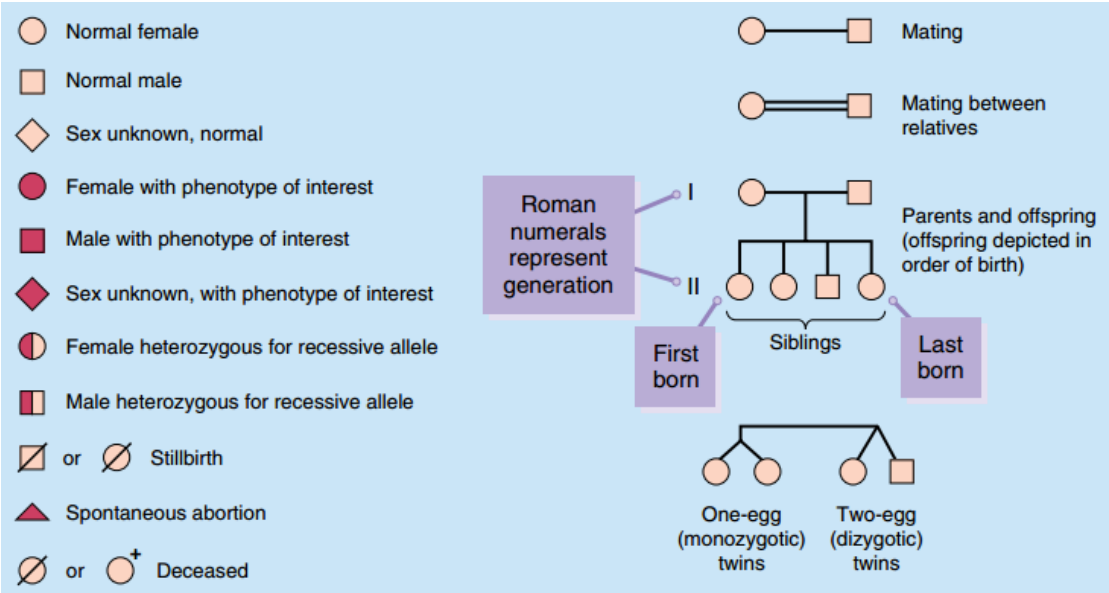
Genes in Individuals

Most human characteristics and common diseases are **polygenic**, whereas many of the disordered phenotypes thought of as "genetic" are **monogenic** but still influenced by other loci in a person's genome. Phenotypes due to alterations at a single gene are frequently referred to as **Mendelian**, Mendel showed that some traits were **dominant** relative to other traits; he called the latter traits **recessive**.

Dominant traits require only one copy of a "factor" to be expressed, regardless of what the other copy is, whereas recessive traits require two copies before expression occurs. We now recognize that the Mendelian factors are genes, and the alternative copies of the gene are alleles.

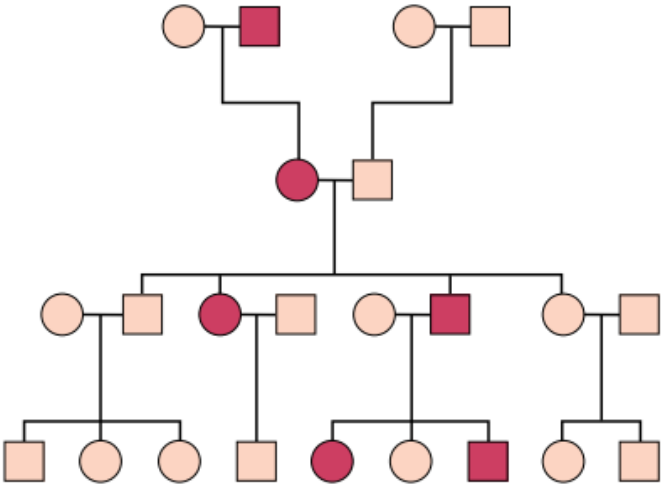
Inheritance Patterns

As described earlier, phenotypes due to alterations at a single gene are characterized as Mendelian, and monogenic human diseases are frequently referred to as Mendelian disorders. The mode of inheritance for a given phenotypic trait or disease is determined by **pedigree analysis**. All affected and unaffected individuals in the family are recorded in a pedigree using standard symbols. The principles of allelic segregation, and the transmission of alleles from parents to children, are illustrated in **Figure**.



