# Chapter 6
# Genes

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This chapter is a review of basic genetics as a preliminary for discussion of evolution.

## 6.1 Human Genes

In the previous chapter, we discussed how we inherit cultural heritage through memes. In this chapter, we will examine how our physical characteristics are inherited. We know now that genes are the basis of hereditary transmission and that they are double-helix DNA strands consisting of four nucleotides, thymine, guanine, cytosine, and adenine. All of the some 30,000 human genes have now been mapped.

All our genes are in the 23 pairs of chromosomes that exist in every cell of our body (except for sperms and eggs that have half the number of chromosomes). The chromosomes consist of 22 pairs of autosomes and two sex chromosomes, XX or XY. The reproductive cells, eggs and sperms, have only one half of the chromosomes, and thus a sperm can have only one X or Y.

Genes have been discussed and argued over long before it was known that they consisted of DNA. Hippocrates, for example, believed in hereditary material accumulating throughout life and that strong impressions, i.e., acquired characteristics, could be transmitted to the offspring. An illustration is his famous defense of a woman who gave birth to a black child as, he believed, she was very impressed with

H. Leigh, *Genes, Memes, Culture, and Mental Illness*,
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an African man (Hippocrates). The idea that acquired characteristics are genetically transmitted was considered to be a well-established fact until the nineteenth century.

## 6.2 Mendelian Genetics

Gregor Johann Mendel (1822–1884) was an Austrian Augustinian monk who is considered to be the father of modern genetics (Bardoe, 2006). He studied the inheritance patterns of specific aspects of the pea plant and discovered that they followed simple mathematical rules. Mendel came to the conclusion that the hereditary determinants were particulate in nature called genes. He believed that each gene consists of a pair of alleles that may be dominant or recessive. Only the dominant allele is expressed as the phenotype unless there are two recessive alleles. Mendel published his work in 1866 as *Experiments on Plant Hybridization* in the *Proceedings of the Natural History Society of Brünn*. His discoveries, however, remained unrecognized until after his death, when in 1900 they were "rediscovered" by Hugo De Vries, Carl Correns, and Erich Von Tschermak.

Now it is known that a heterozygote carrying a copy of both a dominant and a recessive trait may result in a phenotype that contains both traits to a greater or lesser extent.

## 6.3 Genes and Mutation

The function of genes is to tell the cells of the offspring how to build a body that resembles the parents. As an offspring requires the contribution of genes from two parents, there is inevitably a recombination of the genes, and the offspring is never an exact copy of the parent. In addition to such recombinations, mutations occur that may change the offspring drastically.

The *genetic code* is the set of rules by which information encoded in genetic material (DNA or RNA sequences) is translated into proteins. The code maps trinucleotide sequences called *codons* that specify a single amino acid to be produced.

Mutation is a change in the genetic code, which may occur simply by accident or by influences such as chemicals and radiation (see Figs. 6.1 and 6.2). Extra nucleotides may be inserted into a DNA sequence (*Insertion*) or segments of DNA may be *deleted.* There may be a *frame shift*, i.e., the sequence of the codon may be altered by insertion or deletion so that the resulting protein, if it exists, would be incorrect. *Substitution* is a mutation in which there is a substitution of one base for another, e.g., A for G, CTGG**A**G for CTGGGG. Substitution may result in a codon that produces a different amino acid resulting in a small change in the protein produced. An example is the sickle cell anemia caused by a substitution in the beta hemoglobin gene that alters a single amino acid (valine for glutamic acid) resulting in Hemoglobin S. Substitution may change a codon that encodes the same amino acid, resulting in no change in the protein produced (*silent or synonymous*

