).



**Figure 3.20**The protein synthesis machinery includes the large and small subunits of the ribosome, mRNA, and tRNA. (credit: modification of work by NIGMS, NIH)

In *E. coli*, there are 200,000 ribosomes present in every cell at any given time. A ribosome is a complex macromolecule composed of structural and catalytic rRNAs, and many distinct polypeptides. In eukaryotes, the nucleolus is completely specialized for the synthesis and assembly of rRNAs.

Ribosomes are located in the cytoplasm in prokaryotes and in the cytoplasm and endoplasmic reticulum of eukaryotes. Ribosomes are made up of a large and a small subunit that come together for translation. The small subunit is responsible for binding the mRNA template, whereas the large subunit sequentially binds **tRNAs**, a type of RNA molecule that brings amino acids to the growing chain of the polypeptide. Each mRNA molecule is simultaneously translated by many ribosomes, all synthesizing protein in the same direction.

Depending on the species, 40 to 60 types of tRNA exist in the cytoplasm. Serving as adaptors, specific tRNAs bind to sequences on the mRNA template and add the corresponding amino acid to the polypeptide chain. Therefore, tRNAs are the molecules that actually “translate” the language of RNA into the language of proteins. For each tRNA to function, it must have its specific amino acid bonded to it. In the process of tRNA “charging,” each tRNA molecule is bonded to its correct amino acid.

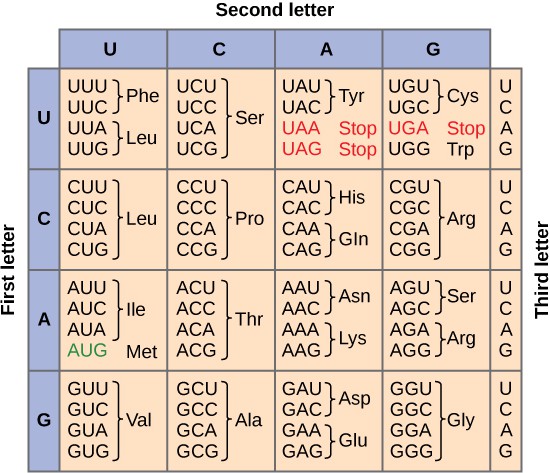
77

#### The Genetic Code

To summarize what we know to this point, the cellular process of transcription generates messenger RNA (mRNA), a mobile molecular copy of one or more genes with an alphabet of A, C, G, and uracil

(U). Translation of the mRNA template converts nucleotide-based genetic information into a protein product. Protein sequences consist of 20 commonly occurring amino acids; therefore, it can be said that the protein alphabet consists of 20 letters. Each amino acid is defined by a three-nucleotide sequence called the triplet **codon**. The relationship between a nucleotide codon and its corresponding amino acid is called the **genetic code**.

Given the different numbers of “letters” in the mRNA and protein “alphabets,” combinations of nucleotides corresponded to single amino acids. Using a three-nucleotide code means that there are a total of 64 (4 × 4 × 4) possible combinations; therefore, a given amino acid is encoded by more than one nucleotide triplet (Figure 3.21).



**Figure 3.21** This figure shows the genetic code for translating each nucleotide triplet, or codon, in mRNA into an amino acid or a termination signal in a nascent protein. (credit: modification of work by NIH)

Three of the 64 codons terminate protein synthesis and release the polypeptide from the translation machinery. These triplets are called **stop codons**. Another codon, AUG, also has a special function. In addition to specifying the amino acid methionine, it also serves as the **start codon** to initiate translation. The reading frame for translation is set by the AUG start codon near the 5' end of the mRNA. The genetic code is universal. With a few exceptions, virtually all species use the same genetic code for protein synthesis, which is powerful evidence that all life on Earth shares a common origin.

#### The Mechanism of Protein Synthesis

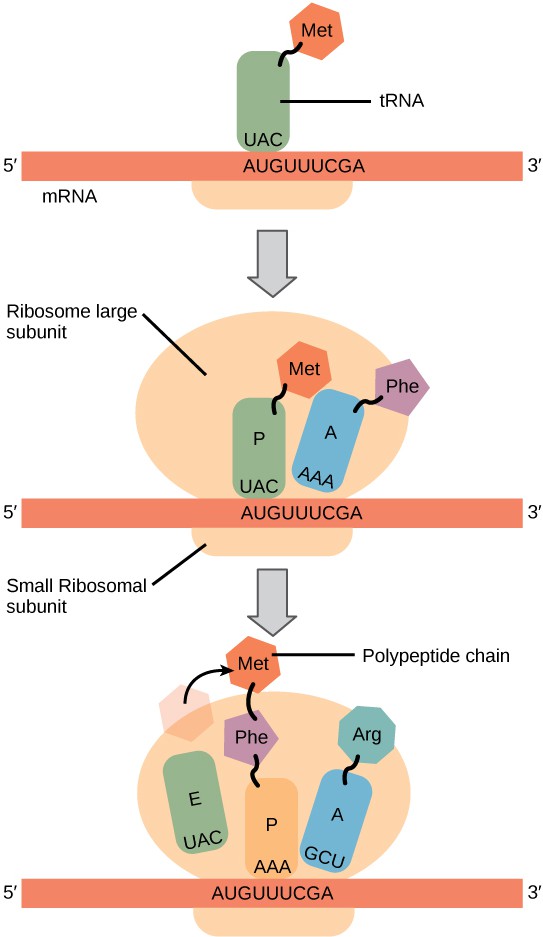
Just as with mRNA synthesis, protein synthesis can be divided into three phases: initiation, elongation, and termination. The process of translation is similar in prokaryotes and eukaryotes. Here we will explore how translation occurs in *E. coli*, a representative prokaryote, and specify any differences between prokaryotic and eukaryotic translation.

Protein synthesis begins with the formation of an initiation complex. In *E. coli*, this complex involves the small ribosome subunit, the mRNA template, three initiation factors, and a special initiator tRNA. The initiator tRNA interacts with the AUG start codon, and links to a special form of the amino acid methionine that is typically removed from the polypeptide after translation is complete.

In prokaryotes and eukaryotes, the basics of polypeptide elongation are the same, so we will review elongation from the perspective of *E. coli*. The large ribosomal subunit of *E. coli* consists of three compartments: the A site binds incoming charged tRNAs (tRNAs with their attached specific amino acids). The P site binds charged tRNAs carrying amino acids that have formed bonds with the growing polypeptide chain but have not yet dissociated from their corresponding tRNA. The E site releases dissociated tRNAs so they can be recharged with free amino acids. The ribosome shifts one codon at a time, catalyzing each process that occurs in the three sites. With each step, a charged tRNA enters the

78

complex, the polypeptide becomes one amino acid longer, and an uncharged tRNA departs. The energy for each bond between amino acids is derived from GTP, a molecule similar to ATP (Figure 3.22). Amazingly, the *E. coli* translation apparatus takes only 0.05 seconds to add each amino acid, meaning that a 200-amino acid polypeptide could be translated in just 10 seconds.



**Figure 3.22** Translation begins when a tRNA anticodon recognizes a codon on the mRNA. The large ribosomal subunit joins the small subunit, and a second tRNA is recruited. As the mRNA moves relative to the ribosome, the polypeptide chain is formed. Entry of a release factor into the A site terminates translation and the components dissociate.

Termination of translation occurs when a stop codon (UAA, UAG, or UGA) is encountered. When the ribosome encounters the stop codon, the growing polypeptide is released and the ribosome subunits dissociate and leave the mRNA. After many ribosomes have completed translation, the mRNA is degraded so the nucleotides can be reused in another transcription reaction.





Transcribe a gene and translate it to protein using complementary pairing and the genetic code at [**this**](http://openstaxcollege.org/l/create_protein2)[**site (http://openstaxcollege.org/l/create\_protein2)**](http://openstaxcollege.org/l/create_protein2).

79

pair; the pairs are bound to each other by hydrogen bonds. The bases pair in such a way that the distance between the backbones of the two strands is the same all along the molecule.

