3 Chromosomal Basis of Inheritance

3.1 Chromosome

Heinrich Wilhelm Gottfried von Waldeyer-Hartz was a German Professor of Anatomy and Histology who coined the word "chromosome" in 1886. DNA, the blueprint of life, is organized into structures called chromosomes. During the interphase between cell divisions, chromosomes are not so easily seen, even with the best dyes. Interphase chromosomes are loosely organized, forming thin threads that are distinguished throughout the nucleus. Consequently, when dyes are applied, the whole nucleus is stained and individual chromosomes cannot be identified. The diffuse network of threads is chromatin. Some regions of the chromatin stain more darkly than others, suggesting an underlying difference in organization. The light and dark regions, respectively called the euchromatin and the heterochromatin, have different densities of chromosomal threads. At the beginning of cell division (S-phase), the DNA is replicated, producing two identical copies of DNA, which are connected to each other at the centromere. This replicated X-like structure is now called a sister chromatid pair. A chromatid is therefore just one of the strands. During mitosis, the sister chromatid pair condenses further, giving rise to the fat X chromosomes that you can see in the karyotype above.

Therefore, chromosomes can be found in 3 forms: (i) thread-like chromatin (during interphase), (ii) thread-like sister chromatids (during S-phase) and (iii) the condense, visible form chromosome (during mitosis). When a cell divides, the sister chromatids separate, and each daughter cell receives one of the strands. The chromatid then decondenses back into a long single chromatin strand when the new cell goes into interphase.

3.1.1 Chromosome Structure

A chromosome is an organized structure of DNA and protein that is found in cells. It is a single piece of coiled DNA containing many genes, regulatory elements and other nucleotide sequences. Chromosomes also contain DNA-bound proteins, which serve to package the DNA and control its functions. The word chromosome comes from the Greek (chroma, color) and (soma, body) due to their property of being very strongly stained by particular dyes.
The structure and location of chromosomes differentiate prokaryotic cells from eukaryotic cells. Every species has a characteristic number of chromosomes; humans have 23 pairs (22 pairs of autosomal, or nonsex, chromosomes and one pair of sex chromosomes). In sexually reproducing organisms, the number of chromosomes in somatic (nonsex) cells is **diploid**, while gametes or sex cells (egg and sperm) produced by meiosis are **haploid**. Fertilization restores the diploid set of chromosomes in the zygote.

In eukaryotes, nuclear chromosomes are packaged by proteins into a condensed structure called **chromatin** (Figure 3.1). This allows the very long DNA molecules to fit into the cell nucleus. The structure of chromosomes and chromatin varies through the cell cycle. Chromosomes are the essential unit for cellular division and must be replicated, divided, and passed successfully to their daughter cells so as to ensure the genetic diversity and survival of their progeny.

*Figure 3.1:* Structure of a eukaryotic chromosome.
In practice "chromosome" is a rather loosely defined term. In prokaryotes and viruses, the term genophore is more appropriate when no chromatin is present. However, a large body of work uses the term chromosome regardless of chromatin content. In prokaryotes DNA is usually arranged as a circle, which is tightly coiled on itself, sometimes accompanied by one or more smaller, circular DNA molecules called plasmids. These small circular genomes are also found in mitochondria and chloroplasts, reflecting their bacterial origins. The simplest genophores are found in viruses: these DNA or RNA molecules are short linear or circular genophores that often lack structural proteins.

3.1.2 Chromosome Number

Within a species, the number of chromosomes is almost always an even multiple of a basic number. In human beings, for example, the basic number is 23; mature eggs and sperms have this number of chromosomes. Most other types of human cells have twice as many (45), although a few kinds, such as some liver cells, have four times (92) the basic number.

The haploid, or basic, chromosome number (n) defines a set of chromosomes called the haploid genome. Most somatic cells contain two of each of the chromo-somes in this set and are therefore diploid (2n). Cells with four of each chromosome are tertaploid (4n), those with eight of each are octaploid (8n), and so on. The basic number of chromosomes varies among species. Chromosome number is unrelated to the size or biological complexity of an organism, with most species containing between 10 and 40 chromosomes in their genome (Table 3.1). The muntjac, a tiny Asian deer, has only three chromosomes in its genome, whereas some species of fern have many hundreds.