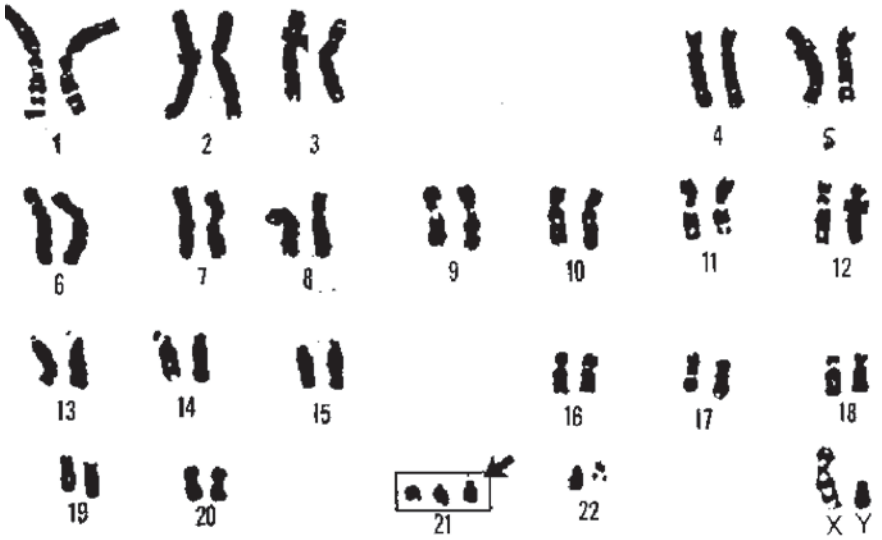


**Fig. 6.1** Human chromosomes in Down's syndrome, which results from trisomy of chromosome 21. (Figure from http://ornl.gov/sci/techresources/Human_Genome/publicat/primer/fig6.html)

*mutation*). At times, an amino acid-coding codon may change to a single "stop" codon, causing an incomplete protein which may not function correctly.

A *single nucleotide polymorphism, or SNP* (pronounced *snip*), is a DNA sequence variation occurring when a single nucleotide (A, T, C, or G) in the genome differs between members of a species or between paired chromosomes in an individual. For example, two DNA fragments from different individuals, AAGC**C**TA and AAGC**T**TA, contain a difference in a single nucleotide, i.e., there are two alleles, C and T, for this gene. Almost all common SNPs have two alleles. SNPs may occur within coding sequences of genes, noncoding regions of genes, or between genes.

*Missence* mutation refers to a substitution of a single nucleotide that results in the production of a different amino acid and, therefore, a different protein (or in some cases, no protein). When an amino acid is replaced by another of very similar chemical properties, the protein may still function normally (*neutral or quiet mutation*). Some amino acids may be encoded by more than one codon (*degenerate coding*), in which case a mutation in one codon would not result in any change in the protein, which would be a synonymous mutation. Some missence mutations cause serious diseases, e.g., epidermolysis bullosa, sickle cell disease, and some forms of amyotrophic lateral sclerosis.

An illustration of Mendelian genetic transmission of a human disease caused by a single nucleotide mutation is sickle cell anemia. Sickle cell anemia is caused by a mutation in the beta hemoglobin gene (HBB) located on the short arm of chromosome 11. The 17th nucleotide of this gene is changed from codon GAG that codes for glutamic acid to GTG, which codes for valine, so the amino acid in position 6 is incorrectly substituted (see Fig. 6.3).