## Errors in Meiosis

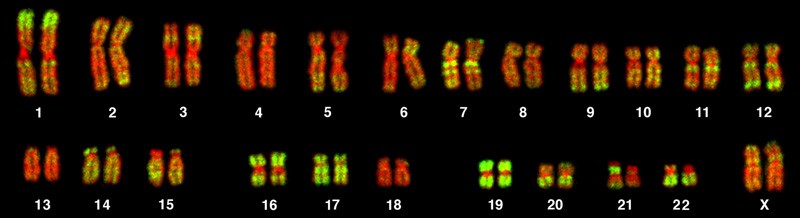
By the end of this section, you will be able to:

* Explain how nondisjunction leads to disorders in chromosome number
* Describe how errors in chromosome structure occur through inversions and translocations

Inherited disorders can arise when chromosomes behave abnormally during meiosis. Chromosome disorders can be divided into two categories: abnormalities in chromosome number and chromosome structural rearrangements. Because even small segments of chromosomes can span many genes, chromosomal disorders are characteristically dramatic and often fatal.

#### Disorders in Chromosome Number

The isolation and microscopic observation of chromosomes forms the basis of cytogenetics and is the primary method by which clinicians detect chromosomal abnormalities in humans. A **karyotype** is the number and appearance of chromosomes, including their length, banding pattern, and centromere position. To obtain a view of an individual’s karyotype, cytologists photograph the chromosomes and then cut and paste each chromosome into a chart, or **karyogram** (Figure 3.23).



**Figure 3.23** This karyogram shows the chromosomes of a female human immune cell during mitosis. (credit: Andreas Bolzer, et al)

80



**Geneticists Use Karyograms to Identify Chromosomal Aberrations**

The karyotype is a method by which traits characterized by chromosomal abnormalities can be identified from a single cell. To observe an individual’s karyotype, a person’s cells (like white blood cells) are first collected from a blood sample or other tissue. In the laboratory, the isolated cells are stimulated to begin actively dividing. A chemical is then applied to the cells to arrest mitosis during metaphase. The cells are then fixed to a slide.

The geneticist then stains chromosomes with one of several dyes to better visualize the distinct and reproducible banding patterns of each chromosome pair. Following staining, chromosomes are viewed using bright-field microscopy. An experienced cytogeneticist can identify each band. In addition to the banding patterns, chromosomes are further identified on the basis of size and centromere location. To obtain the classic depiction of the karyotype in which homologous pairs of chromosomes are aligned in numerical order from longest to shortest, the geneticist obtains a digital image, identifies each chromosome, and manually arranges the chromosomes into this pattern ([**Figure 7.7**](#_bookmark729)).

At its most basic, the karyogram may reveal genetic abnormalities in which an individual has too many or too few chromosomes per cell. Examples of this are Down syndrome, which is identified by a third copy of chromosome 21, and Turner syndrome, which is characterized by the presence of only one X chromosome in women instead of two. Geneticists can also identify large deletions or insertions of DNA. For instance, Jacobsen syndrome, which involves distinctive facial features as well as heart and bleeding defects, is identified by a deletion on chromosome 11. Finally, the karyotype can pinpoint **translocations**, which occur when a segment of genetic material breaks from one chromosome and reattaches to another chromosome or to a different part of the same chromosome. Translocations are implicated in certain cancers, including chronic myelogenous leukemia.

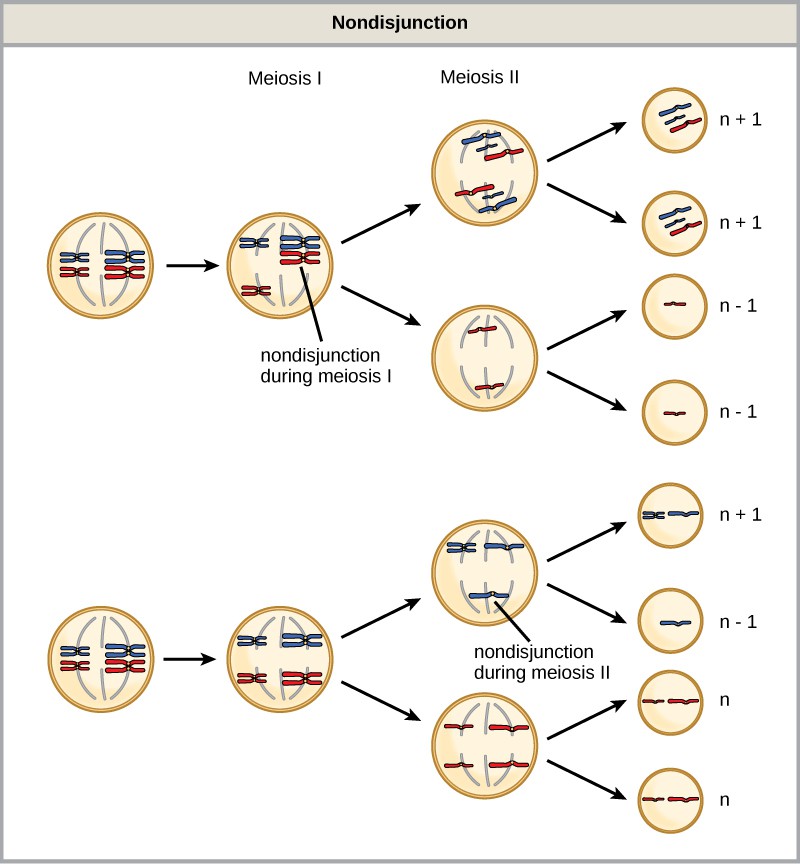
By observing a karyogram, geneticists can actually visualize the chromosomal composition of an individual to confirm or predict genetic abnormalities in offspring even before birth.

Nondisjunctions, Duplications, and Deletions

Of all the chromosomal disorders, abnormalities in chromosome number are the most easily identifiable from a karyogram. Disorders of chromosome number include the duplication or loss of entire chromosomes, as well as changes in the number of complete sets of chromosomes. They are caused by **nondisjunction**, which occurs when pairs of homologous chromosomes or sister chromatids fail to separate during meiosis. The risk of nondisjunction increases with the age of the parents.

Nondisjunction can occur during either meiosis I or II, with different results ([**Figure**](#_bookmark732) **3.24**). If homologous chromosomes fail to separate during meiosis I, the result is two gametes that lack that chromosome and two gametes with two copies of the chromosome. If sister chromatids fail to separate during meiosis II, the result is one gamete that lacks that chromosome, two normal gametes with one copy of the chromosome, and one gamete with two copies of the chromosome.

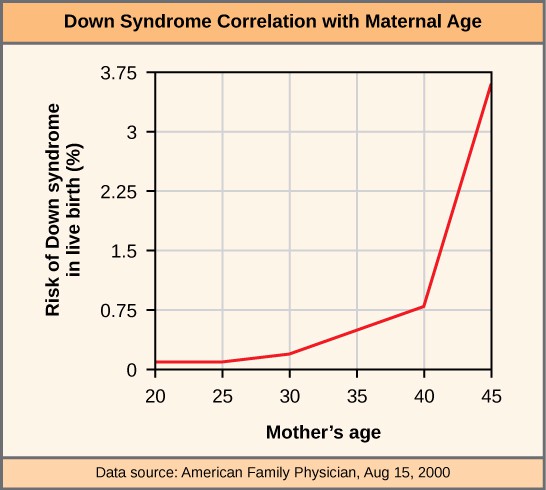
81



**Figure 3.24** Following meiosis, each gamete has one copy of each chromosome. Nondisjunction occurs when homologous chromosomes (meiosis I) or sister chromatids (meiosis II) fail to separate during meiosis.

An individual with the appropriate number of chromosomes for their species is called **euploid**; in humans, euploidy corresponds to 22 pairs of **autosomes** and one pair of sex chromosomes. An individual with an error in chromosome number is described as **aneuploid**, a term that includes **monosomy** (loss of one chromosome) or **trisomy** (gain of an extraneous chromosome). Monosomic human zygotes missing any one copy of an autosome invariably fail to develop to birth because they have only one copy of essential genes. Most autosomal trisomies also fail to develop to birth; however, duplications of some of the smaller chromosomes (13, 15, 18, 21, or 22) can result in offspring that survive for several weeks to many years. Trisomic individuals suffer from a different type of genetic imbalance: an excess in gene dose. Cell functions are calibrated to the amount of gene product produced by two copies (doses) of each gene; adding a third copy (dose) disrupts this balance. The most common trisomy is that of chromosome 21, which leads to Down syndrome. Individuals with this inherited disorder have characteristic physical features and developmental delays in growth and cognition. The incidence of Down syndrome is correlated with maternal age, such that older women are more likely to give birth to children with Down syndrome (Figure 3.25).