Autosomal Dominant Inheritance

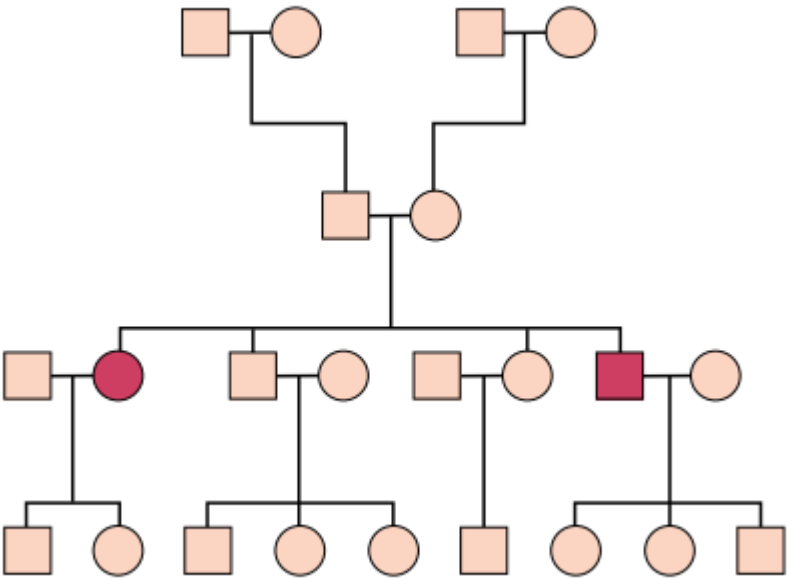
Autosomal dominant disorders are relevant because mutations in a single allele to cause the disease **(Figure).** In contrast to recessive disorders, in which disease pathogenesis is relatively straightforward because there is loss of gene function, dominant disorders can be caused by various disease mechanisms, many of which are unique to the function of the genetic pathway involved.



A pedigree illustrating autosomal dominant inheritance. Square symbols indicate males and circles indicate females; open symbols indicate that the person is phenotypically unaffected, and filed symbols indicate that the phenotype is present to some extent**.**

Autosomal Recessive Inheritance

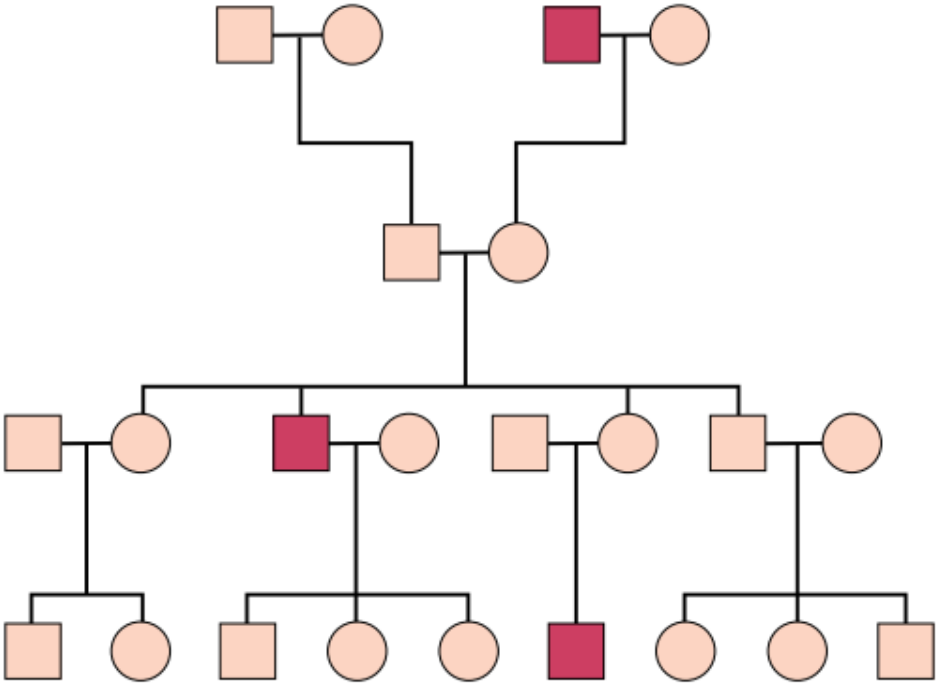
In the case of recessive disorders, mutated alleles result in a complete or partial loss of function. An example of a pedigree of autosomal recessive inheritance is shown in **(Figure)**. Recessive disorders frequently involve enzymes in metabolic pathways, receptors, or proteins in signaling cascades. The affected individual can be of either sex and either a homozygote or compound heterozygote for a single-gene defect.