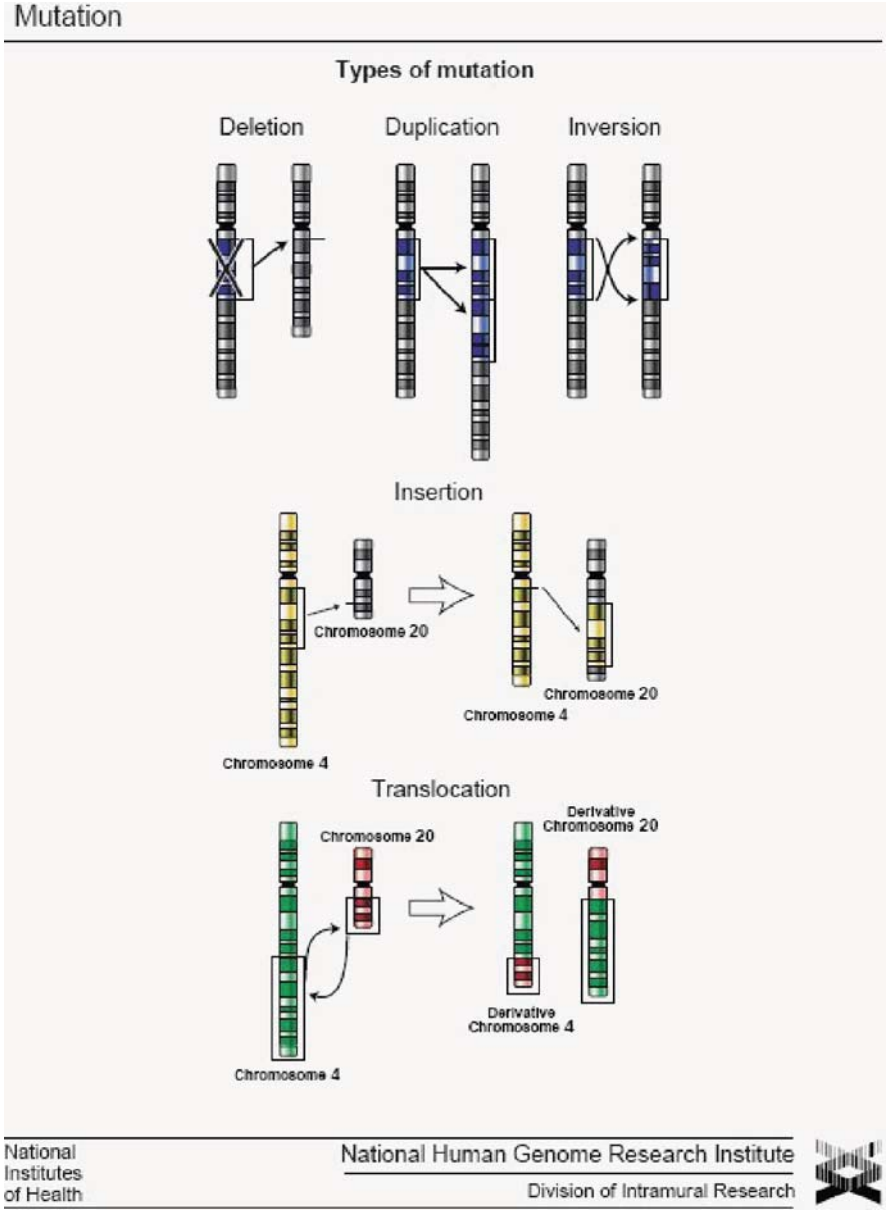


**Fig. 6.2** Gene mutations

This mutation results in production of abnormal Hemoglobin S, which tends to stick together and form long, rigid molecules. The rigid HbS molecules bend red blood cells into a sickle (crescent) shape. These abnormal cells die prematurely, which may lead to anemia. The sickle-shaped cells can also occlude small

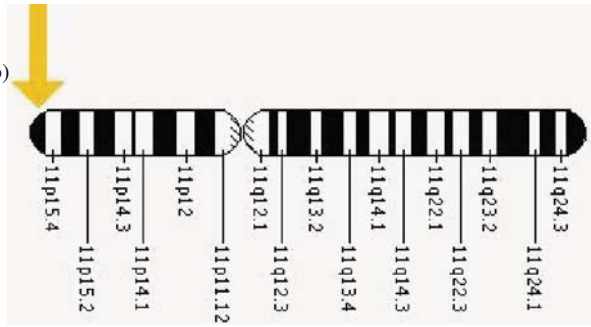


**Fig. 6.3** Chromosome 11 and HBB. (From http://ghr.nlm.nih.gov/gene=hbb)

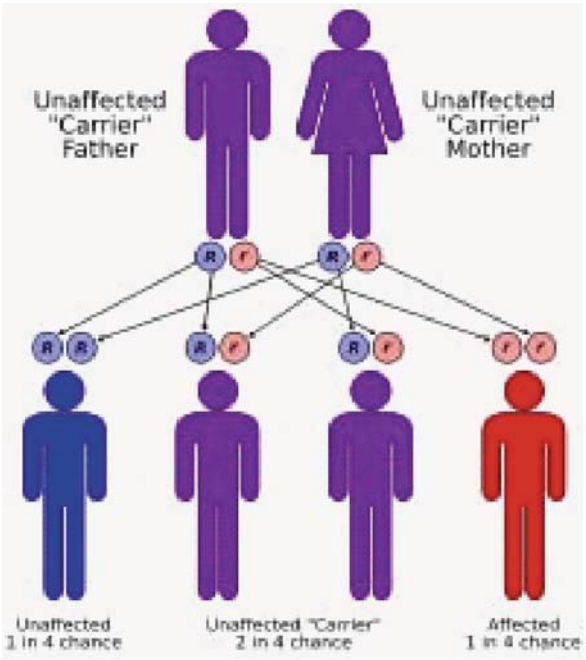


**Fig. 6.4** Genetics of sickle cell disease

blood vessels, causing pain and tissue damage (http://ghr.nlm.nih.gov/gene=hbb) (Figs. 6.4 and 6.5).