82



**Figure 3.25** The incidence of having a fetus with trisomy 21 increases dramatically with maternal age.





Visualize the addition of a chromosome that leads to Down syndrome in this [**video simulation**](http://openstaxcollege.org/l/down_syndrome2)[**(http://openstaxcollege.org/l/down\_syndrome2)**](http://openstaxcollege.org/l/down_syndrome2).

Humans display dramatic deleterious effects with autosomal trisomies and monosomies. Therefore, it may seem counterintuitive that human females and males can function normally, despite carrying different numbers of the X chromosome. In part, this occurs because of a process called **X inactivation**. Early in development, when female mammalian embryos consist of just a few thousand cells, one X chromosome in each cell inactivates by condensing into a structure called a Barr body. The genes on the inactive X chromosome are not expressed. The particular X chromosome (maternally or paternally derived) that is inactivated in each cell is random, but once the inactivation occurs, all cells descended from that cell will have the same inactive X chromosome. By this process, females compensate for their double genetic dose of X chromosome.

In so-called “tortoiseshell” cats, X inactivation is observed as coat-color variegation (Figure 3.26). Females heterozygous for an X-linked coat color gene will express one of two different coat colors over different regions of their body, corresponding to whichever X chromosome is inactivated in the embryonic cell progenitor of that region. When you see a tortoiseshell cat, you will know that it has to be a female.

83



**Figure 3.26** Embryonic inactivation of one of two different X chromosomes encoding different coat colors gives rise to the tortoiseshell phenotype in cats. (credit: Michael Bodega)

In an individual carrying an abnormal number of X chromosomes, cellular mechanisms will inactivate all but one X in each of her cells. As a result, X-chromosomal abnormalities are typically associated with mild mental and physical defects, as well as sterility. If the X chromosome is absent altogether, the individual will not develop.

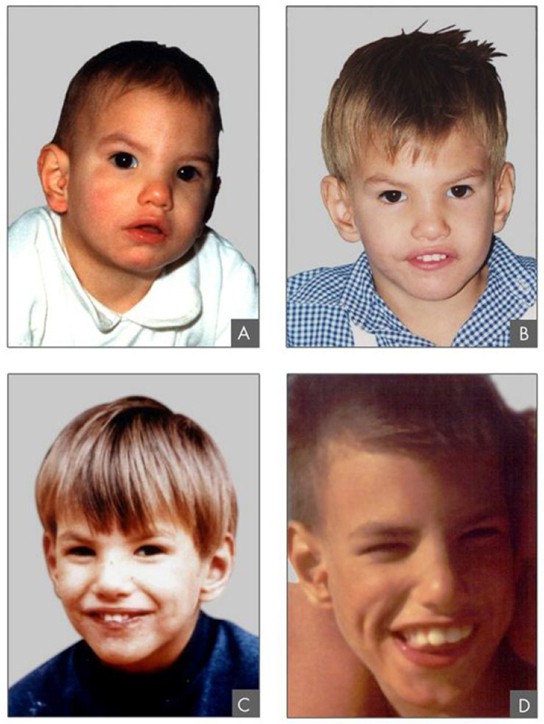
Several errors in sex chromosome number have been characterized. Individuals with three X chromosomes, called triplo-X, appear female but express developmental delays and reduced fertility. The XXY chromosome complement, corresponding to one type of Klinefelter syndrome, corresponds to male individuals with small testes, enlarged breasts, and reduced body hair. The extra X chromosome undergoes inactivation to compensate for the excess genetic dosage. Turner syndrome, characterized as an X0 chromosome complement (i.e., only a single sex chromosome), corresponds to a female individual with short stature, webbed skin in the neck region, hearing and cardiac impairments, and sterility.

An individual with more than the correct number of chromosome sets (two for diploid species) is called **polyploid**. For instance, fertilization of an abnormal diploid egg with a normal haploid sperm would yield a triploid zygote. Polyploid animals are extremely rare, with only a few examples among the flatworms, crustaceans, amphibians, fish, and lizards. Triploid animals are sterile because meiosis cannot proceed normally with an odd number of chromosome sets. In contrast, polyploidy is very common in the plant kingdom, and polyploid plants tend to be larger and more robust than euploids of their species.

#### Chromosome Structural Rearrangements

Cytologists have characterized numerous structural rearrangements in chromosomes, including partial duplications, deletions, inversions, and translocations. Duplications and deletions often produce offspring that survive but exhibit physical and mental abnormalities. Cri-du-chat (from the French for “cry of the cat”) is a syndrome associated with nervous system abnormalities and identifiable physical features that results from a deletion of most of the small arm of chromosome 5 (Figure 3.27). Infants with this genotype emit a characteristic high-pitched cry upon which the disorder’s name is based.

84



**Figure 3.27** This individual with cri-du-chat syndrome is shown at various ages: (A) age two, (B) age four, (C) age nine, and (D) age 12. (credit: Paola Cerruti Mainardi)

Chromosome inversions and translocations can be identified by observing cells during meiosis because homologous chromosomes with a rearrangement in one of the pair must contort to maintain appropriate gene alignment and pair effectively during prophase I.

A **chromosome inversion** is the detachment, 180° rotation, and reinsertion of part of a chromosome (Figure 3.28). Unless they disrupt a gene sequence, inversions only change the orientation of genes and are likely to have more mild effects than aneuploid errors.

85



**The Chromosome 18 Inversion**

Not all structural rearrangements of chromosomes produce nonviable, impaired, or infertile individuals. In rare instances, such a change can result in the evolution of a new species. In fact, an inversion in chromosome 18 appears to have contributed to the evolution of humans. This inversion is not present in our closest genetic relatives, the chimpanzees.

The chromosome 18 inversion is believed to have occurred in early humans following their divergence from a common ancestor with chimpanzees approximately five million years ago. Researchers have suggested that a long stretch of DNA was duplicated on chromosome 18 of an ancestor to humans, but that during the duplication it was inverted (inserted into the chromosome in reverse orientation.

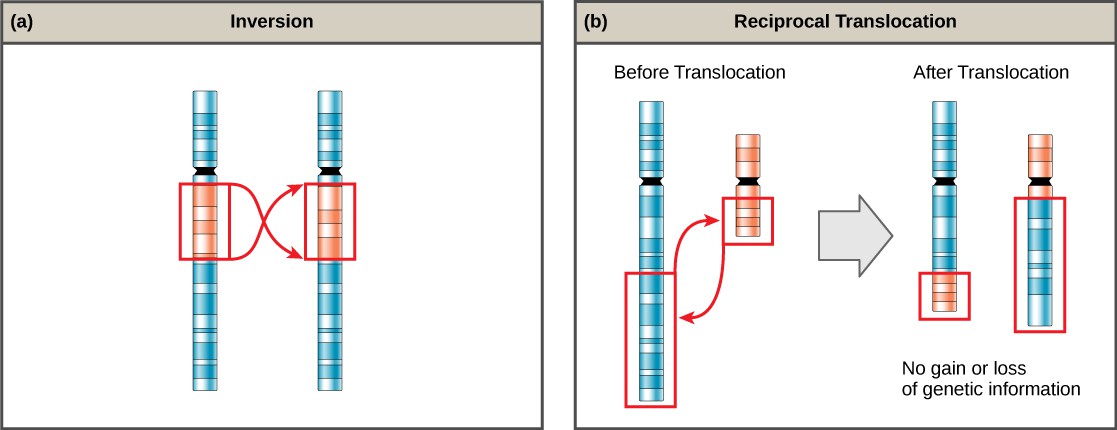
A comparison of human and chimpanzee genes in the region of this inversion indicates that two genes—*ROCK1* and *USP14*—are farther apart on human chromosome 18 than they are on the corresponding chimpanzee chromosome. This suggests that one of the inversion breakpoints occurred between these two genes. Interestingly, humans and chimpanzees express *USP14* at distinct levels in specific cell types, including cortical cells and fibroblasts. Perhaps the chromosome 18 inversion in an ancestral human repositioned specific genes and reset their expression levels in a useful way. Because both *ROCK1* and *USP14* code for enzymes, a change in their expression could alter cellular function.

It is not known how this inversion contributed to hominid evolution, but it appears to be a

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significant factor in the divergence of humans from other primates.

A translocation occurs when a segment of a chromosome dissociates and reattaches to a different, nonhomologous chromosome. Translocations can be benign or have devastating effects, depending on how the positions of genes are altered with respect to regulatory sequences. Notably, specific translocations have been associated with several cancers and with schizophrenia. Reciprocal translocations result from the exchange of chromosome segments between two nonhomologous chromosomes such that there is no gain or loss of genetic information (Figure 3.27).



