CHAPTER 17

Introduction to genetics

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All living organisms, including human beings, need to reproduce, so that at the end of their life span they have produced at least one, often several, other individuals to replace themselves. This ensures the continuation of their species. Offspring inherit from their parents a copy of all information needed to develop into a functioning organism; this information is carried as deoxyribonucleic acid (DNA), mainly within the cell nucleus. DNA is organised into functional units called genes, which themselves are part of much bigger structures, the chromosomes. Collectively, all the genetic material in a cell is called its *genome*. Genetics is the study of genes, and advancing knowledge in this area has a profound effect on many aspects of daily life, e.g. for genetic counselling in families carrying inherited diseases and the production of human insulin from genetically engineered micro-organisms.

The Human Genome project, an international collaboration, was initiated in 1990. Its aim was to identify and sequence every gene on every chromosome, and to be able to draw a map of each chromosome, showing the position of all its genes. It has yielded a great deal of important information regarding human genetic disorders.

At the end of the chapter, the effects of ageing on chromosomes, cell division and heredity are considered, and this is followed by a section on some common genetic abnormalities.

Chromosomes, genes and DNA

Learning outcomes

After studying this section, you should be able to:

- explain the structural relationship between chromosomes, genes and DNA
- describe the molecular structure of DNA
- explain the terms autosomes and sex chromosomes
- define the terms genome, haploid, diploid and karyotype.

Chromosomes

Nearly every body cell contains, within its nucleus, an identical copy of the entire complement of the individual's genetic material. Two important exceptions are red blood cells (which have no nucleus) and the gametes or sex cells. In a resting cell, the *chromatin* (genetic material, see Fig. 3.8) is diffuse and hard to see under the microscope, but when the cell prepares to divide, it is collected into highly visible, compact, sausage-shaped structures called *chromosomes*. Each chromosome is one of a pair, one inherited from the mother and one from the father, so the human cell has 46 chromosomes that can be arranged as 23 pairs. A cell with 23 pairs of chromosomes is termed *diploid*. Gametes (spermatozoa and ova) with only half of the normal complement, i.e. 23 chromosomes instead of 46, are described as *haploid*. Chromosomes belonging to the same pair are called *homologous* chromosomes. The complete set of chromosomes from a cell is its *karyotype* (Fig. 17.1). **17.1**

Each pair of chromosomes is numbered, the largest pair being no. 1. The first 22 pairs are collectively known as *autosomes*, and the chromosomes of each pair contain the same amount of genetic material. The chromosomes of pair 23 are called the *sex chromosomes* (Fig. 17.2) because they determine the individual's gender. Unlike autosomes, these two chromosomes are not necessarily the same size; the Y chromosome is much shorter than the X and is carried only by males. A child inheriting two X chromosomes (XX), one from each parent, is female, and a child inheriting an X from his mother and a Y from his father (XY) is male. **17.2**

Each end of the chromosome is capped with a length of DNA called a *telomere*, which seals the chromosome and is structurally essential. During replication, the telomere is shortened, which would damage the chromosome, and so it is repaired with an enzyme called *telomerase*. Reduced telomerase activity with age is related to cell *senescence* (p. 445).

Genes

Along the length of the chromosomes are the genes. Each gene contains information in code that allows the cell to make (almost always) a specific protein, the so-called *gene product*. Each gene codes for one specific protein, and research puts the number of genes in the human genome at between 25 000 and 30 000.

Genes normally exist in pairs, because the gene on one chromosome is matched at the equivalent site (locus) on the other chromosome of the pair.

DNA

Genes are composed mainly of very long strands of DNA; the total length of DNA in each cell is about a metre. Because this is packaged into chromosomes, which are micrometres (10^{-6} m) long, this means that the DNA must be tightly wrapped up to condense it into such a small space.

DNA is a double-stranded molecule, made up of two chains of *nucleotides*. Nucleotides consist of three subunits:

- a sugar
- a phosphate group
- a base.

The DNA molecule is sometimes likened to a twisted ladder, with the uprights formed by alternating chains of

