14.2 Human Genetic Disorders

Key Questions

How do small changes in DNA molecules affect human traits?

What are the effects of errors in meiosis?

Vocabulary

nondisjunction

Taking Notes

Two-Column Chart Before you read, make a two-column chart. In the first column, write three questions you have about genetic disorders. As you read, fill in answers to your questions in the second column. When you have finished, research the answers to your remaining questions.

THINK ABOUT IT Have you ever heard the expression "It runs in the family"? Relatives or friends might have said that about your smile or the shape of your ears, but what could it mean when they talk of diseases and disorders? What, exactly, is a genetic disorder?

From Molecule to Phenotype

How do small changes in DNA molecules affect human traits?

We know that genes are made of DNA and that they interact with the environment to produce an individual organism's characteristics, or phenotype. However, when a gene fails to work or works improperly, serious problems can result.

Molecular research techniques have shown us a direct link between genotype and phenotype. For example, the wax that sometimes builds up in our ear canals can be one of two forms: wet or dry. People of African and European ancestry are more likely to have wet earwax—the dominant form. Those of Asian or Native American ancestry most often have the dry form, which is recessive. A single DNA base in the gene for a membrane-transport protein is the culprit. A simple base change from guanine (G) to adenine (A) causes this protein to produce dry earwax instead of wet earwax.

The connection between molecule and trait, and between genotype and phenotype, is often that simple, and just as direct. **Changes in a gene's DNA sequence can change proteins by altering their amino acid sequences, which may directly affect one's phenotype.** In other words, there is a molecular basis for genetic disorders.

Disorders Caused by Individual Genes

Thousands of genetic disorders are caused by changes in individual genes. These changes often affect specific proteins associated with important cellular functions.

▶ ***Sickle Cell Disease*** This disorder is caused by a defective allele for beta-globin, one of two polypeptides in hemoglobin, the oxygen-carrying protein in red blood cells. The defective polypeptide makes hemoglobin a bit less soluble, causing hemoglobin molecules to stick together when the blood's oxygen level decreases. The molecules clump into long fibers, forcing cells into a distinctive sickle shape, which gives the disorder its name.

Sickle-shaped cells are more rigid than normal red blood cells, and, therefore, they tend to get stuck in the capillaries—the narrowest blood vessels in the body. If the blood stops moving through the capillaries, damage to cells, tissues, and even organs can result.

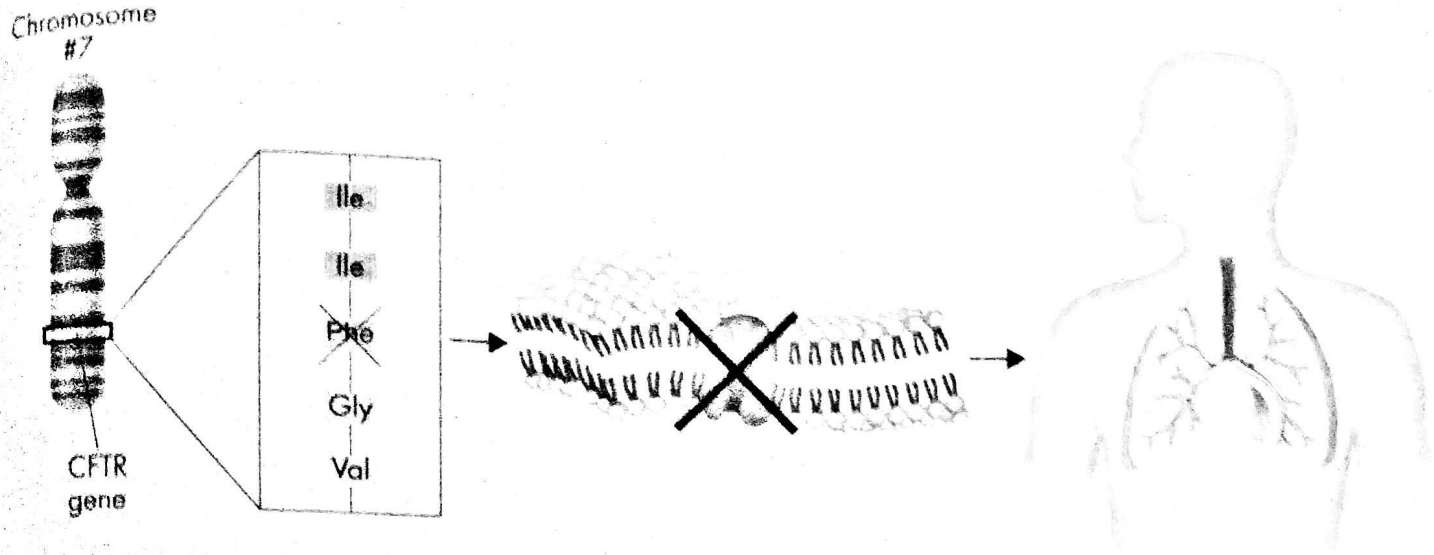


FIGURE 14–8 Mutations Cause Cystic Fibrosis CF is usually caused by the deletion of three bases in the DNA of a single gene. As a result, the body does not produce normal CFTR, a protein needed to transport chloride ions. Infer *Why isn't the cause of CF considered a frameshift mutation?*