Sickle cell anemia is a Mendelian autosomal recessive disease, and one quarter of the offsprings of carrier parents are expected to be affected. Sickle cell trait is a heterozygous form of this illness with variable severity of symptomatology. The sickle cell gene is quite common in sub-Saharan Africa where malaria is prevalent (Makani et al., 2007). This is no wonder as sickle cells are resistant to malarial infection, and thus confers protection against it (Timmann et al., 2007).

**Fig. 6.5** Sickle cells

## 6.4 Sex-Linked Genes

The genes that reside in the sex chromosomes, X and Y, not only cause sexual differentiation but also may be associated with disease. The genes in the Y chromosomes can only be manifested in males – only a few genes in the Y chromosomes have been identified, one of them the testis-determining factor that causes the male phenotype to develop. Even one X-linked recessive trait will be expressed in a male (lacking another X chromosome that might carry the dominant trait) but in a female only if she carries another X chromosome with the same recessive trait.

An example of sex-linked condition is red-green color blindness, which is an X-linked recessive trait. Thus, the children of a color-blind father (X′Y) and a carrier mother (X′X) would result in X′X′, X′X, YX′, and YX, so that 50% of the male children and 50% of the female children would be color blind. On the other hand, if the father is not color blind (XY) and mother is a carrier (X′X), then the children would be XX′, XX, YX′, and YX, i.e., 50% of the male children and no female children would be phenotypically color blind (Wiggs, 2000).

If the father is color blind (X′Y) and mother is not a carrier (XX), then none of the sons would be color blind, while 50% of the daughters would be carriers.

## 6.5 Polygenic Inheritance

Many genetic traits and conditions such as size, intelligence, and behavioral dispositions in humans and animals are determined by the interaction of many different genes as well as with environment as discussed in Chapters 1 and 2. One gene makes one protein but the effects of the proteins usually interact. The term, epistasis, is used to denote the interference of one gene in the expression of another.

There are many genes that have more than two alleles, such as the ABO blood type in humans. Multiple alleles result from different mutations of the same gene. Human ABO blood types are determined by alleles, A, B, and O. Both A and B alleles are codominant over O. Thus, AA and AO types produce A antigen, BB and BO produce B antigen, AB produces both A and B antigens, and OO type produces neither antigen.

Polygenic traits are usually expressed as a gradation of small differences (continuous variation) rather than discrete characteristics as in simple Mendelian inheritance. Such variations usually result in a bell-shaped curve, as in height, weight, skin color, etc. Traits showing continuous variation may be controlled by two or more separate gene pairs. The inheritance of each gene in such polygenic inheritance does follow Mendelian rules (Farabee, 2001).