Table 3.1: Chromosome number in different organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Haploid Chromosome No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast (<em>Saccharomyces cerevisiae</em>)</td>
<td>16</td>
</tr>
<tr>
<td>Maize (<em>Zea mays</em>)</td>
<td>10</td>
</tr>
<tr>
<td>Wheat (<em>Triticum aestivum</em>)</td>
<td>21</td>
</tr>
<tr>
<td>Giant sequoia (<em>Sequoia sempivirens</em>)</td>
<td>11</td>
</tr>
<tr>
<td>Fruit fly (<em>Drosophila melanogaster</em>)</td>
<td>4</td>
</tr>
<tr>
<td>Human being (<em>Homo sapiens</em>)</td>
<td>23</td>
</tr>
<tr>
<td>Mouse (<em>Mus musculus</em>)</td>
<td>20</td>
</tr>
</tbody>
</table>
3.1.3 The Chromosome Theory of Heredity

In 1910 American biologist Thomas H Morgan discovered a particular eye colour mutation in the fruit fly, Drosophila melanogaster, was inherited along with the X chromosome, suggesting that a gene for eye colour was physically situated on the X chromosome. Later, one of his students, Calvin B Bridges, obtained definitive proof for this Chromosome Theory of Heredity.

Morgan and his students carried out additional experiments to confirm the elements of his hypothesis. They soon identified other X-linked genes in Drosophila. These early studies with Drosophila greatly strengthened the view that all genes were located on chromosomes and that Mendel’s principles could be explained by the transmissional properties of chromosomes during reproduction. This idea, called the Chromosome Theory of Heredity, stands as one of the most important achievements in biology and has provided a unifying framework for all studies of inheritance.

3.2 Sex Chromosomes

3.2.1 XX and XO

In some animal species—for example, grasshopper—females have one more chromosome than male. This extra chromosome, originally observed in other insects, is called X chromosome. Females of these species have two X chromosomes, males have only one; thus females are cytologically XX and males are XO, where “O” denotes the absence of a chromosome. During meiosis in the female, two X chromosomes pair and then separate, producing eggs that contain a single X chromosome. During meiosis in the male, the solitary X chromosome moves independently of all the other chromosomes and is incorporated into half the sperm; other half receive no X chromosome. Thus, when sperms and eggs unite, two kinds of zygotes are produced: XX, which develop into female, and XO, which develop into males. Because each of these types is equally likely, the reproductive mechanism preserves a 1:1 ratio of males to female in these species.

3.2.2 XX and XY

In many other animals, including human beings, males and females have the same number of chromosomes. This numerical equality is due to the presence of a chromosome in the male, called the Y chromosome, which pairs with X during meiosis. The Y chromosome is morphologically distinguishable from the X
chromosome. In humans, for example, the Y is much shorter than the X, and its centromere is located closer to one of the ends. The material common to X and Y chromosomes is limited, consisting mainly of short terminal segments.

During meiosis in the male, the X and Y chromosomes separate from each other, producing two kinds of sperms, X-bearing and Y-bearing; the frequencies of the two types are approximately equal. XX females produce only one kind of egg, which is X-bearing. If fertilization were to occur randomly, approximately half the zygotes would be XX and the other half would be XY, leading to a 1:1 sex ratio at conception. However, in human beings, Y-bearing sperms have a fertilization advantage, and the zygotic sex ratio is about 1.3:1. During development, the excess of males is diminishes by differential viability of XX and XY embryos, and at birth, males are only slightly more numerous than females (sex ratio 1.07:1). By the age of reproduction and the sex ratio is very close to 1:1. The X and Y chromosomes are called sex chromosomes. All the other chromosomes in the genome are called autosomes.

3.2.3 Sex-Linked Genes in Human Being

In human beings recessive X-linked traits are much more easily identified than are recessive autosomal traits. A male needs only to inherit one recessive allele to show an X-linked trait; however, a female needs to inherit two—one from each of her parents. Thus, the preponderance who show X-linked traits are male.

3.2.3.1 Haemophilia, an X-Linked Blood-Clotting Disorder

In human beings, a certain type of haemophilia is one of the best-known examples of an X-linked trait. People with this disease are unable to produce a factor needed for blood clotting; the cuts and wounds of haemophiliacs continue to bleed and, if not stopped by therapeutic treatment, can cause death. Nearly all the individuals affected with X-linked haemophilia are male. Other blood-clotting disorders are found in both males and females because they are due to mutations in autosomal genes.

