

Lesson Overview

15.2 Human Genetic Disorders

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 is a genetic disorder?

From Molecule to Phenotype

 How do small changes in DNA molecules affect human traits?

From Molecule to Phenotype



How do small changes in DNA molecules affect human traits?



Changes in a gene's DNA sequence can change proteins by altering their amino acid sequences, which may directly affect one's phenotype.

From Molecule to Phenotype

Molecular research techniques have shown a direct link between genotype and phenotype.

For example, people of African and European ancestry are more likely to have wet earwax—the dominant form.

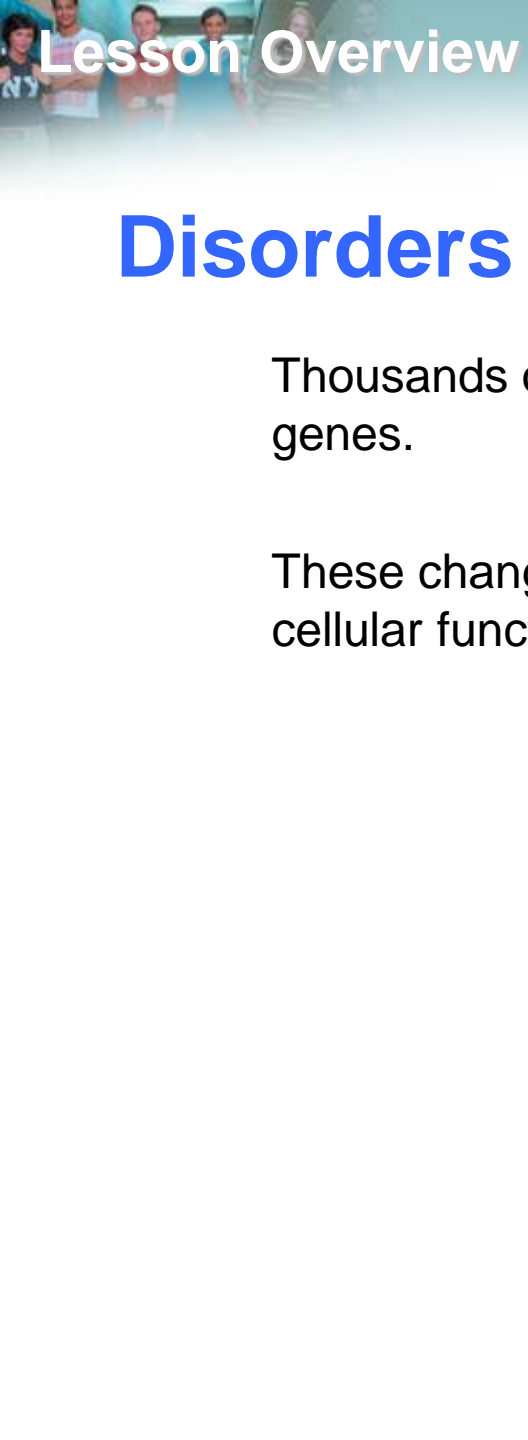
Those of Asian or Native American ancestry most often have the dry form, which is recessive.

A single DNA base change from guanine (G) to adenine (A) in the gene for a membrane-transport protein causes this protein to produce dry earwax instead of wet earwax.

From Molecule to Phenotype

There is a direct connection between molecule and trait, and between genotype and phenotype. In other words, there is a molecular basis for genetic disorders.

Changes in a gene's DNA sequence can change proteins by altering their amino acid sequences, which may directly affect one's phenotype.



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 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 Cell Disease

Sickle-shaped cells are more rigid than normal red blood cells, and they tend to get stuck in the capillaries.

If the blood stops moving through the capillaries, damage to cells, tissues, and even organs can result.

Cystic Fibrosis

Cystic fibrosis (CF) is most common among people of European ancestry.

Most cases result from the deletion of just three bases in the gene for a protein called cystic fibrosis transmembrane conductance regulator (CFTR). As a result, the amino acid phenylalanine is missing from the protein.

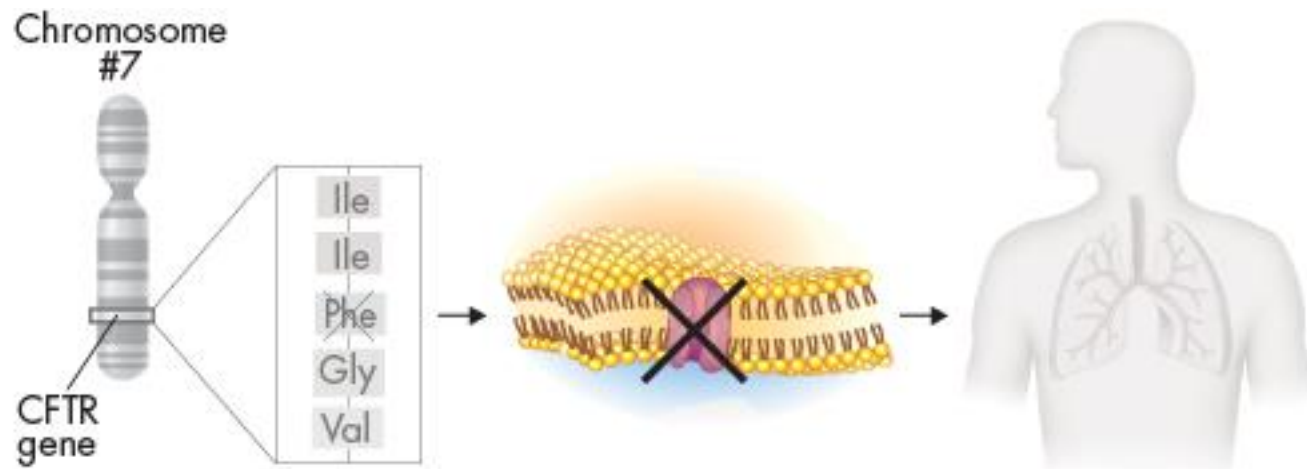


Cystic Fibrosis

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.