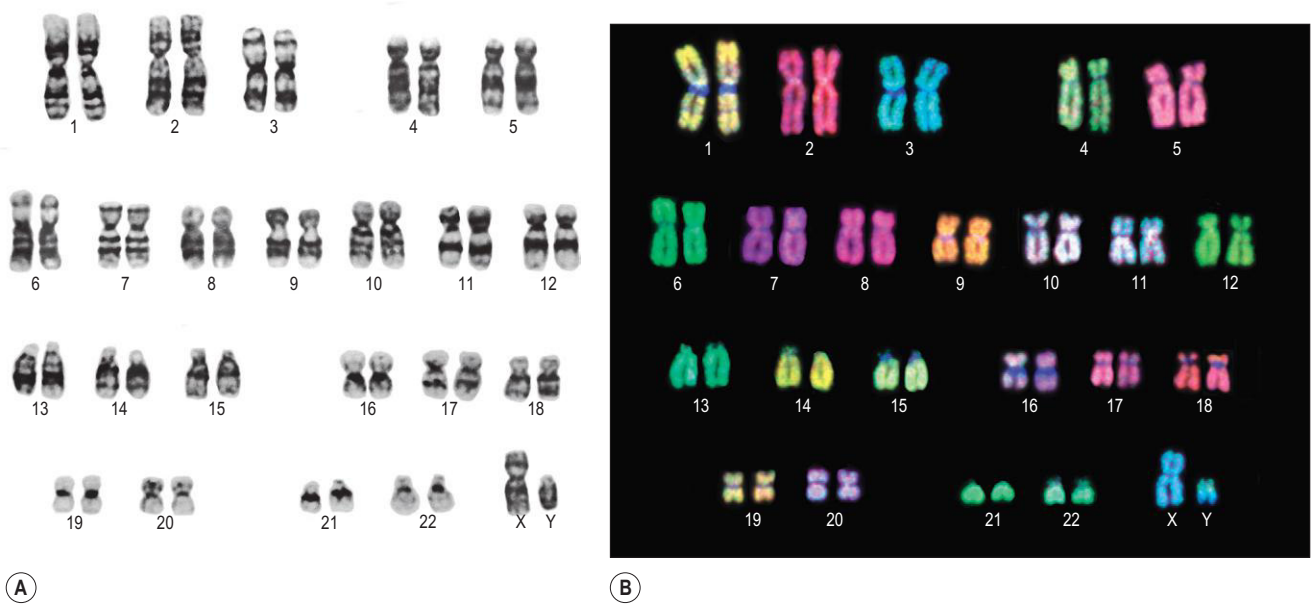

Figure 17.1 Chromosomal complement (karyotype) of a normal human male, showing 22 pairs of autosomes and sex chromosomes (XY, pair 23).

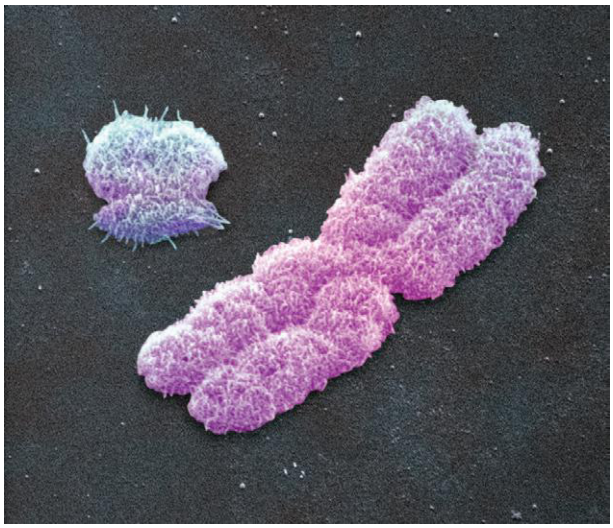

Figure 17.2 Coloured scanning electron micrograph of replicated human sex chromosomes: Y upper left, X centre.

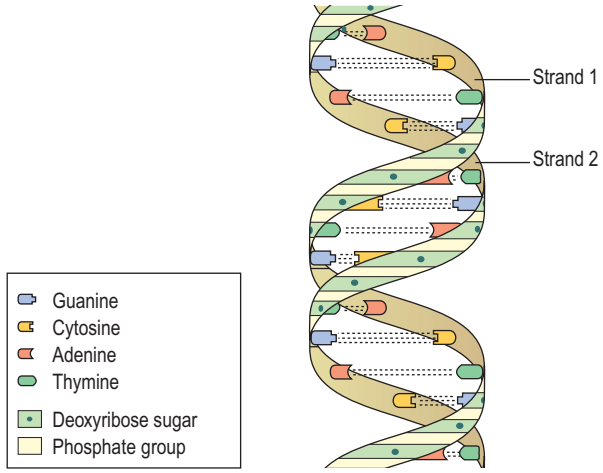

Figure 17.3 Deoxyribonucleic acid (DNA).

sugar and phosphate units (Fig. 17.3). In DNA, the sugar is deoxyribose, thus DNA. The bases are linked to the sugars, and each base binds to another base on the other sugar/phosphate chain, forming the rungs of the ladder. The two chains are twisted around one another, giving a double helix (twisted ladder) arrangement. The double helix itself is further twisted and wrapped in a highly organised way around structural proteins called *histones*, which are important in maintaining the heavily coiled three-dimensional shape of the DNA. The term given to the DNA–histone material is *chromatin*. The chromatin is supercoiled and packaged into the chromosomes shortly before the cell divides (Fig. 17.4).

The genetic code

DNA carries a huge amount of information that determines all biological activities of an organism, and which is transmitted from one generation to the next. The key to how this information is kept is found in the bases within DNA. There are four bases:

- adenine (A)
- guanine (G)
- thymine (T)
- cytosine (C).