**Figure 3.28** An (a) inversion occurs when a chromosome segment breaks from the chromosome, reverses its orientation, and then reattaches in the original position. A (b) reciprocal translocation occurs between two nonhomologous chromosomes and does not cause any genetic information to be lost or duplicated. (credit: modification of work by National Human Genome Research Institute (USA)

Genetics

Genetics is the study of heredity. Johann Gregor Mendel set the framework for genetics long before chromosomes or genes had been identified, at a time when meiosis was not well understood. Mendel selected a simple biological system and conducted methodical, quantitative analyses using large sample sizes. Because of Mendel’s work, the fundamental principles of heredity were revealed. We now know that genes, carried on chromosomes, are the basic functional units of heredity with the ability to be replicated, expressed, or mutated. Today, the postulates put forth by Mendel form the basis of classical, or Mendelian, genetics. Not all genes are transmitted from parents to offspring according to Mendelian genetics, but Mendel’s experiments serve as an excellent starting point for thinking about inheritance. 86

## Mendel’s Experiments



**Figure 3.29** Johann Gregor Mendel set the framework for the study of genetics.

Johann Gregor Mendel (1822–1884) (Figure 3.29) was a lifelong learner, teacher, scientist, and man of faith. As a young adult, he joined the Augustinian Abbey of St. Thomas in Brno in what is now the Czech Republic. Supported by the monastery, he taught physics, botany, and natural science courses at the secondary and university levels. In 1856, he began a decade-long research pursuit involving inheritance patterns in honeybees and plants, ultimately settling on pea plants as his primary **model system** (a system with convenient characteristics that is used to study a specific biological phenomenon to gain understanding to be applied to other systems). In 1865, Mendel presented the results of his experiments with nearly 30,000 pea plants to the local natural history society. He demonstrated that traits are transmitted faithfully from parents to offspring in specific patterns. In 1866, he published his work,

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*Experiments in Plant Hybridization,* in the proceedings of the Natural History Society of Brünn.

Mendel’s work went virtually unnoticed by the scientific community, which incorrectly believed that the process of inheritance involved a blending of parental traits that produced an intermediate physical appearance in offspring. This hypothetical process appeared to be correct because of what we know now as continuous variation. **Continuous variation** is the range of small differences we see among individuals in a characteristic like human height. It does appear that offspring are a “blend” of their parents’ traits when we look at characteristics that exhibit continuous variation. Mendel worked instead with traits that show **discontinuous variation**. Discontinuous variation is the variation seen among individuals when each individual shows one of two—or a very few—easily distinguishable traits, such as violet or white flowers. Mendel’s choice of these kinds of traits allowed him to see experimentally that the traits were not blended in the offspring as would have been expected at the time, but that they were inherited as distinct traits. In 1868, Mendel became abbot of the monastery and exchanged his scientific pursuits for his pastoral duties. He was not recognized for his extraordinary scientific contributions during his lifetime; in fact, it was not until 1900 that his work was rediscovered, reproduced, and revitalized by scientists on the brink of discovering the chromosomal basis of heredity.

#### Mendel’s Crosses

Mendel’s seminal work was accomplished using the garden pea, *Pisum sativum*, to study inheritance. This species naturally self-fertilizes, meaning that pollen encounters ova within the same flower. The

1. Johann Gregor Mendel, “Versuche über Pflanzenhybriden.” *Verhandlungen des naturforschenden Vereines in Brünn*, Bd. IV für das Jahr, 1865 Abhandlungen (1866):3–47. [for English translation, see [http://www.mendelweb.org/Mendel.plain.html]](http://www.mendelweb.org/Mendel.plain.html)

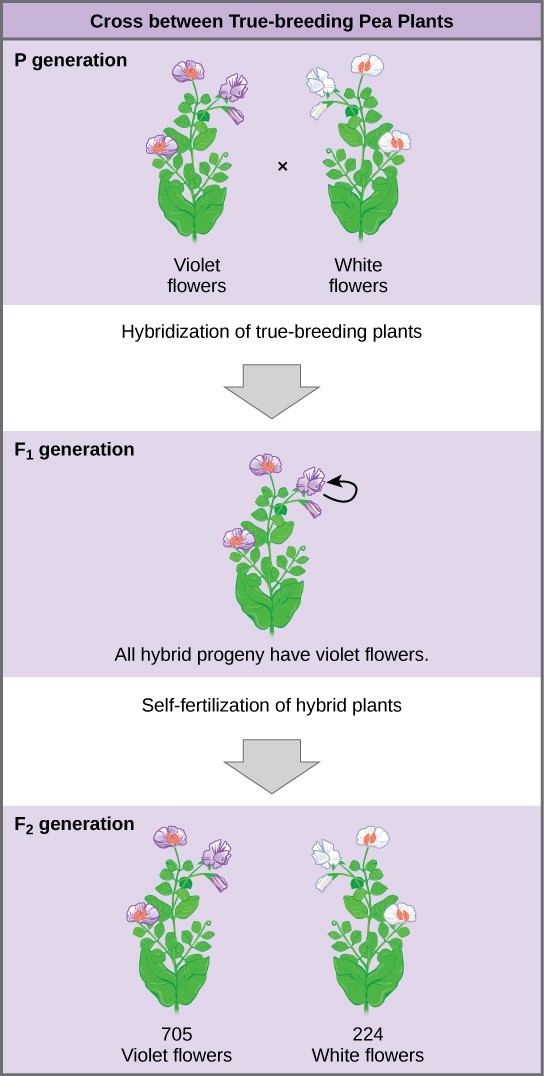
88

flower petals remain sealed tightly until pollination is completed to prevent the pollination of other plants. The result is highly inbred, or “true-breeding,” pea plants. These are plants that always produce offspring that look like the parent. By experimenting with true-breeding pea plants, Mendel avoided the appearance of unexpected traits in offspring that might occur if the plants were not true breeding. The garden pea also grows to maturity within one season, meaning that several generations could be evaluated over a relatively short time. Finally, large quantities of garden peas could be cultivated simultaneously, allowing Mendel to conclude that his results did not come about simply by chance.

Mendel performed **hybridizations**, which involve mating two true-breeding individuals that have different traits. In the pea, which is naturally self-pollinating, this is done by manually transferring pollen from the anther of a mature pea plant of one variety to the stigma of a separate mature pea plant of the second variety.

Plants used in first-generation crosses were called **P**, or parental generation, plants (Figure 3.30). Mendel collected the seeds produced by the P plants that resulted from each cross and grew them the following season. These offspring were called the **F1**, or the first filial (filial = daughter or son), generation. Once Mendel examined the characteristics in the F1 generation of plants, he allowed them to self-fertilize naturally. He then collected and grew the seeds from the F1 plants to produce the **F2**, or second filial, generation. Mendel’s experiments extended beyond the F2 generation to the F3 generation, F4 generation, and so on, but it was the ratio of characteristics in the P, F1, and F2 generations that were the most intriguing and became the basis of Mendel’s postulates.