The most famous case of X-linked haemophilia occurred in the Russian imperial family at the beginning of the twentieth century (Figure 3.2). Czar Nicholas and Czarina Alexandra had four daughters and one son. The son, Alexis, suffered from haemophilia. The X-linked mutation responsible for Alexis’ disease was transmitted to him by his mother, who was a heterozygous carrier. Czarina Alexandra was a granddaughter of Queen Victoria of Great Britain, who was also a carrier. Pedigree
records show that *Victoria* transmitted the mutant allele to three of her nine children: *Alice*, who was *Alexandra’s* mother, *Beatrice*, who had two sons with the disease, and *Leopold*, who had the disease himself. The allele that *Victoria* carried evidently arose as a new mutation in the germ cells of one of her parents, or in those of a more distant maternal ancestor.

*Figure 3.2:* Royal hemophilia. (a) The Russian imperial family of Czar Nicholas II. (b) X-linked hemophilia in the royal families of Europe. Through intermarriage, the mutant allele for hemophilia was transmitted from the British royal family to the German, Russian, and Spanish royal families.
3.2.3.2 Colour Blindness, an X-Linked Vision Disorder

In human beings, colour perception is mediated by light-absorbing proteins in the specialized cone cells of the retina in the eye. Three such proteins have been identified—one to absorb blue light, one to absorb green light, and one to absorb red light. Colour blindness may be caused by an abnormality in any of these receptor proteins. The classic type of colour blindness, involving faulty perception of red and green light, follows an X-linked pattern of inheritance. About 5 to 10 percent of human males are red-green colour blind; however, a much smaller fraction of female, less than 1 percent, has this disability, suggesting that the mutant alleles are recessive.

Molecular studies have shown that there are two distinct genes for colour perception on the X chromosome; one encodes the receptor for green light, and the other encodes the receptor for red light. Detailed analyses have demonstrated that these two receptors are structurally very similar, probably because the genes encoding them evolved from an ancient colour-receptor gene. A third gene for colour perception, the one encoding the receptor for blue light, is located on an autosome.

3.2.3.3 The Fragile X Syndrome and Mental Retardation

In human beings, many cases of mental retardation appear to follow an X-linked pattern of inheritance. Most of these are associated with a cytological anomaly that is detectable in cells that have been cultured in the absence of certain nucleotides. This anomaly—a constriction near the tip of the long arm of the X chromosome—gives the impression that the tip is ready to detach from the rest of the chromosome; hence the name fragile X chromosome. The clinical features of the fragile X syndrome vary considerably, making diagnosis difficult. Most patients show significant mental impairment, and some exhibit facial and behavioural abnormalities; both male and females can be affected. Among children, the incidence of the fragile X syndrome is about one in 2000.

The fragile X syndrome has been described as an X-linked dominant disorder with incomplete penetrance. Affected females are heterozygous for the fragile X chromosome, and affected males are hemizygous for this chromosome. However, some carriers of the chromosome, both male and female, are asymptomatic for the disorder.
3.2.4 Genes on the Human Y Chromosome

Very few genes have been localized to the human Y chromosome. This failure to find Y-linked genes is somewhat surprising, since a mutation in one of these genes should have an immediate phenotypic effect on the man who carries it. Furthermore, such a mutation should be passed on to all the man's sons but to none of his daughters. A Y-linked gene should therefore be the easiest kind of gene to identify in conventional pedigree analysis.

To date, however, only a few Y-linked genes have been discovered. One is responsible for the synthesis of a male-specific substance called the H-Y antigen, which is found on cell surfaces. Another is involved in the production of a factor that is critical for the differentiation of the testes and the subsequent acquisition of male sexual characteristics.

Advances in molecular genetics have provided new techniques to identify other Y-linked genes, but even with these, the view that the Y chromosome has fewer genes than any other human chromosome probably will not change.

3.2.5 Genes on Both the X and Y Chromosomes

Some genes are present on both the X and Y chromosomes, mostly near the ends of the short arms. Alleles of these genes do not follow a distinct X- or Y-linked pattern of inheritance. Instead, they are transmitted from mothers and fathers to sons and daughters alike, mimicking the inheritance of an autosomal gene. Such genes are therefore called pseudoautosomal genes. In males, the regions that contain these genes seem to mediate pairing between the X and Y chromosomes.