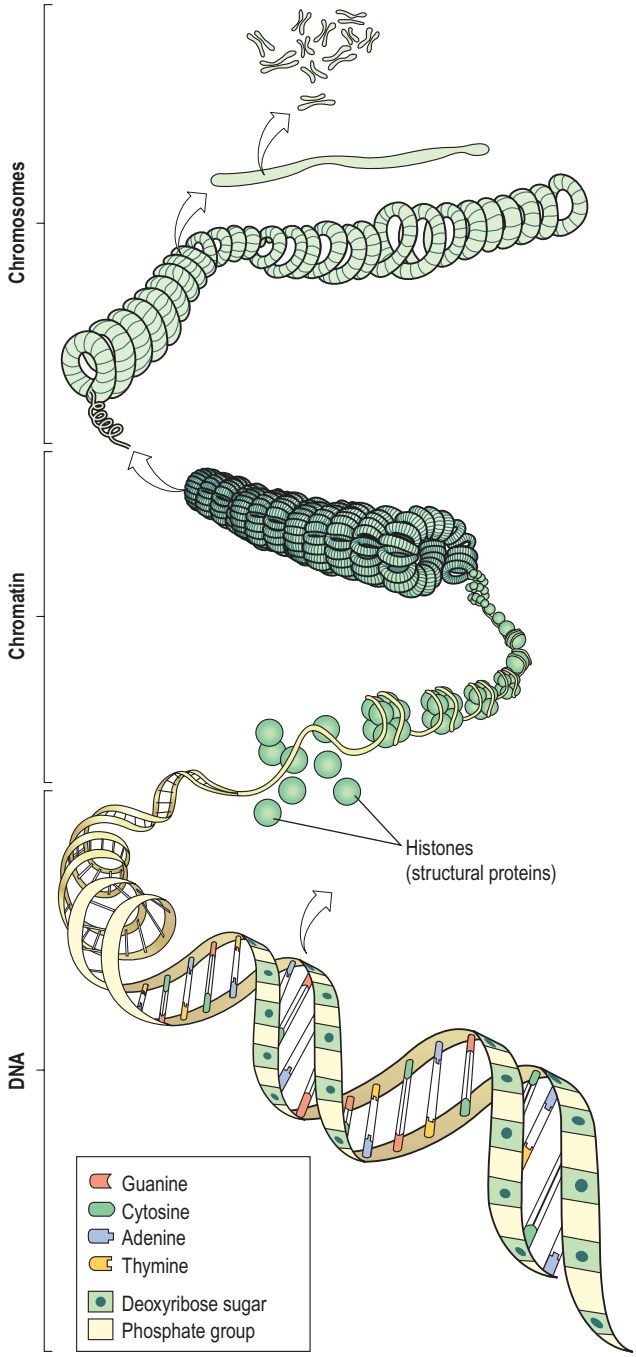

Figure 17.4 The structural relationship between DNA, chromatin and chromosomes.

They are arranged in a precise order along the DNA molecule, making a base code that can be read when protein synthesis is required. Each base along one strand of DNA pairs with a base on the other strand in a precise and predictable way. This is known as *complementary base pairing*. Adenine always pairs with thymine (and vice versa), and cytosine and guanine always go together. The bases on opposite strands run down the middle of the helix and bind to one another with hydrogen bonds (Fig. 17.3). 17.3

Mitochondrial DNA

Each body cell has, on average, 5000 mitochondria (p. 33) that hold a quantity of DNA (mitochondrial DNA), which codes, for example, for enzymes important in energy production. This DNA is passed from one generation to another via the ovum (p. 463), so the offspring's complement of mitochondrial DNA is inherited from the mother. Certain rare inherited disorders that arise from faulty mitochondrial DNA are therefore passed through generations via the maternal line.

Mutation

Mutation means an inheritable alteration in the normal genetic make-up of a cell. Most mutations occur spontaneously, because of the countless millions of DNA replications and cell divisions that occur normally throughout life. Others may be caused by external factors, such as X-rays, ultraviolet rays or exposure to certain chemicals. Any factor capable of mutating DNA is called a *mutagen* (p. 55). Most mutations are immediately repaired by an army of enzymes present in the cell nucleus, and therefore cause no permanent problems.

Sometimes the mutation is lethal, because it disrupts some essential cellular function, causing cell death and the mutation is destroyed along with the cell. Often, the mutated cell is detected by immune cells and destroyed because it is abnormal (p. 379). Other mutations do not kill the cell but alter its function in some way that may cause disease, e.g. in cancer (p. 55). A persistent mutation in the genome that has not led to cell death can be passed from parent to child and may cause inherited disease, e.g. phenylketonuria (p. 446) or cystic fibrosis (p. 266).

Protein synthesis

Learning outcomes

After studying this section, you should be able to:

- describe the origin and structure of mRNA
- explain the mechanism of transcription
- outline the mechanism of translation.

DNA holds the cell's essential biological information, written within the base code in the centre of the double helix. The products of this information are almost always proteins. Proteins are essential to all aspects of body function, forming the major structural elements of the body as well as the enzymes (p. 28) essential for all biochemical

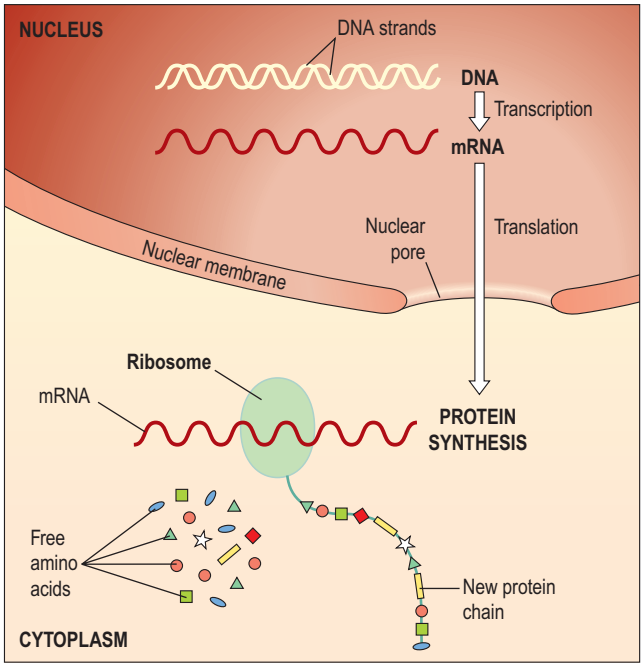

Figure 17.5 The relationship between DNA, RNA and protein synthesis.

processes within it. The building blocks of human proteins are about 20 different amino acids. As the cell's DNA is too big to leave the nucleus, an intermediary molecule is needed to carry the genetic instructions from the nucleus to the cytoplasm, where proteins are made. This is called *messenger* (*m*)RNA. Protein synthesis is summarised in Figure 17.5.

Messenger ribonucleic acid (mRNA)

mRNA is a single-stranded chain of nucleotides synthesised in the nucleus from the appropriate gene, whenever the cell requires to make the protein for which that gene codes. There are three main differences between the structures of RNA and DNA:

- it is single instead of double stranded
- it contains the sugar ribose instead of deoxyribose
- it uses the base uracil instead of thymine.

Using the DNA as a template, a piece of mRNA is made from the gene to be used. This process is called *transcription*. The mRNA then leaves the nucleus through the nuclear pores and carries its information to the ribosomes in the cytoplasm.