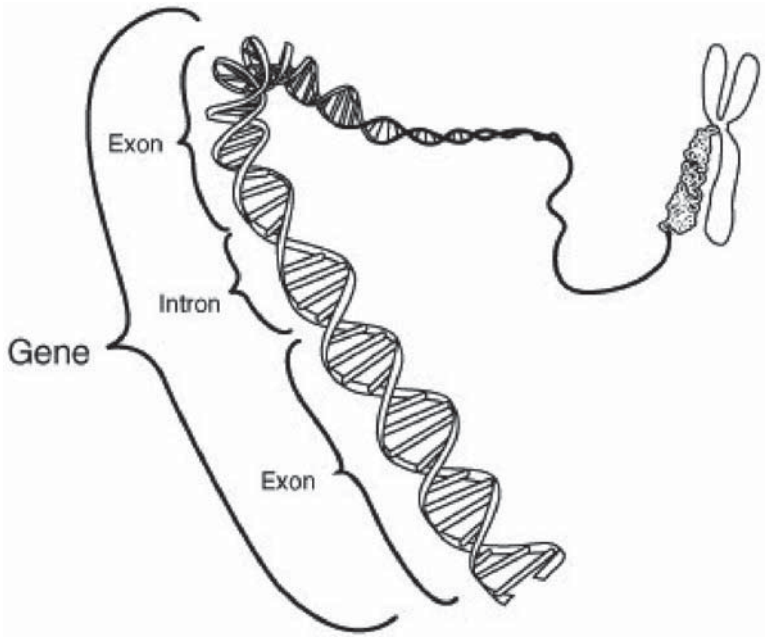


**Fig. 6.6** Structure of a gene

## 6.6 How Do Genes Work?

Genes are segments of the chromosome that contain strands of DNA that make messenger RNAs (ribonucleic acid, mRNA). Genes are associated with a promoter, the DNA region that is usually upstream to the coding sequence. The promoter binds and directs RNA polymerase (RNAP, RNApol) to the correct transcriptional start site and thus permits the initiation of *transcription.* Through this process, a copy of RNA complementary to the DNA template is produced.

Of particular interest is polymorphism of gene promoters such as the serotonin transporter promoter gene (5-HTTLPR) mentioned in Chapters 1 and 2.

RNA polymerase can also elongate the mRNA chain by adding nucleotides to it. The mRNA leaves the nucleus of the cell and becomes ribosomal RNA (mRNA) that makes a protein using the amino acids presented to it by the transport RNA (tRNA). The only function of genes is to make proteins.

However, not all the DNAs that make up the chromosome are genes. There are large portions of the DNA that do not code for proteins, and even in a gene, there are

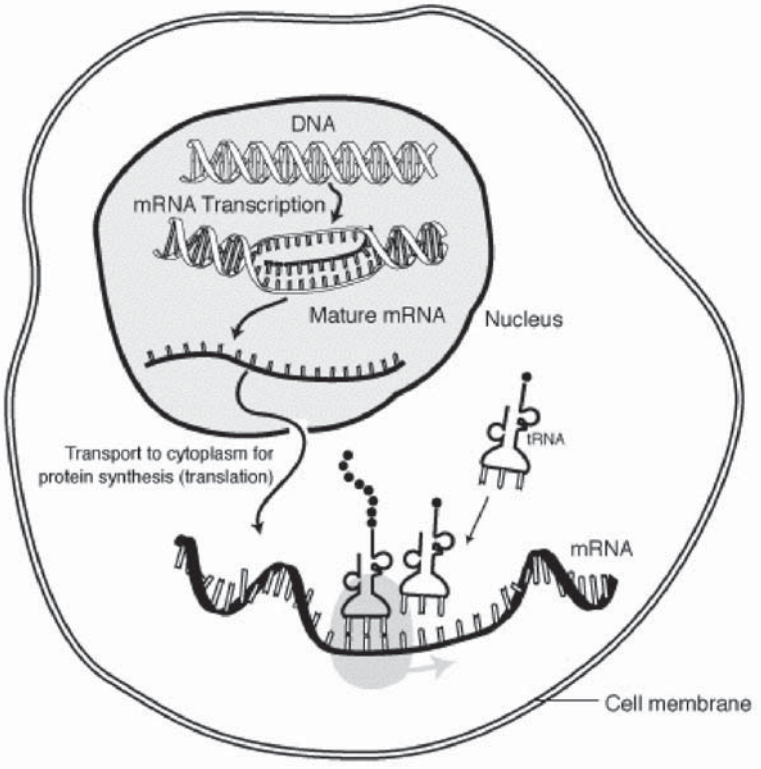


**Fig. 6.7** DNA and RNA. (This image is in the *public domain* because it contains materials that originally came from the *National Institutes of Health*)

segments that do not make proteins. That segment of the gene that is expressed to make proteins is called an exon, and the silent portion is called an intron (Fig. 6.6). The DNA that does not produce proteins has been called collectively "junk DNA." Even when a DNA has made an RNA, some portions of the RNA may not get translated into protein (untranslated RNA, UTR) (Fig. 6.7).

It turns out that such "junk DNA" and UTR are not junk at all, but seem to have important functions in regulating the genes and, even at times, reverse engineering the genes (Andolfatto, 2005; Lolle et al., 2005).

Each cell has the entire DNA code, but cells in different tissues are different and serve different functions, i.e., only certain genes are activated and others are not. What activates the specific genes to make specific cells? It seems the DNA produces cell type-specific noncoding RNA that attracts molecules called *epigenetic activators*, which, in turn, bind to DNA elements in the target gene, activating or silencing it (Beisel et al., 2002; Brene et al., 2000; Sanchez-Elsner et al., 2006).

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