3.3 Sex Determination

In the animal kingdom, sex is perhaps the most conspicuous phenotype. Animals with distinct males and females are sexually dimorphic. Sometimes this dimorphism is established by environmental factors. In one species of turtles, for example, sex is determined by temperature. Eggs that have been incubated above 30° hatch into females, whereas eggs that have been incubated at a lower temperature hatch into males. In many other species, sexual dimorphism is established by genetic factors, often involving a pair of sex chromosomes.
3.3.1 Sex Determination in Human Beings

3.3.1.1 The Process of Sex Determination in Humans

The discovery that human females are XX and that human males are XY suggested that sex might be determined by the number of X chromosomes or by the presence or absence of a Y chromosome. As we now know, the second hypothesis is correct. In humans and other placental mammals, maleness is due to a dominant effect of the Y chromosome (Figure 3.3). The evidence for this fact comes from the study of individuals with an abnormal number of sex chromosomes. XO animals develop as females, and XXY animals develop as males. The dominant effect of the Y chromosome is manifested early in development, when it directs the primordial gonads to develop into testes. Once the testes have formed, they secrete testosterone, a hormone that stimulates the development of male secondary sexual characteristics.

**Figure 3.3**: The process of sex determination in humans. Male sexual development depends on the production of the testis-determining factor (TDF) by a gene on the Y chromosome. In the absence of this factor, the embryo develops as a female.
3.3.1.2 Molecular Basis of Sex Determination in Humans

Researchers have shown that the **testis-determining factor (TDF)** is the product of a gene called **SRY** (for **sex-determining region Y**), which is located just outside the pseudoautosomal region in the short arm of the Y chromosome. The discovery of SRY was made possible by the identification of unusual individuals whose sex was inconsistent with their chromosome constitution—XX males and XY females (**Figure 3.4**). Some of the XX males were found to carry a small piece of the Y chromosome inserted into one of the X chromosomes. This piece evidently carried a gene responsible for maleness. Some of the XY females were found to carry an incomplete Y chromosome. The part of the Y chromosome that was missing corresponded to the piece that was present in the XX males; its absence in the XY females apparently prevented them from developing testes. These complementary lines of evidence showed that a particular segment of the Y chromosome was needed for male development. Molecular analyses subsequently identified the SRY gene in this male-determining segment. Additional research has shown that an SRY gene is present on the Y chromosome of the mouse, and that—like the human SRY gene—it triggers male development.

![Figure 3.4](image)

**Figure 3.4**: Evidence localizing the gene for the testis-determining factor (TDF) to the short arm of the Y chromosome in normal males. The TDF is the product of the SRY gene. In XX males, a small region containing this gene has been inserted into one of the X chromosomes, and in XY females, it has been deleted from the Y chromosome.

After the testes have formed, testosterone secretion initiates the development of male sexual characteristics. Testosterone is a hormone that binds to receptors in many kinds of cells. Once bound, the hormone–receptor complex transmits a signal to the nucleus, instructing the cell in how to differentiate. The concerted differentiation of many types of cells leads to the development of distinctly male
characteristics such as heavy musculature, beard, and deep voice. If the testosterone signaling system fails, these characteristics do not appear and the individual develops as a female.

One reason for failure is an inability to make the testosterone receptor (Figure 3.5). XY individuals with this biochemical deficiency initially develop as males—testes are formed and testosterone is produced. However, the testosterone has no effect because it cannot transmit the developmental signal inside its target cells. Individuals lacking the testosterone receptor therefore acquire female sexual characteristics. They do not, however, develop ovaries and are therefore sterile. This syndrome, called testicular feminization, results from a mutation in an X-linked gene, Tfm, which encodes the testosterone receptor. The tfm mutation is transmitted from mothers to their hemizygous XY offspring (who are phenotypically female) in a typical X-linked pattern.
Figure 3.5: Testicular feminization, a condition caused by an X-linked mutation, \( t_{fm} \), that prevents the production of the testosterone receptor. (a) Normal male. (b) Feminized male with the \( t_{fm} \) mutation.

### 3.3.2 Sex Determination in *Drosophila*

The Y chromosome in *Drosophila*—unlike that in humans—plays no role in sex determination. Instead, the sex of the fly is determined by the ratio of X chromosomes to autosomes (Table 3.2). Normal diploid flies have a pair of sex chromosomes, either XX or XY, and three pairs of autosomes, usually denoted AA; here A represents one haploid set of chromosomes.