89



**Figure 3.30** Mendel’s process for performing crosses included examining flower color.

#### Garden Pea Characteristics Revealed the Basics of Heredity

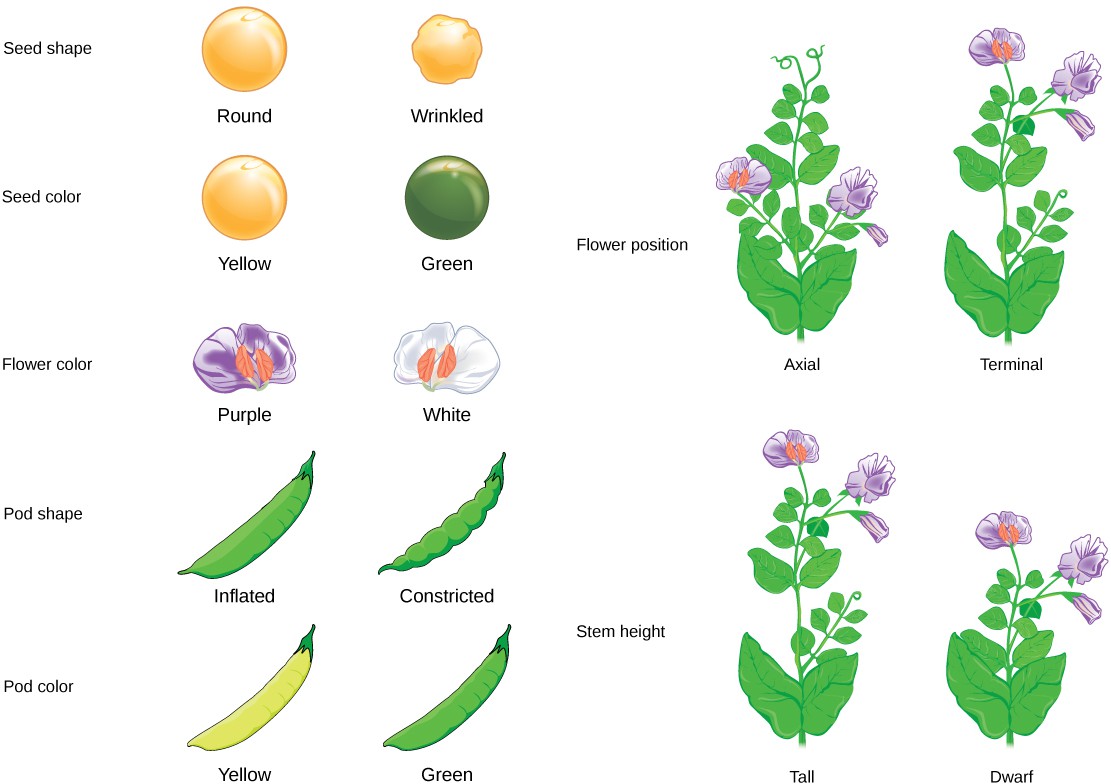
In his 1865 publication, Mendel reported the results of his crosses involving seven different characteristics, each with two contrasting traits. A **trait** is defined as a variation in the physical appearance of a heritable characteristic. The characteristics included plant height, seed texture, seed color, flower color, pea-pod size, pea-pod color, and flower position. For the characteristic of flower color, for example, the two contrasting traits were white versus violet. To fully examine each characteristic, Mendel generated large numbers of F1 and F2 plants and reported results from thousands of F2 plants.

What results did Mendel find in his crosses for flower color? First, Mendel confirmed that he was using plants that bred true for white or violet flower color. Irrespective of the number of generations that Mendel examined, all self-crossed offspring of parents with white flowers had white flowers, and all self-crossed offspring of parents with violet flowers had violet flowers. In addition, Mendel confirmed that, other than flower color, the pea plants were physically identical. This was an important check to make sure that the two varieties of pea plants only differed with respect to one trait, flower color.

90

Once these validations were complete, Mendel applied the pollen from a plant with violet flowers to the stigma of a plant with white flowers. After gathering and sowing the seeds that resulted from this cross, Mendel found that 100 percent of the F1 hybrid generation had violet flowers. Conventional wisdom at that time would have predicted the hybrid flowers to be pale violet or for hybrid plants to have equal numbers of white and violet flowers. In other words, the contrasting parental traits were expected to blend in the offspring. Instead, Mendel’s results demonstrated that the white flower trait had completely disappeared in the F1 generation.

Importantly, Mendel did not stop his experimentation there. He allowed the F1 plants to self-fertilize and found that 705 plants in the F2 generation had violet flowers and 224 had white flowers. This was a ratio of 3.15 violet flowers to one white flower, or approximately 3:1. When Mendel transferred pollen from a plant with violet flowers to the stigma of a plant with white flowers and vice versa, he obtained approximately the same ratio irrespective of which parent—male or female—contributed which trait. This is called a **reciprocal cross**—a paired cross in which the respective traits of the male and female in one cross become the respective traits of the female and male in the other cross. For the other six characteristics that Mendel examined, the F1 and F2 generations behaved in the same way that they behaved for flower color. One of the two traits would disappear completely from the F1 generation, only to reappear in the F2 generation at a ratio of roughly 3:1 (Figure 3.31).



**Figure 3.31** Mendel identified seven pea plant characteristics.

Upon compiling his results for many thousands of plants, Mendel concluded that the characteristics could be divided into expressed and latent traits. He called these dominant and recessive traits, respectively. **Dominant** traits are those that are inherited unchanged in a hybridization. **Recessive** traits become latent, or disappear in the offspring of a hybridization. The recessive trait does, however, reappear in the progeny of the hybrid offspring. An example of a dominant trait is the violet-colored flower trait. For this same characteristic (flower color), white-colored flowers are a recessive trait. The fact that the recessive trait reappeared in the F2 generation meant that the traits remained separate (and were not blended) in the plants of the F1 generation. Mendel proposed that this was because the plants possessed two copies of the trait for the flower-color characteristic, and that each parent transmitted one of their two copies to their offspring, where they came together. Moreover, the physical observation of a dominant trait could mean that the genetic composition of the organism included two dominant versions of the characteristic, or that it included one dominant and one recessive version. Conversely, the observation of a recessive trait meant that the organism lacked any dominant versions of this characteristic.

91





For an excellent review of Mendel’s experiments and to perform your own crosses and identify patterns of inheritance, visit the [**Mendel’s Peas (http://openstaxcollege.org/l/mendels\_peas)**](http://openstaxcollege.org/l/mendels_peas)web lab.

## Laws of Inheritance

The seven characteristics that Mendel evaluated in his pea plants were each expressed as one of two versions, or traits. Mendel deduced from his results that each individual had two discrete copies of the characteristic that are passed individually to offspring. We now call those two copies genes, which are carried on chromosomes. The reason we have two copies of each gene is that we inherit one from each parent. In fact, it is the chromosomes we inherit and the two copies of each gene are located on paired chromosomes. Recall that in meiosis these chromosomes are separated out into haploid gametes. This separation, or segregation, of the homologous chromosomes means also that only one of the copies of the gene gets moved into a gamete. The offspring are formed when that gamete unites with one from another parent and the two copies of each gene (and chromosome) are restored.

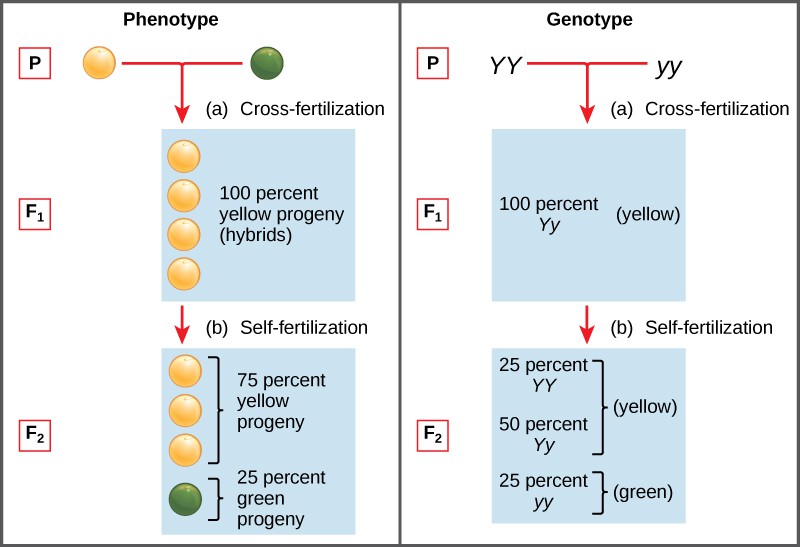
For cases in which a single gene controls a single characteristic, a diploid organism has two genetic copies that may or may not encode the same version of that characteristic. For example, one individual may carry a gene that determines white flower color and a gene that determines violet flower color. Gene variants that arise by mutation and exist at the same relative locations on homologous chromosomes are called **alleles**. Mendel examined the inheritance of genes with just two allele forms, but it is common to encounter more than two alleles for any given gene in a natural population.

#### Phenotypes and Genotypes

Two alleles for a given gene in a diploid organism are expressed and interact to produce physical characteristics. The observable traits expressed by an organism are referred to as its **phenotype**. An organism’s underlying genetic makeup, consisting of both the physically visible and the non-expressed alleles, is called its **genotype**. Mendel’s hybridization experiments demonstrate the difference between phenotype and genotype. For example, the phenotypes that Mendel observed in his crosses between pea plants with differing traits are connected to the diploid genotypes of the plants in the P, F1, and F2 generations. We will use a second trait that Mendel investigated, seed color, as an example. Seed color is governed by a single gene with two alleles. The yellow-seed allele is dominant and the green-seed allele is recessive. When true-breeding plants were cross-fertilized, in which one parent had yellow seeds and one had green seeds, all of the F1 hybrid offspring had yellow seeds. That is, the hybrid offspring were phenotypically identical to the true-breeding parent with yellow seeds. However, we know that the allele donated by the parent with green seeds was not simply lost because it reappeared in some of the F2 offspring (Figure 3.32). Therefore, the F1 plants must have been genotypically different from the parent with yellow seeds.