A pedigree illustrating autosomal recessive inheritance.

X-Linked Inheritance

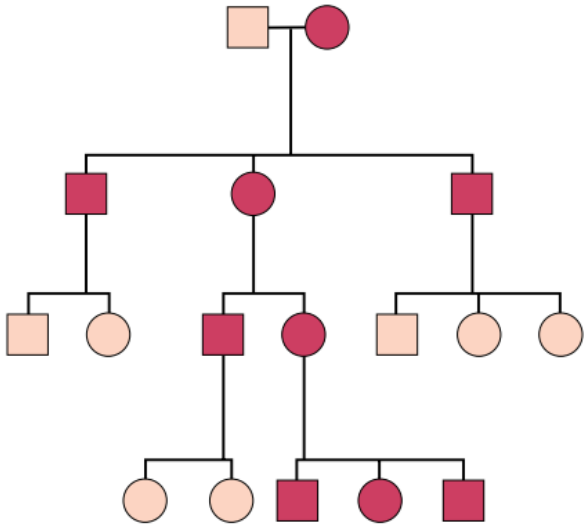
Because males have only one X chromosome, a daughter will always inherit her father's X chromosome in addition to one of her mother's two X chromosomes. Conversely, a son inherits the Y chromosome from his father and one maternal X chromosome, so the risk of developing disease due to a mutant X-chromosomal gene differs in the two sexes. Because of the presence of one X chromosome, males are said to be homozygous for the mutant allele on that chromosome. Therefore, they are more likely to develop the mutant phenotype, regardless of whether the mutation is dominant or recessive. A female with two X chromosomes may be either heterozygous or homozygous for the mutant allele, which may be dominant or recessive. Therefore, the terms "X-linked dominant" and "X-linked recessive" are applicable to expression of the mutant phenotype only in women.



A pedigree illustrating X-linked inheritance.

Mitochondrial Inheritance

As described earlier, transmission of genes encoded by DNA contained in the nuclear chromosomes follows the principles of Mendelian inheritance. In addition, each mitochondrion contains several copies of a small circular chromosome that encodes tRNA, ribosomal RNA (rRNA), and proteins that are involved in oxidative phosphorylation and ATP generation. The mitochondrial genome does not recombine and is inherited through the maternal line because sperm does not contribute significant cytoplasmic components to the zygote. Mutations in the genes encoded by the mitochondrial chromosome cause a variety of diseases that affect (in particular) organs highly dependent on oxidative metabolism, such as the retina, brain, kidneys, and heart.



Mitochondrial (“maternal”) inheritance.

An affected woman can pass the defective mitochondrial chromosome to all of her offspring, whereas an affected man has little risk of passing his mutation to a child.

Human Genome Project

Genomics is the study of all the genes in a person as well as the interactions of these genes with one another and with the individual’s environment. All people are 99.9% identical in genetic makeup, but differences in the remaining 0.1% offer important clues about health and disease. The goals of the Human Genome Project were to determine the complete sequence of the 3 billion DNA subunits (bases), identify all human genes, and make that information accessible for further biological study. The project was completed in 2003 and identified approximately 25,000 genes in human DNA **(Box)**.

The completion of the Human Genome Project has inspired much excitement regarding the many potential applications using this information:
(1) improved disease diagnosis,

(2) ability to detect genetic predispositions to disease,

(3) development of drugs based on molecular information,

(4) use of gene therapy and control systems as drugs, and

(5) creation of “custom drugs” based on individual genetic profiles.