<table>
<thead>
<tr>
<th>X Chromosome (X) and Sets of Autosomes (A)</th>
<th>X:A Ratio</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1X 2A</td>
<td>0.5</td>
<td>Male</td>
</tr>
<tr>
<td>2X 2A</td>
<td>1.0</td>
<td>Female</td>
</tr>
<tr>
<td>3X 2A</td>
<td>1.5</td>
<td>Metafemale</td>
</tr>
<tr>
<td>4X 3A</td>
<td>1.33</td>
<td>Metafemale</td>
</tr>
<tr>
<td>4X 4A</td>
<td>1.0</td>
<td>Tetraploid female</td>
</tr>
<tr>
<td>3X 3A</td>
<td>1.0</td>
<td>Triploid female</td>
</tr>
<tr>
<td>3X 4A</td>
<td>0.75</td>
<td>Intersex</td>
</tr>
<tr>
<td>2X 3A</td>
<td>0.67</td>
<td>Intersex</td>
</tr>
<tr>
<td>2X 4A</td>
<td>0.5</td>
<td>Tetraploid male</td>
</tr>
<tr>
<td>1X 3A</td>
<td>0.33</td>
<td>Metamale</td>
</tr>
</tbody>
</table>
Whenever the ratio of X’s to A’s is 1.0 or greater, the fly is female, and whenever it is 0.5 or less, the fly is male. Flies with an X:A ratio between 0.5 and 1.0 developed characteristics of both sexes; thus they are called intersexes. Flies with the Y chromosome have no effect on the sexual phenotype, however it is required for male fertility.

### 3.3.3 Sex Determination in Other animals

In both *Drosophila* and humans, males produce two kinds of gametes, X-bearing and Y-bearing. For this reason, they are referred to as the heterogametic sex; in these species females are the homogametic sex. In birds, butterflies, and some reptiles, this situation is reversed (Figure 3.6). Males are homogametic (usually denoted ZZ) and females are heterogametic (ZW). However, little is known about the mechanism of sex determination in the Z–W sex chromosome system.

![Figure 3.6: Sex determination in birds. The female is heterogametic (ZW), and the male is homogametic (ZZ). The sex of the offspring is determined by which of the sex chromosomes, Z or W, is transmitted by the female.](image)

In honeybees, sex is determined by whether the animal is haploid or diploid (Figure 3.7). Diploid embryos, which develop from fertilized eggs, become females; haploid embryos, which develop from unfertilized eggs, become males. Whether or not a given female will mature into a reproductive form (queen) depends on how she was nourished as a larva. In this system, a queen can control the ratio of males to females by regulating the proportion of unfertilized eggs that she lays. Because this number is small, most of the progeny are female, albeit sterile, and serve as workers
for the hive. In a **haplo-diplo system** of sex determination, eggs are produced through meiosis in the queen, and sperm are produced through mitosis in the male. This system ensures that fertilized eggs will have the diploid chromosome number and that unfertilized eggs will have the haploid number.

![Figure 3.7: Sex determination in honeybees. Females, which are derived from fertilized eggs, are diploid, and males, which are derived from unfertilized eggs, are haploid.](image)

Some wasps also have a haplo-diplo method of sex determination. In these species diploid males are sometimes produced, but they are always sterile. Detailed genetic analysis in one species, *Bracon hebetor*, has indicated that the diploid males are homozygous for a sex-determining locus, called $X$; diploid females are always heterozygous for this locus. Evidently, the sex locus in *Bracon* has many alleles; crosses between unrelated males and females therefore almost always produce heterozygous diploid females. However, when the mates are related, there is an appreciable chance that their offspring will be homozygous for the sex locus, in which case they develop into sterile males.

### 3.4 Dosage Compensation of X-linked Genes

Animal development is usually sensitive to an imbalance in the number of genes. Normally, each gene is present in two copies. Departure from this conditions either up or down, can cause abnormal phenotypes and sometimes even death. It is therefore puzzling that so many species should have a sex-determination system based on females with two $X$ chromosomes and males with only one. In these species, how is the numerical difference of $X$-linked genes accommodated?
A priori, two mechanisms may compensate for this differences: (i) each X-linked gene works twice as hard in males as it does in females, or (2) one copy of each X-linked gene is inactivated in females. Extensive research has shown that both mechanisms are utilised, the first in *Drosophila* and the second in mammals.

### 3.4.1 Hyperactivation of X-Linked Genes in Male *Drosophila*

In *Drosophila*, dosage compensation of X-linked genes is achieved by an increase in the activity of these genes in males. This phenomenon is called **hyperactivation**, involving the *Sex-lethal (Sxl)* gene, which also plays a key role in sex determination ([Figure 3.8](#)). The Sxl gene is turned on in females and off in males. When the Sxl gene product is absent (as it is in male), a complex of different proteins binds to many sites on the X chromosome and triggers a doubling of gene activity. When the Sxl gene product is present (as it is in females), this protein complex does not bind, and hyperactivation of X-linked genes does not occur. In this way, total X-linked gene activity in males and females is approximately equalized.