92

The P plants that Mendel used in his experiments were each homozygous for the trait he was studying. Diploid organisms that are **homozygous** for a gene have two identical alleles, one on each of their homologous chromosomes. The genotype is often written as *YY* or *yy*, for which each letter represents one of the two alleles in the genotype. The dominant allele is capitalized and the recessive allele is lower case. The letter used for the gene (seed color in this case) is usually related to the dominant trait (yellow allele, in this case, or “*Y*”). Mendel’s parental pea plants always bred true because both produced gametes carried the same allele. When P plants with contrasting traits were cross-fertilized, all of the offspring were **heterozygous** for the contrasting trait, meaning their genotype had different alleles for the gene being examined. For example, the F1 yellow plants that received a *Y* allele from their yellow parent and a *y* allele from their green parent had the genotype *Yy*.



**Figure 3.32** Phenotypes are physical expressions of traits that are transmitted by alleles. Capital letters represent dominant alleles and lowercase letters represent recessive alleles. The phenotypic ratios are the ratios of visible characteristics. The genotypic ratios are the ratios of gene combinations in the offspring, and these are not always distinguishable in the phenotypes.

Law of Dominance

Our discussion of homozygous and heterozygous organisms brings us to why the F1 heterozygous offspring were identical to one of the parents, rather than expressing both alleles. In all seven pea- plant characteristics, one of the two contrasting alleles was dominant, and the other was recessive. Mendel called the dominant allele the expressed unit factor; the recessive allele was referred to as the latent unit factor. We now know that these so-called unit factors are actually genes on homologous chromosomes. For a gene that is expressed in a dominant and recessive pattern, homozygous dominant and heterozygous organisms will look identical (that is, they will have different genotypes but the same phenotype), and the recessive allele will only be observed in homozygous recessive individuals ([**Table**](#_bookmark813) 3.3).

##### Correspondence between Genotype and Phenotype for a Dominant- Recessive Characteristic.

|  |  |  |  |
| --- | --- | --- | --- |
| **Homozygous** | | **Heterozygous** | **Homozygous** |
| Genotype | *YY* | *Yy* | *yy* |
| Phenotype | yellow | yellow | green |

Table 3.3

Mendel’s **law of dominance** states that in a heterozygote, one trait will conceal the presence of another trait for the same characteristic. For example, when crossing true-breeding violet-flowered plants with true-breeding white-flowered plants, all of the offspring were violet-flowered, even though they all had one allele for violet and one allele for white. Rather than both alleles contributing to a phenotype,

93

the dominant allele will be expressed exclusively. The recessive allele will remain latent, but will be transmitted to offspring in the same manner as that by which the dominant allele is transmitted. The recessive trait will only be expressed by offspring that have two copies of this allele (Figure 3.33), and these offspring will breed true when self-crossed.



**Figure 3.33** The allele for albinism, expressed here in humans, is recessive. Both of this child’s parents carried the recessive allele.

## Extensions of the Laws of Inheritance

Mendel studied traits with only one mode of inheritance in pea plants. The inheritance of the traits he studied all followed the relatively simple pattern of dominant and recessive alleles for a single characteristic. There are several important modes of inheritance, discovered after Mendel’s work, that do not follow the dominant and recessive, single-gene model.

#### Alternatives to Dominance and Recessiveness

Mendel’s experiments with pea plants suggested that: 1) two types of “units” or alleles exist for every gene; 2) alleles maintain their integrity in each generation (no blending); and 3) in the presence of the dominant allele, the recessive allele is hidden, with no contribution to the phenotype. Therefore, recessive alleles can be “carried” and not expressed by individuals. Such heterozygous individuals are sometimes referred to as “carriers.” Since then, genetic studies in other organisms have shown that much more complexity exists, but that the fundamental principles of Mendelian genetics still hold true. In the sections to follow, we consider some of the extensions of Mendelism.

Incomplete Dominance

Mendel’s results, demonstrating that traits are inherited as dominant and recessive pairs, contradicted the view at that time that offspring exhibited a blend of their parents’ traits. However, the heterozygote

94

phenotype occasionally does appear to be intermediate between the two parents. For example, in the snapdragon, *Antirrhinum majus* (Figure 3,34), a cross between a homozygous parent with white flowers (*CWCW*) and a homozygous parent with red flowers (*CRCR*) will produce offspring with pink flowers (*CRCW*). (Note that different genotypic abbreviations are used for Mendelian extensions to distinguish these patterns from simple dominance and recessiveness.) This pattern of inheritance is described as **incomplete dominance**, meaning that one of the alleles appears in the phenotype in the heterozygote, but not to the exclusion of the other, which can also be seen. The allele for red flowers is incompletely dominant over the allele for white flowers. However, the results of a heterozygote self-cross can still be predicted, just as with Mendelian dominant and recessive crosses. In this case, the genotypic ratio would be 1 *CRCR*:2 *CRCW*:1 *CWCW*, and the phenotypic ratio would be 1:2:1 for red:pink:white. The basis for the intermediate color in the heterozygote is simply that the pigment produced by the red allele (anthocyanin) is diluted in the heterozygote and therefore appears pink because of the white background of the flower petals.

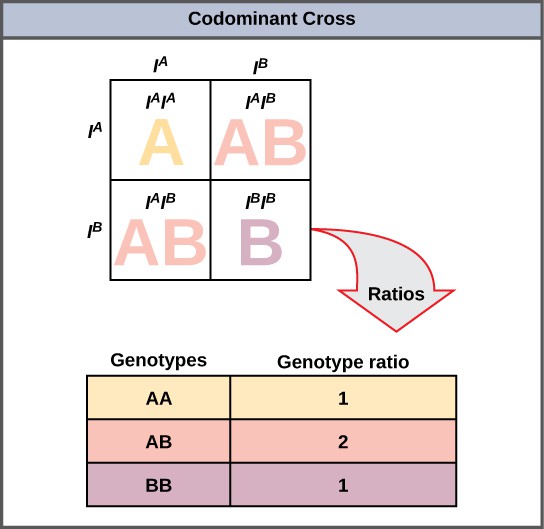


**Figure 3.34**These pink flowers of a heterozygote snapdragon result from incomplete dominance. (credit: "storebukkebruse"/Flickr)

Codominance

A variation on incomplete dominance is **codominance**, in which both alleles for the same characteristic are simultaneously expressed in the heterozygote. An example of codominance occurs in the ABO blood groups of humans. The A and B alleles are expressed in the form of A or B molecules present on the surface of red blood cells. Homozygotes (*IAIA* and *IBIB*) express either the A or the B phenotype, and heterozygotes (*IAIB*) express both phenotypes equally. The *IAIB* individual has blood type AB. In a self- cross between heterozygotes expressing a codominant trait, the three possible offspring genotypes are phenotypically distinct. However, the 1:2:1 genotypic ratio characteristic of a Mendelian monohybrid cross still applies (Figure 3.35).

95



**Figure 3.35** This Punnet square shows an AB/AB blood type cross

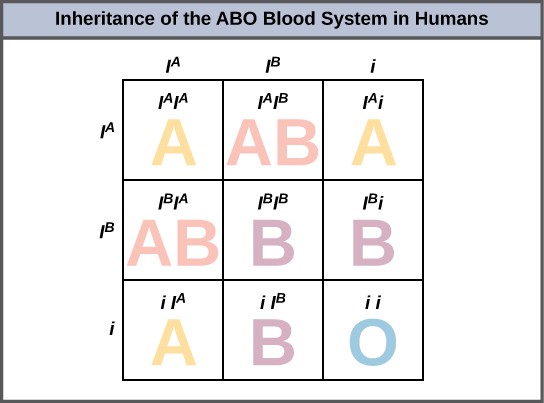
Multiple Alleles

Mendel implied that only two alleles, one dominant and one recessive, could exist for a given gene. We now know that this is an oversimplification. Although individual humans (and all diploid organisms) can only have two alleles for a given gene, multiple alleles may exist at the population level, such that many combinations of two alleles are observed. Note that when many alleles exist for the same gene, the convention is to denote the most common phenotype or genotype in the natural population as the **wild type** (often abbreviated “+”). All other phenotypes or genotypes are considered variants (mutants) of this typical form, meaning they deviate from the wild type. The variant may be recessive or dominant to the wild-type allele.