Transcription 17.4

Because the code is buried within the DNA molecule, the first step is to open up the helix to expose the bases. Only the gene to be transcribed is opened; the remainder of the chromosome remains coiled. Opening up the helix exposes both base strands, but the enzyme that makes the

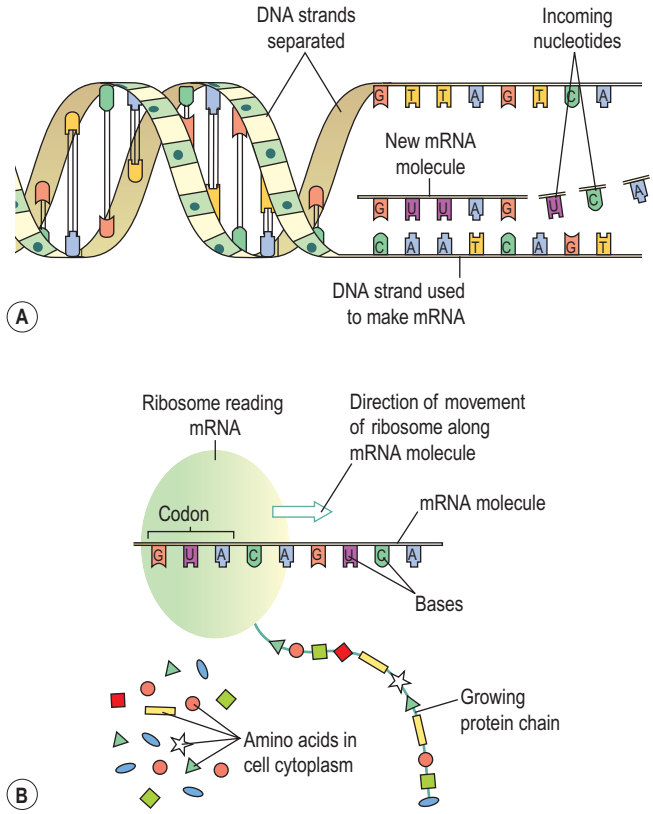

Figure 17.6 Transcription (A) and translation (B).

mRNA uses only one of them, so the mRNA molecule is single, not double stranded. As the enzyme moves along the opened DNA strand, reading its code, it adds the complementary base to the mRNA. Therefore, if the DNA base is cytosine, guanine is added to the mRNA molecule (and vice versa); if it is thymine, adenine is added; if it is adenine, uracil is added (remember there is no thymine in RNA, but uracil instead) (Fig. 17.6A). When the enzyme gets to a 'stop' signal, it terminates synthesis of the mRNA molecule, and the mRNA is released. The DNA is zipped up again by other enzymes, and the mRNA then leaves the nucleus.

Translation 17.5

Translation is synthesis of the final protein using the information carried on mRNA. It takes place on free ribosomes (p. 34) in the cytoplasm and those attached to rough endoplasmic reticulum. First, the mRNA attaches to the ribosome. The ribosome then 'reads' the base sequence of the mRNA (Fig. 17.6B).

Because proteins are built from up to 20 different amino acids, it is not possible to use the four bases individually in a simple one-to-one code. To give enough options, the base code in RNA is read in triplets, giving a possible 64 base combinations, which allows a coded instruction for each amino acid as well as other codes, e.g. stop and start instructions. Each of these specific triplet

sequences is called a *codon*; for example, the base sequence ACA (adenine, cytosine, adenine) codes for the amino acid cysteine.

The first codon is a start codon, which initiates protein synthesis. The ribosome slides along the mRNA, reading the codons and adding the appropriate amino acids to the growing protein molecule as it goes. The ribosome continues assembling the new protein molecule until it arrives at a stop codon, at which point it terminates synthesis and releases the new protein. Some new proteins are used within the cell itself, and others are exported, e.g. insulin synthesised by pancreatic β-islet cells is released into the bloodstream.

Gene expression

Although all nucleated cells (except gametes) have an identical set of genes, each cell type uses only those genes related directly to its own particular function. For example, the only cell type *containing* haemoglobin is the red blood cell, although all body cells carry the haemoglobin gene. This selective gene expression is controlled by various regulatory substances, and the genes not needed by the cell are kept switched off.

Cell division

Learning outcomes

After studying this section, you should be able to:

- explain the mechanism of DNA replication
- compare and contrast the processes of mitosis and meiosis
- describe the basis of genetic diversity from generation to generation.

Most body cells are capable of division, even in adulthood. Cell division usually leads to production of two identical diploid daughter cells, *mitosis* (p. 35) and is important in body growth and repair. Production of gametes is different in that the daughter cells have only half the normal chromosome number – 23 instead of 46, i.e. they are haploid. Gametes are produced by a form of cell division called *meiosis*. DNA replication takes place before mitosis and meiosis.

DNA replication

DNA is the only biological molecule capable of self-replication. Mistakes in copying may lead to production of non-functioning or poorly functional cells, or cells that do not respond to normal cell controls (this could lead to the development of a tumour). Accurate copying of DNA is therefore essential.

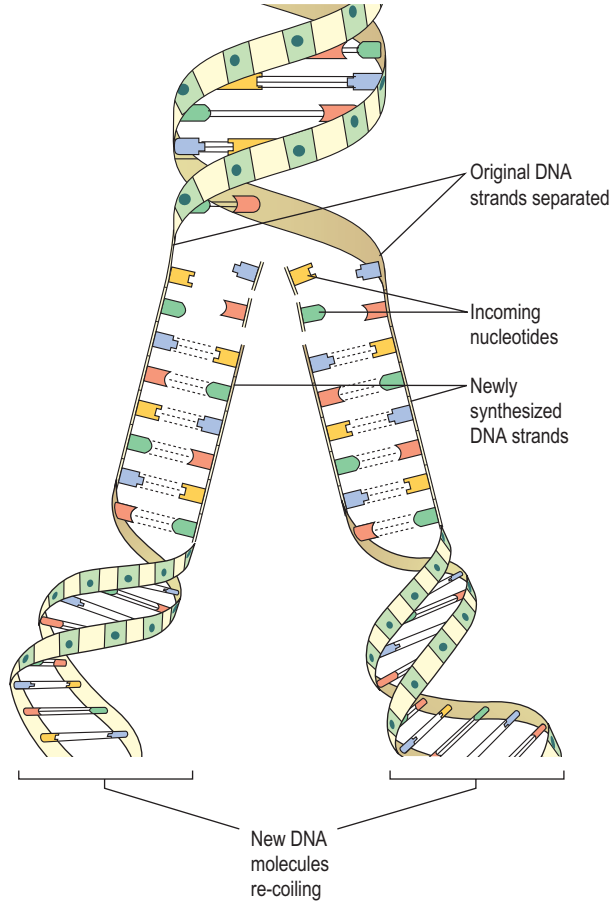

Figure 17.7 DNA replication.