Cystic Fibrosis

With cell membranes unable to transport chloride ions, tissues throughout the body malfunction. Children with CF have serious digestive problems and produce thick, heavy mucus that clogs their lungs and breathing passageways.



Cystic Fibrosis

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.

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.

Genetic Advantages

Disorders such as sickle cell disease and CF are still common in human populations.

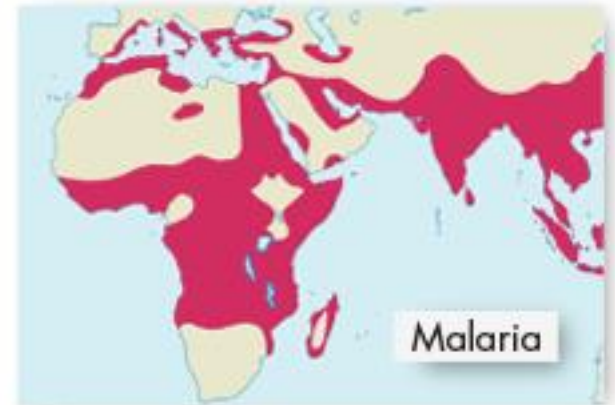
In the United States, the sickle cell allele is carried by approximately 1 person in 12 of African ancestry, and the CF allele is carried by roughly 1 person in 25 of European ancestry.

Why are these alleles still around if they can be fatal for those who carry them?

Genetic Advantages

Most African Americans today are descended from populations that originally lived in west central Africa, where malaria is common.

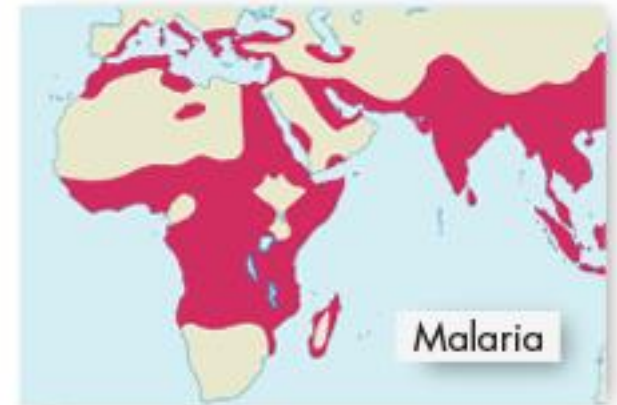
Malaria is a mosquito-borne infection caused by a parasite that lives inside red blood cells.



Genetic Advantages

Individuals with just one copy of the sickle cell allele are generally healthy, and are also highly resistant to the parasite, giving them a great advantage against malaria.

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.



Genetic Advantages

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?

Chromosomal Disorders



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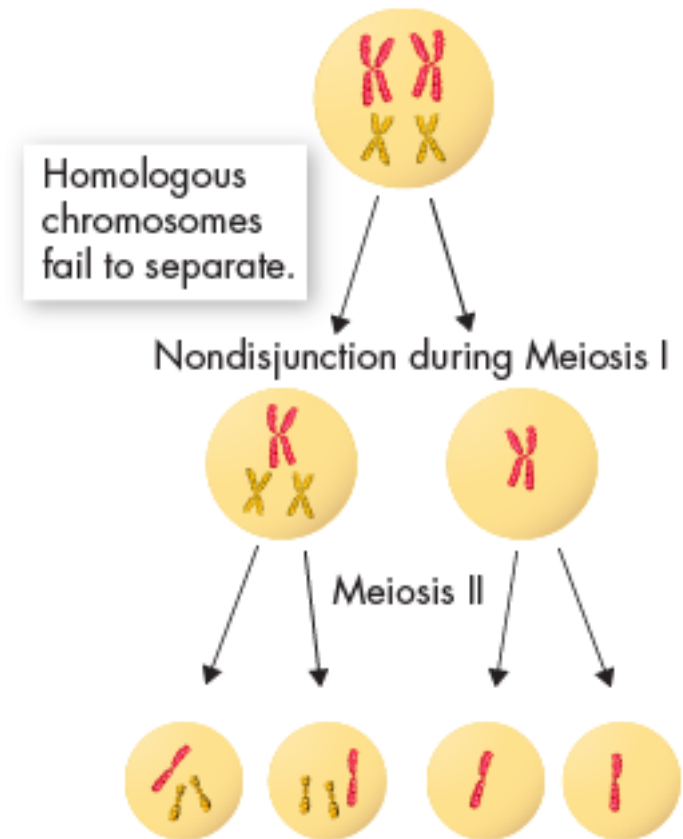


If nondisjunction occurs during meiosis, gametes with an abnormal number of chromosomes may result, leading to a disorder of chromosome numbers.

Chromosomal Disorders

The most common error in meiosis occurs when homologous chromosomes fail to separate. This mistake is known as **nondisjunction**, which means “not coming apart.”

Nondisjunction may result in gametes with an abnormal number of chromosomes, which can lead to a disorder of chromosome numbers.



Chromosomal Disorders

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 often characterized by mild to severe mental retardation and a high frequency of certain birth defects.

Chromosomal Disorders

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.

Chromosomal Disorders

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.