An example of multiple alleles is the ABO blood-type system in humans. In this case, there are three alleles circulating in the population. The *IA* allele codes for A molecules on the red blood cells, the *IB* allele codes for B molecules on the surface of red blood cells, and the *i* allele codes for no molecules on the red blood cells. In this case, the *IA* and *IB* alleles are codominant with each other and are both dominant over the *i* allele. Although there are three alleles present in a population, each individual only gets two of the alleles from their parents. This produces the genotypes and phenotypes shown in [**Figure**](#_bookmark833)

3.36. Notice that instead of three genotypes, there are six different genotypes when there are three alleles. The number of possible phenotypes depends on the dominance relationships between the three alleles.

96



**Figure 3.36** Inheritance of the ABO blood system in humans is shown.



**Multiple Alleles Confer Drug Resistance in the Malaria Parasite**

Malaria is a parasitic disease in humans that is transmitted by infected female mosquitoes, including *Anopheles gambiae*, and is characterized by cyclic high fevers, chills, flu-like symptoms, and severe anemia. *Plasmodium falciparum* and *P. vivax* are the most common causative agents of malaria, and *P. falciparum* is the most deadly. When promptly and correctly treated, *P. falciparum* malaria has a mortality rate of 0.1 percent. However, in some parts of the world, the parasite has evolved resistance to commonly used malaria treatments, so the most effective malarial treatments can vary by geographic region.

In Southeast Asia, Africa, and South America, *P. falciparum* has developed resistance to the anti-malarial drugs chloroquine, mefloquine, and sulfadoxine-pyrimethamine. *P. falciparum*, which is haploid during the life stage in which it is infective to humans, has evolved multiple drug-resistant mutant alleles of the *dhps* gene. Varying degrees of sulfadoxine resistance are associated with each of these alleles. Being haploid, *P. falciparum* needs only one drug-resistant allele to express this trait.

In Southeast Asia, different sulfadoxine-resistant alleles of the *dhps* gene are localized to different geographic regions. This is a common evolutionary phenomenon that comes about because drug-resistant mutants arise in a population and interbreed with other *P. falciparum* isolates in close proximity. Sulfadoxine-resistant parasites cause considerable human hardship in regions in which this drug is widely used as an over-the-counter malaria remedy. As is common with pathogens that multiply to large numbers within an infection cycle, *P. falciparum* evolves relatively rapidly (over a decade or so) in response to the selective pressure of commonly used anti-malarial drugs. For this reason, scientists must constantly work to develop new drugs or drug combinations to combat the worldwide

[2]

malaria burden.

Sex-Linked Traits

In humans, as well as in many other animals and some plants, the sex of the individual is determined by sex chromosomes—one pair of non-homologous chromosomes. Until now, we have only considered inheritance patterns among non-sex chromosomes, or autosomes. In addition to 22 homologous pairs of autosomes, human females have a homologous pair of X chromosomes, whereas human males have

1. Sumiti Vinayak et al., “Origin and Evolution of Sulfadoxine Resistant *Plasmodium falciparum,” PLoS Pathogens* 6 (2010): e1000830.

97

an XY chromosome pair. Although the Y chromosome contains a small region of similarity to the X chromosome so that they can pair during meiosis, the Y chromosome is much shorter and contains fewer genes. When a gene being examined is present on the X, but not the Y, chromosome, it is **X-linked**.

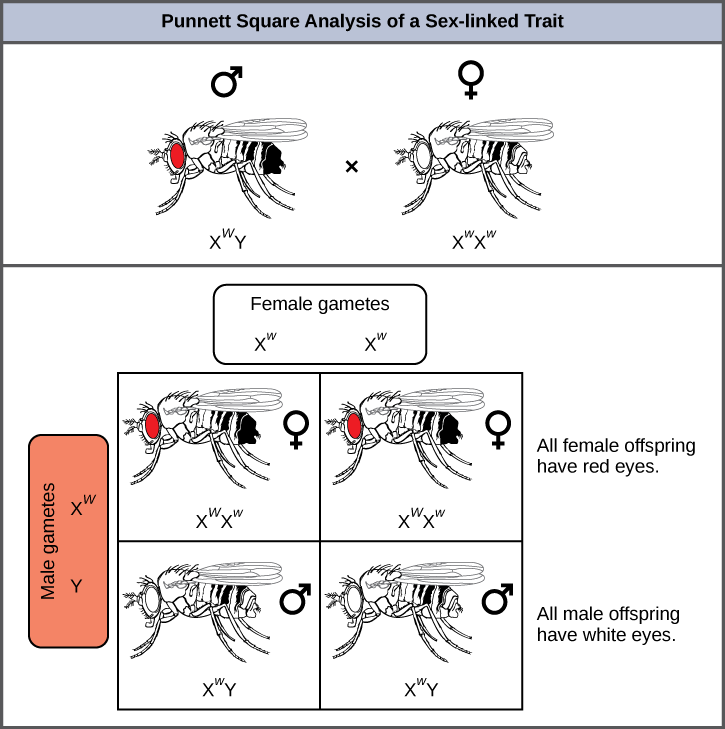
Eye color in *Drosophila*, the common fruit fly, was the first X-linked trait to be identified. Thomas Hunt Morgan mapped this trait to the X chromosome in 1910. Like humans, *Drosophila* males have an XY chromosome pair, and females are XX. In flies the wild-type eye color is red (X*W*) and is dominant to white eye color (X*w*) (Figure 3.37). Because of the location of the eye-color gene, reciprocal crosses do not produce the same offspring ratios. Males are said to be **hemizygous**, in that they have only one allele for any X-linked characteristic. Hemizygosity makes descriptions of dominance and recessiveness irrelevant for XY males. *Drosophila* males lack the white gene on the Y chromosome; that is, their genotype can only be XWY or X*w*Y. In contrast, females have two allele copies of this gene and can be X*W*X*W*, X*W*X*w*, or X*w*X*w*.



**Figure 3.37** In *Drosophila*, the gene for eye color is located on the X chromosome. Red eye color is wild-type and is dominant to white eye color.

In an X-linked cross, the genotypes of F1 and F2 offspring depend on whether the recessive trait was expressed by the male or the female in the P generation. With respect to *Drosophila* eye color, when the P male expresses the white-eye phenotype and the female is homozygously red-eyed, all members of the F1 generation exhibit red eyes (Figure 3.38). The F1 females are heterozygous (X*W*X*w*), and the males are all X*W*Y, having received their X chromosome from the homozygous dominant P female and their Y chromosome from the P male. A subsequent cross between the X*W*X*w* female and the X*W*Y male would produce only red-eyed females (with X*W*X*W* or X*W*X*w* genotypes) and both red- and white-eyed males (with X*W*Y or XwY genotypes). Now, consider a cross between a homozygous white-eyed female and a male with red eyes. The F1 generation would exhibit only heterozygous red-eyed females (XWXw) and only white-eyed males (XwY). Half of the F2 females would be red-eyed (XWXw) and half would be white-eyed (XwXw). Similarly, half of the F2 males would be red-eyed (XWY) and half would be white- eyed (XwY).

98



**Figure 3.38** Crosses involving sex-linked traits often give rise to different phenotypes for the different sexes of offspring, as is the case for this cross involving red and white eye color in *Drosophila*. In the diagram, *w* is the white-eye mutant allele and *W* is the wild-type, red-eye allele.

**Figure 8.16** Crosses involving sex-linked traits often give rise to different phenotypes for the different sexes of offspring, as is the case for this cross involving red and white eye color in *Drosophila*. In the diagram, *w* is the white-eye mutant allele and *W* is the wild-type, red-eye allele.

What ratio of offspring would result from a cross between a white-eyed male and a female that is heterozygous for red eye color?

Discoveries in fruit fly genetics can be applied to human genetics. When a female parent is homozygous for a recessive X-linked trait, she will pass the trait on to 100 percent of her male offspring, because the males will receive the Y chromosome from the male parent. In humans, the alleles for certain conditions (some color-blindness, hemophilia, and muscular dystrophy) are X-linked. Females who are heterozygous for these diseases are said to be carriers and may not exhibit any phenotypic effects. These females will pass the disease to half of their sons and will pass carrier status to half of their daughters; therefore, X-linked traits appear more frequently in males than females.