The initial step in DNA replication is the unfolding of the double helix and the unzipping of the two strands to expose the bases, as happens in transcription. Both strands of the parent DNA molecule are copied. The enzyme responsible for DNA replication moves along the base sequence on each strand, reading the genetic code and adding the complementary base to the newly forming chain. This means that each strand of opened bases becomes a double strand and the end result is two identical DNA molecules (Fig. 17.7). As each new double strand is formed, other enzymes cause it to twist and coil back into its normal highly folded form.

Mitosis

This is described on page 35.

Meiosis

Meiosis is the final step in gamete production. On fertilisation, when the male gamete (sperm cell) and the female gamete (ovum) unite, the resulting zygote is diploid, because each gamete was haploid.

Unlike mitosis, meiosis involves two distinct cell divisions rather than one (Fig. 17.8). Additionally, meiosis

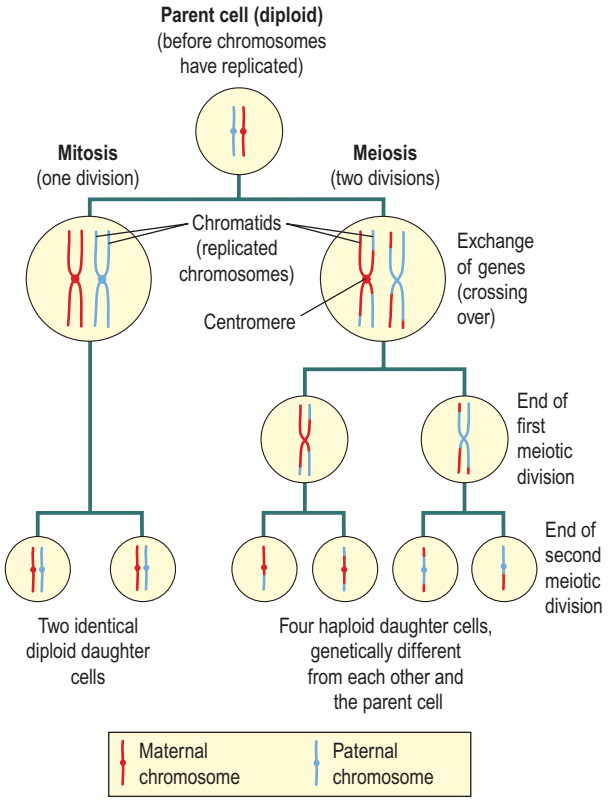

Figure 17.8 Mitosis and meiosis, showing only one pair of chromosomes for clarity.

produces four daughter cells, not two, all different from the parent cells and from each other. This is the basis of genetic diversity and the uniqueness of each human individual.

First meiotic division

This stage (Fig. 17.8) produces two genetically different daughter cells.

DNA replication occurred beforehand, so each pair of chromosomes is now four chromatids, and they gather together into a tight bundle. Because the chromosomes are so tightly associated, it is possible for them to exchange genes. This process is called *crossing over* **17.6**, and results in the four chromatids acquiring different combinations of genes. Following crossing over, the pairs of chromosomes then separate in preparation for the first meiotic division, and transfer of maternal and paternal chromosomes to either daughter cell is random. This means that the two daughter cells have an unpredictable assortment of maternal and paternal DNA, giving rise to a huge number of possible combinations of chromosomes in them. This explains why a child inherits a combination of its mother's and father's characteristics and why children from the same parents can be very different from one another.

Each pair of chromosomes separates and one travels to each end of the cell, guided by a spindle as in mitosis, producing two genetically unique diploid daughter cells.

Second meiotic division

For a gamete to be produced, the amount of genetic material present in the two daughter cells following the first meiotic division must be halved. This is accomplished by a second division (Fig. 17.8). The centromeres separate and the two sister chromatids travel to opposite ends of the cell, which then divides. Each of the four haploid daughter cells now has only one chromosome from each original pair. Fusion with another gamete creates a zygote (fertilised ovum), a diploid cell which can then go on to grow and develop into a human being by mitosis.

The genetic basis of inheritance

Learning outcomes

After studying this section, you should be able to:

- describe the basis of autosomal inheritance, including the relevance of recessive and dominant genes
- explain how sex-linked characteristics are passed from one generation to the next.

Mixing up of parental genes during meiosis leads to the huge genetic variety of the human race. It is important to understand how genes interact to produce inherited characteristics.

Autosomal inheritance

Each of a pair of homologous chromosomes contains genes for the same traits. For example, the ability to roll one's tongue is coded for on a single gene. Because one chromosome of each pair is inherited from the father and one from the mother, an individual has two genes controlling the ability to roll the tongue. Such paired genes are called *alleles*. Corresponding alleles contain genes concerned with the same trait, but they need not be identical. An individual may have:

- two identical forms of the gene (*homozygous*)
- two different forms of the gene (*heterozygous*).