▶ ***Cystic Fibrosis*** Known as CF for short, cystic fibrosis is most common among people of European ancestry. CF is caused by a genetic change almost as small as the earwax allele. Most cases result from the deletion of just three bases in the gene for a protein called cystic fibrosis transmembrane conductance regulator (CFTR). CFTR normally allows chloride ions (Cl^-) to pass across cell membranes. The loss of these bases removes a single amino acid—phenylalanine—from CFTR, causing the protein to fold improperly. The misfolded protein is then destroyed. With cell membranes unable to transport chloride ions, tissues throughout the body malfunction.

People with one normal copy of the CF allele are unaffected by CF, because they can produce enough CFTR to allow their cells to work properly. Two copies of the defective allele are needed to produce the disorder, which means the CF allele is recessive. Children with CF have serious digestive problems and produce thick, heavy mucus that clogs their lungs and breathing passageways.

▶ ***Huntington's Disease*** Huntington's disease is caused by a dominant allele for a protein found in brain cells. The allele for this disease contains a long string of bases in which the codon CAG—coding for the amino acid glutamine—repeats over and over again, more than 40 times. Despite intensive study, the reason why these long strings of glutamine cause disease is still not clear. The symptoms of Huntington's disease, namely mental deterioration and uncontrollable movements, usually do not appear until middle age. The greater the number of codon repeats, the earlier the disease appears, and the more severe are its symptoms.

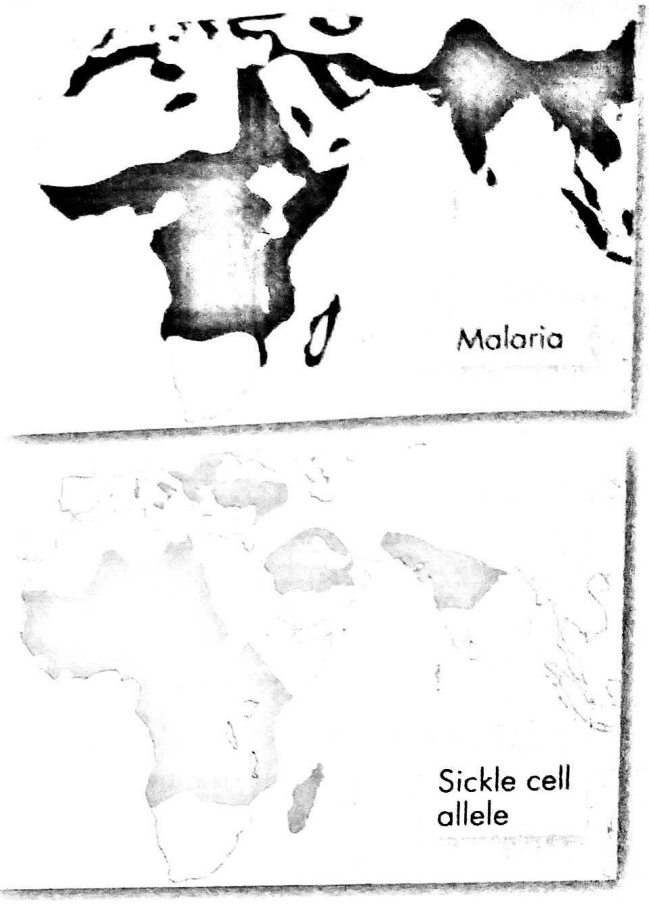
MYSTERY CLUE

Individuals with sickle cell disease have a different amino acid in one of their hemoglobin proteins than people without the disease. What could produce this change?

Analyzing Data

The Geography of Malaria

Malaria is a potentially fatal disease transmitted by mosquitoes. Its cause is a parasite that lives inside red blood cells. The upper map shows the parts of the world where malaria is common. The lower map shows regions where people have the sickle cell allele.



1. Analyze Data What is the relationship between the places where malaria and the sickle cell allele are found?

2. Infer In 1805, a Scottish explorer named Mungo Park led an expedition of European geographers to find the source of the Niger River in Africa. The journey began with a party of 45 Europeans. During the expedition, most of these men perished from malaria. Why do you think their native African guides survived?

3. Form a Hypothesis As the map shows, the sickle cell allele is not found in African populations that are native to southern Africa. Propose an explanation for this discrepancy.

BUILD Vocabulary

WORD ORIGINS The term *malaria* was coined in the mid-eighteenth century from the Italian phrase, *mala aria*, meaning "bad air." It originally referred to the unpleasant odors caused by the release of marsh gases, to which the disease was initially attributed.