In some groups of organisms with sex chromosomes, the sex with the non-homologous sex chromosomes is the female rather than the male. This is the case for all birds. In this case, sex-linked traits will be more likely to appear in the female, in whom they are hemizygous.

99





Watch [**this video (http://openstaxcollege.org/l/sex-linked\_trts)**](http://openstaxcollege.org/l/sex-linked_trts)to learn more about sex-linked traits.

Summary

**The Genome**

Prokaryotes have a single loop chromosome, whereas eukaryotes have multiple, linear chromosomes surrounded by a nuclear membrane. Human somatic cells have 46 chromosomes consisting of two sets of 22 homologous chromosomes and a pair of nonhomologous sex chromosomes. This is the 2n, or diploid, state. Human gametes have 23 chromosomes or one complete set of chromosomes. This is the n, or haploid, state. Genes are segments of DNA that code for a specific protein or RNA molecule. An organism’s traits are determined in large part by the genes inherited from each parent, but also by the environment that they experience. Genes are expressed as characteristics of the organism and each characteristic may have different variants called traits that are caused by differences in the DNA sequence for a gene.

**Errors in Meiosis**

The number, size, shape, and banding pattern of chromosomes make them easily identifiable in a karyogram and allow for the assessment of many chromosomal abnormalities. Disorders in chromosome number, or aneuploidies, are typically lethal to the embryo, although a few trisomic genotypes are viable. Because of X inactivation, aberrations in sex chromosomes typically have milder effects on an individual. Aneuploidies also include instances in which segments of a chromosome are duplicated or deleted. Chromosome structures also may be rearranged, for example by inversion or translocation. Both of these aberrations can result in negative effects on development, or death. Because they force chromosomes to assume contorted pairings during meiosis I, inversions and translocations are often associated with reduced fertility because of the likelihood of nondisjunction.

**Mendel’s Experiments**

Working with garden pea plants, Mendel found that crosses between parents that differed for one trait produced F1 offspring that all expressed one parent’s traits. The traits that were visible in the F1 generation are referred to as dominant, and traits that disappear in the F1 generation are described as recessive. When the F1 plants in Mendel’s experiment were self-crossed, the F2 offspring exhibited the dominant trait or the recessive trait in a 3:1 ratio, confirming that the recessive trait had been transmitted faithfully from the original P parent. Reciprocal crosses generated identical F1 and F2 offspring ratios. By examining sample sizes, Mendel showed that traits were inherited as independent events.

When true-breeding, or homozygous, individuals that differ for a certain trait are crossed, all of the offspring will be heterozygous for that trait. If the traits are inherited as dominant and recessive, the F1 offspring will all exhibit the same phenotype as the parent homozygous for the dominant trait. If these heterozygous offspring are self-crossed, the resulting F2 offspring will be equally likely to inherit gametes carrying the dominant or recessive trait, giving rise to offspring of which one quarter are homozygous dominant, half are heterozygous, and one quarter are homozygous recessive.

Because homozygous dominant and heterozygous individuals are phenotypically identical, the observed traits in the F2 offspring will exhibit a ratio of three dominant to one recessive

Mendel postulated that genes (characteristics) are inherited as pairs of alleles (traits) that behave in a dominant and recessive pattern. Alleles segregate into gametes such that each gamete is equally likely to receive either one of the two alleles present in a diploid individual. In addition, genes are assorted into gametes independently of one another. That is, in general, alleles are not more likely to segregate into a gamete with a particular allele of another gene.

**Extensions of the Laws of Inheritance**

Alleles do not always behave in dominant and recessive patterns. Incomplete dominance describes situations in which the heterozygote exhibits a phenotype that is intermediate between the homozygous phenotypes. Codominance describes the simultaneous expression of both of the alleles in the heterozygote. Although diploid organisms can only have two alleles for any given gene, it is common for more than two alleles for a gene to exist in a population. In humans, as in many animals and some plants, females have two X chromosomes and males have one X and one Y chromosome. Genes that are present on the X but not the Y chromosome are said to be X-linked, such that males only inherit one allele for the gene, and females inherit two.

**The Structure of DNA**

The model of the double-helix structure of DNA was proposed by Watson and Crick. The DNA molecule is a polymer of nucleotides. Each nucleotide is composed of a nitrogenous base, a five-carbon sugar (deoxyribose), and a phosphate group. There are four nitrogenous bases in DNA, two purines (adenine and guanine) and two pyrimidines (cytosine and thymine). A DNA molecule is composed of two strands. Each strand is composed of nucleotides bonded together covalently between the phosphate group of one and the deoxyribose sugar of the next. From this backbone extend the bases. The bases of one strand bond to the bases of the second strand with hydrogen bonds. Adenine always bonds with thymine, and cytosine always bonds with guanine. The bonding causes the two strands to spiral around each other in a shape called a double helix. Ribonucleic acid (RNA) is a second nucleic acid found in cells. RNA is a single-stranded polymer of nucleotides. It also differs from DNA in that it contains the sugar ribose, rather than deoxyribose, and the nucleotide uracil rather than thymine. Various RNA molecules function in the process of forming proteins from the genetic code in DNA.

Prokaryotes contain a single, double-stranded circular chromosome. Eukaryotes contain double- stranded linear DNA molecules packaged into chromosomes. The DNA helix is wrapped around proteins to form nucleosomes. The protein coils are further coiled, and during mitosis and meiosis, the chromosomes become even more greatly coiled to facilitate their movement. Chromosomes have two distinct regions which can be distinguished by staining, reflecting different degrees of packaging and determined by whether the DNA in a region is being expressed (euchromatin) or not (heterochromatin).

**Transcription**

In prokaryotes, mRNA synthesis is initiated at a promoter sequence on the DNA template. Elongation synthesizes new mRNA. Termination liberates the mRNA and occurs by mechanisms that stall the RNA polymerase and cause it to fall off the DNA template. Newly transcribed eukaryotic mRNAs are modified with a cap and a poly-A tail. These structures protect the mature mRNA from degradation and help export it from the nucleus. Eukaryotic mRNAs also undergo splicing, in which introns are removed and exons are reconnected with single-nucleotide accuracy. Only finished mRNAs are exported from the nucleus to the cytoplasm.

**Translation**

The central dogma describes the flow of genetic information in the cell from genes to mRNA to proteins. Genes are used to make mRNA by the process of transcription; mRNA is used to synthesize proteins by the process of translation. The genetic code is the correspondence between the three- nucleotide mRNA codon and an amino acid. The genetic code is “translated” by the tRNA molecules, which associate a specific codon with a specific amino acid. The genetic code is degenerate because 64 triplet codons in mRNA specify only 20 amino acids and three stop codons. This means that more than one codon corresponds to an amino acid. Almost every species on the planet uses the same genetic code.

**Review Questions**

1. Which of the following does cytosine pair with?

a. guanine

b. thymine

c. adenine

d. a pyrimidine

2. Prokaryotes contain a \_\_\_\_\_\_\_\_\_\_\_\_chromosome, and eukaryotes contain \_\_\_\_\_\_\_\_\_\_\_\_chromosomes.

a. single-stranded circular; single-stranded linear

b. single-stranded linear; single-stranded circular

c. double-stranded circular; double- stranded linear

d. double-stranded linear; double-stranded circular

3. How long would the peptide be that is translated from this MRNA sequence: 5'- AUGGGCUACCGA-3'?

a. 0

b. 2

c. 3

d. 4

4. The observable traits expressed by an organism are described as its .

a. phenotype

b. genotype

c. alleles

d. zygote

5. If black and white true-breeding mice are mated and the result is all gray offspring, what inheritance pattern would this be indicative of?

a. dominance

b. codominance

c. multiple alleles

d. incomplete dominance

102

6. If a muscle cell of a typical organism has 32 chromosomes, how many chromosomes will be in a gamete of that same organism?

a. 8

b. 16

c. 32

d. 64

7. The genotype XXY corresponds to:

a. Klinefelter syndrome

b. Turner syndrome

c. Triplo-X

d. Jacob syndrome

OpenStax College, *Concepts of Biology*. OpenStax College. 25 April 2013. <<http://openstaxcollege.org/textbooks/concepts-of-biology/get>>.

103