One copy of the tongue-rolling gene may code for the ability to roll the tongue, but the corresponding gene on the other chromosome of the pair may be a different form and code for inability to tongue roll. This simple example involves only two forms of the same gene, but other characteristics are more complex. Eye colour is a diverse trait with a wide range of pigment colours and patterns possible, and is controlled by more than one gene.

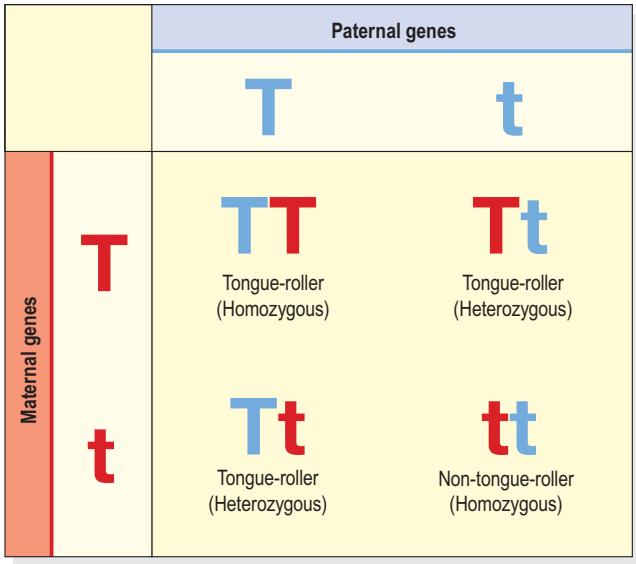

Figure 17.9 Autosomal inheritance. Example shows all possible combinations of tongue-rolling genes in children of parents heterozygous for the trait. T: dominant gene (tongue rolling); t: recessive gene (non-tongue rolling).

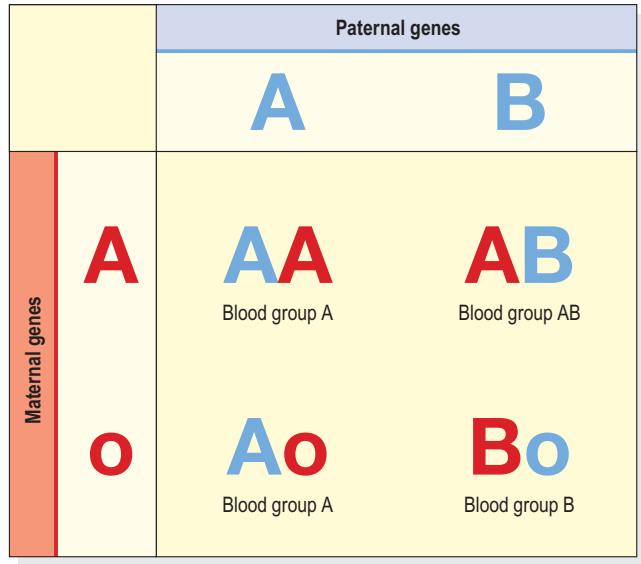

Figure 17.10 Co-dominant inheritance of ABO blood groups.

Should an individual inherit a tongue-rolling gene from one parent, and the non-rolling gene from the other, he will still be able to roll his tongue. This is because the tongue-rolling form of the gene is *dominant*, and takes priority over the non-rolling gene, which is *recessive*. Dominant genes are always *expressed* (active) in preference over recessive genes, and only one copy of a dominant gene is required for that characteristic to be expressed. A recessive gene can only be expressed if it is present on both chromosomes, i.e. individuals unable to tongue-roll have two copies of the recessive, non-rolling gene.

Individuals homozygous for a gene have two identical copies, of either the dominant or the recessive form. Heterozygous individuals have one dominant and one recessive gene. **17.7**

Punnett squares **17.8**

The probability of inheriting either form of a gene depends upon parental make-up. Simple autosomal inheritance can be illustrated using a Punnett square. Figure 17.9 shows all the possible combinations of the tongue-rolling gene in children whose parents are heterozygous for the trait. Using this example, there is a 3 in 4 (75%) chance that the child of these parents will be a tongue roller (TT or Tt), and only a 1 in 4 chance that they would inherit two recessive genes (tt), making them a non-roller.

Prediction of the probability that a baby will be born with an inherited disease, e.g. cystic fibrosis, page 266, forms the basis of genetic counselling.

Co-dominance

For some traits, there can be more than two alleles that code for it, and more than one allele can be dominant. An example of this is the inheritance of A and B type antigens on the surface of red blood cells, determined clinically as the ABO system of blood grouping (p. 67). There are three possible alleles here: one allele codes for production of A type antigens (A), one allele codes for production of B type antigens (B) and a third allele codes for no antigen at all (o). An individual may have any combination of two of these three alleles: AA, AB, BB, Ao, Bo, or oo. Both A and B are dominant, and both express themselves wherever they are present. This is called co-dominance. O is recessive, and so only expresses itself in a homozygous recessive genotype. This means that individuals with an oo genotype have neither A nor B antigens on their red cell surface and are blood group O. An individual with genotype AB has both A and B and is blood group AB. An individual with genotype Ao or AA has only A type antigens and is blood group A; someone with genotype Bo or BB has only B type antigens and is blood group B.

Figure 17.10 shows a Punnett square illustrating the possible blood types of children produced by a mother with genotype AO (phenotype blood group A) and a father with genotype AB (phenotype blood group AB).