Genetic Advantages Disorders such as sickle cell disease and CF are still common in human populations. In the United States, the sickle cell allele is carried by approximately 1 person in 12 of African ancestry, and the CF allele is carried by roughly 1 person in 25 of European ancestry. Why are these alleles still around if they can be fatal for those who carry them? The answers may surprise you.

Most African Americans today are descended from populations that originally lived in west central Africa, where malaria is common. Malaria is a mosquito-borne infection caused by a parasite that lives inside red blood cells. Individuals with just one copy of the sickle cell allele are generally healthy and are also highly resistant to the parasite. This resistance gives them a great advantage against malaria, which even today claims more than a million lives every year.

More than 1000 years ago, the cities of medieval Europe were ravaged by epidemics of typhoid fever. Typhoid is caused by a bacterium that enters the body through cells in the digestive system. The protein produced by the CF allele helps block the entry of this bacterium. Individuals heterozygous for CF would have had an advantage when living in cities with poor sanitation and polluted water, and—because they also carried a normal allele—these individuals would not have suffered from cystic fibrosis.

Chromosomal Disorders

What are the effects of errors in meiosis?

Most of the time, the process of meiosis works perfectly and each human gamete gets exactly 23 chromosomes. Every now and then, however, something goes wrong. The most common error in meiosis occurs when homologous chromosomes fail to separate. This mistake is known as **nondisjunction,** which means "not coming apart." Figure 14–9 illustrates the process.

If nondisjunction occurs during meiosis, gametes with an abnormal number of chromosomes may result, leading to a disorder of chromosome numbers. For example, if two copies of an autosomal chromosome fail to separate during meiosis, an individual may be born with three copies of that chromosome. This condition is known as a trisomy, meaning "three bodies." The most common form of trisomy, involving three copies of chromosome 21, is Down syndrome, which is associated with a range of cognitive disabilities and a high frequency of certain birth defects.

Nondisjunction of the X chromosomes can lead to a disorder known as Turner's syndrome. A female with Turner's syndrome usually inherits only one X chromosome. Women with Turner's syndrome are sterile, which means that they are unable to reproduce. Their sex organs do not develop properly at puberty.

In males, nondisjunction may cause Klinefelter's syndrome, resulting from the inheritance of an extra X chromosome, which interferes with meiosis and usually prevents these individuals from reproducing. There have been no reported instances of babies being born without an X chromosome, indicating that this chromosome contains genes that are vital for the survival and development of the embryo.

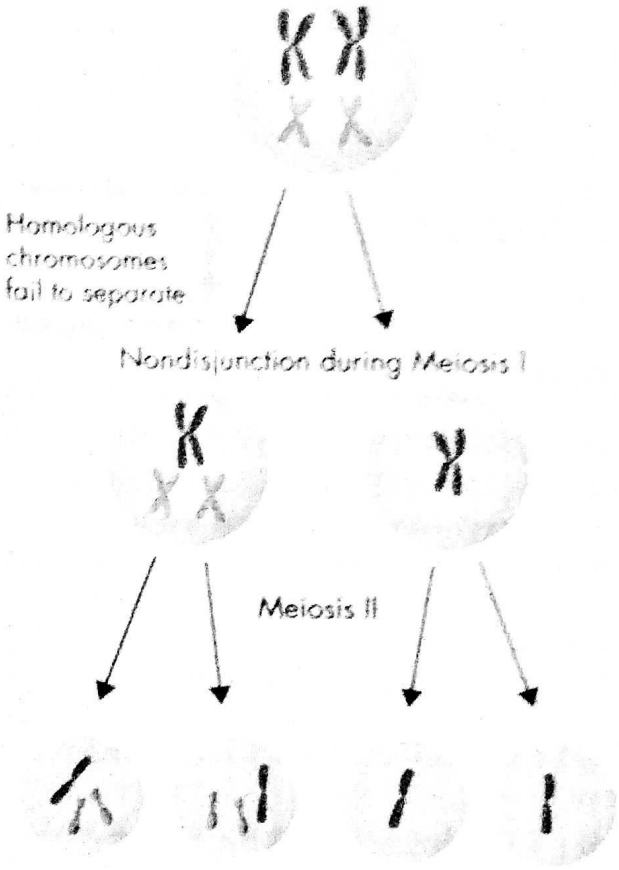


FIGURE 14–9 Nondisjunction This failure of meiosis causes gametes to have an abnormal number of chromosomes. **Apply Concepts** *Which phase of meiosis is shown in the first cell?*

14.2 Assessment

Review Key Concepts

1. a. Review How can a small change in a person's DNA cause a genetic disorder?

b. Infer How do genetic disorders such as CF support the theory of evolution?

2. a. Review Describe two sex chromosome disorders.

b. Apply Concepts How does nondisjunction cause chromosomal disorders?

WRITE ABOUT SCIENCE

Description

3. Write a paragraph explaining the process of nondisjunction. (*Hint:* To organize your writing, create a flowchart that shows the steps in the process.)