Sex-linked inheritance **17.9**

Figure 17.2 shows clearly that the Y chromosome is much smaller than the X chromosome. It is not surprising then to find that the Y chromosome carries only 86 genes compared with the X chromosome's 2000, and the vast majority of genes on the X-chromosome are not matched on the Y. This means that a male has only one copy of most of the genes on his sex chromosomes. Traits coded for on the section of the X chromosome that has no corresponding material on the Y are said to be sex linked. The gene that codes for normal colour vision is one example, and

is therefore carried on X chromosomes only. It is the dominant form of the gene. There is a rare, recessive form of this gene, which is faulty and codes for red–green colour blindness. If a female inherits a faulty copy of the gene, she is statistically likely to have a normal gene on her other X chromosome, giving normal colour vision. A female carrying the colour blindness gene, even though she is not colour blind, may pass the faulty gene on to her children and is said to be a *carrier*. If the gene is abnormal in a male, he will be colour blind because, having only one X-chromosome, he has only one copy of the gene. Inheritance of colour blindness is shown in Figure 17.11. This illustrates the possible genetic combinations of the children of a carrier mother (one normal gene and one faulty gene) and a normal father (one normal gene).

There is a 50% chance of a son being colour blind, a 50% chance of a son having normal vision, a 50% chance of a daughter being a carrier (with normal vision herself) and a 50% chance of a daughter being normal.

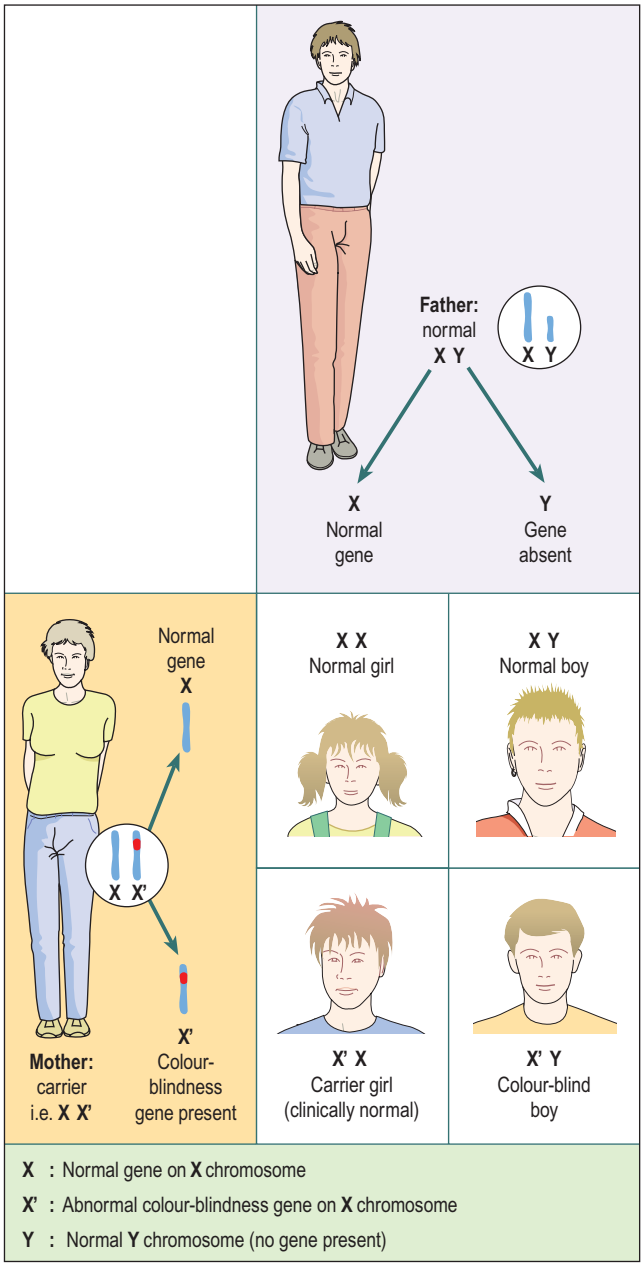

Figure 17.11 Inheritance of sex-linked red–green colour blindness gene between generations.

Ageing and genetics

Learning outcomes

At the end of this section, you should be able to:

- describe the main effects of ageing on the genetic material of cells
- outline the genetic mechanisms of senescence.

Ageing and DNA

Cumulative exposure over a lifetime to potential mutagens as well as a diminishing ability to repair DNA means the cell's genome gradually accumulates mutations, which can lead to diminished function and increased risk of disease, e.g. cancer. Mitochondrial DNA is more prone to mutations than nuclear DNA and as it ages and develops 'wear and tear' damage, it causes progressive impairment of cell function.

Cell senescence (ageing). The number of times a cell can divide is somewhere between 50 and 60 divisions. One important factor in this is thought to relate to the effects of ageing on telomerase function. Telomerase is the enzyme that repairs the telomeres (chromosome tips) following DNA replication. It declines in function with age. This restricts the number of cell replications possible, since without effective telomerase activity, the chromosomes become progressively shorter with each division and eventually become too short to be replicated and the cell can no longer divide.

Genetic basis of disease

Learning outcomes

After studying this section, you should be able to:

- outline the link between cancer and cell mutation
- distinguish between genetic disorders caused by gene mutation and chromosomal abnormalities, giving examples of each.

Cancer

Cancer (malignant growth of new tissue, p. 55) is caused by mutation (p. 440) of cellular DNA, causing its growth pattern to become disorganised and uncontrolled.

Inherited disease

Box 17.1 lists a number of diseases with an inherited component.

Gene mutations

Many diseases, such as cystic fibrosis (p. 266) and haemophilia (p. 79), are passed directly from parent to child via a faulty gene. Many of these genes have been located by mapping of the human genome, e.g. the gene for cystic fibrosis is carried on chromosome 7. Other diseases, e.g. asthma, some cancers and cardiovascular disease, have a genetic component (run in the family). In these cases, a single faulty gene has not been identified, and inheritance is not as predictable as when a single gene is responsible. The likelihood of an individual developing the disease depends not only on their genetic make-up, but also on the influence of other factors, such as lifestyle and environment.

Phenylketonuria

In this disorder, an example of an *inborn error of metabolism*, the gene responsible for producing the enzyme phenylalanine hydroxylase is faulty, and the enzyme is absent. This enzyme normally converts phenylalanine to tyrosine in the liver, but in its absence phenylalanine accumulates in the liver and overflows into the blood (Fig. 17.12). In high quantities, phenylalanine is toxic to the central nervous system and, if untreated, results in brain damage and mental retardation within a few

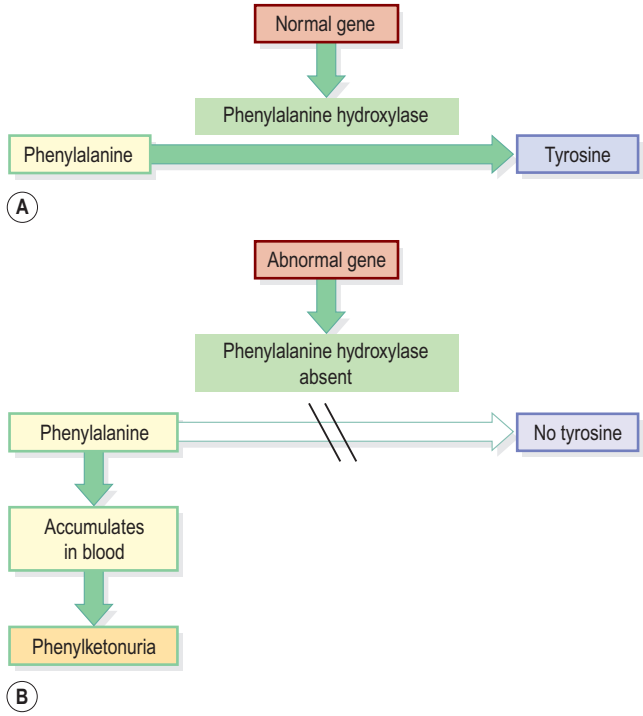

Figure 17.12 Phenylketonuria. A. Gene function normal. **B.** Abnormal gene.

Box 17.1 Some disorders with an inherited component

Single gene disorders
Phenylketonuria
Duchenne muscular dystrophy (p. 435)
Huntington disease
Haemophilia (p. 79)
Achondroplasia (p. 432)
Some cancers, including a proportion of breast, ovarian and bowel cancers
Myotonic dystrophy
Cystic fibrosis (p. 266)
Polycystic kidney disease (p. 354)

More complex inheritance: more than one gene likely to be involved, leading to increased susceptibility and 'running in families'. Lifestyle and other factors involved in determining risk.
Asthma (p. 264)
Cleft lip (p. 320)
Hypertension (p. 131)
Atheroma (p. 120)
Some cancers, e.g. breast and gastric cancer
Types I and II diabetes mellitus (p. 236)
Epilepsy
Schizophrenia
Neural tube defects, e.g. spina bifida (p. 188)

months. Because there are low levels of tyrosine, which is needed to make melanin, depigmentation occurs and affected children are fair skinned and blonde. The incidence of this disease is now low in developed countries because screening of newborn babies detects the condition and treatment is provided.

Mitochondrial abnormalities

Mitochondrial DNA contains only 37 genes but defects in these genes can cause inherited disorders with a very wide range of potentially fatal signs and symptoms, most commonly involving the CNS and skeletal or cardiac muscle. Spontaneous mutations in this DNA can also occur in maturity, leading to onset of disease in adults. There is evidence that mitochondrial mutations may be associated with some forms of important diseases, e.g. diabetes mellitus, Parkinson disease and Alzheimer disease.

Chromosomal abnormalities

Sometimes a fault during meiosis produces a gamete carrying abnormal chromosomes – too many, too few, abnormally shaped, or with segments missing. Often, these aberrations are lethal and a pregnancy involving such a gamete miscarries in the early stages. Non-lethal conditions include Down syndrome and cri-du-chat syndrome.

Down syndrome

In this disorder, there are three copies of chromosome 21 (trisomy 21), meaning that an extra chromosome is present, caused by failure of chromosomes to separate normally during meiosis. People with Down syndrome are usually short of stature, with pronounced eyelid folds and flat, round faces. The tongue may be too large for the mouth and habitually protrudes. Learning disability is present, ranging from mild to severe. Life expectancy is shorter than normal, with a higher than average incidence of cardiovascular and respiratory disease, and a high incidence of early dementia. Down syndrome is associated with increasing maternal age, especially over 35 years.

Cri-du-chat syndrome

Cri-du-chat (cat's cry) refers to the characteristic meowing cry of an affected child. This syndrome is caused when part of chromosome 5 is missing, and is associated with learning disabilities and anatomical abnormalities, including gastrointestinal and cardiovascular problems.

Abnormalities of the sex chromosomes

If the sex chromosomes fail to separate normally during meiosis, the daughter cells will have an incorrect number, either too many or too few. A child born with such an abnormality will not follow normal sexual development without treatment, and may have additional problems such as learning disability.

Turner syndrome. This is usually associated with having only one sex chromosome, an X, as well as 22 normal pairs of autosomes. The karyotype is therefore usually XO, and affected individuals are female. They have female external genitalia and ovaries, but are infertile because the ovaries fail to develop during fetal life, and secondary sexual characteristics do not develop at puberty unless oestrogen treatment is given. Other features include short stature and coarctation of the aorta (in 15%, p. 130). Intelligence is usually normal.

Klinefelter syndrome. The karyotype in this condition is XXY, so affected individuals are male, with 47 chromosomes instead of 46. This condition is commoner than Turner syndrome and is associated with a greater than average height and mild learning disability. The genitalia are male but the testes are underdeveloped and affected individuals are infertile. At puberty, development of feminine characteristics such as enlarged breasts (gynaecomastia) and rounded hips is common, and there is no development of male secondary sexual characteristics unless testosterone treatment is given.

For a range of self-assessment exercises on the topics in this chapter, visit Evolve online resources: https://evolve.elsevier.com/Waugh/anatomy/