![Figure 3.8: Dosage Compensation in *Drosophila*](#)

### 3.4.2 Inactivation of X-Linked Genes in Female Mammals

In placental mammals, dosage compensation of X-linked genes is achieved by the *inactivation* of one of the female’s X chromosomes. This mechanism was first proposed in 1961 by the British geneticist Mary Lyon, who inferred it from studies on mice. Subsequent research by Lyon and others has shown that the inactivation event
occurs when the mouse embryo consists of a few thousand cells. At this time, each cell makes an independent decision to silence one of its X chromosomes.

The chromosome to be inactivated is chosen at random; once chosen, however, it remains inactivated in all the descendants of that cell. Thus, female mammals are genetic mosaics containing two types of cell lineages; the maternally inherited X chromosome is inactivated in roughly half of these cells, and the paternally inherited X is inactivated in the other half. A female that is heterozygous for an X-linked gene is therefore able to show two different phenotypes. One of the best examples of this phenotypic mosaicism comes from the study of fur coloration in cats and mice (Figure 3.9). In both of these species, the X chromosome carries a gene for pigmentation of the fur. Females heterozygous for different alleles of this gene show patches of light and dark fur. The light patches express one allele, and the dark patches express the other. In cats, where one allele produces black pigment and the other produces orange pigment, this patchy phenotype is called tortoiseshell. Each patch of fur defines a clone of pigment-producing cells, or melanocytes, that were derived by mitosis from a precursor cell present at the time of X chromosome inactivation.

Figure 3.9: Color mosaics resulting from X chromosome inactivation in female mammals. One X chromosome in the zygote carries the allele for dark fur color, and the other X chromosome carries the allele for light fur color. In each cell of the early embryo, one of the two X chromosomes is randomly inactivated. Whichever X chromosome is chosen remains inactive in all the descendants of that cell. Thus, the developing embryo comes to consist of clones of cells that express only one of the fur color alleles. This genetic mosaicism produces the patches of light and dark fur that are characteristic of tortoiseshell cats.
3.5 Changes in Chromosome Number and Structure

The large change in chromosome number and structure is referred to as chromosomal aberration. There are two basic types of chromosomal aberrations:

1. **Changes in Chromosome Number**: It involves the addition or loss of entire chromosomes or sets of chromosomes.

2. **Changes in Chromosome Structure**: It involves the addition, deletion, or rearrangement of large portions of individual chromosomes.

Chromosomal aberrations represent some of the most important mutations in genetics. Their importance in human medicine, agriculture, and genetic research is widely recognized. In human, chromosomal aberrations may affect one gene, hundreds of genes, or thousands of genes, and they may have profound effects on an individual’s phenotype. For example, the phenotype in human known as *Down syndrome* results from a chromosomal abnormality in which an extra copy of chromosome 21 is present. Down syndrome individuals have a wide range of developmental abnormalities and health problems, even though they may not have any mutant alleles on chromosome 21.

On the other hand, chromosomal aberrations are not always deleterious but, in fact, can produce highly beneficial phenotypes. Many of the plants we use every day for food or fibre (wheat, coffee, strawberries, cotton, potatoes, and bananas) and many of the flowers (roses, chrysanthemums, and tulips) we enjoy in our gardens have chromosomal aberrations. For example, modern cultivated wheat, *Triticum aestivum*, is a hybrid of at least three different species. Its progenitors were low-yielding grasses that grew in Syria, Iran, Iraq, and Turkey. Some of these grasses appear to have been cultivated by the ancient peoples of this region. Two of the grasses apparently interbred, producing a species that excelled as a crop plant. Through human cultivation, this hybrid was selectively improved, and then it, too, interbred with a third species, yielding a triple-hybrid that was even better suited for agriculture. Modern wheat is descendent from these triple-hybrid plants, and has six sets of chromosomes. These result in larger grains, greater harvests, and the ability to adapt to a wide range of environmental conditions. The study of chromosomal aberrations has also given us considerable information about how chromosomal structure affects gene function. Some of the unique properties of chromosomal aberrations make them especially useful as tools in genetic experiments.
### 3.6 Changes in Chromosome Number

The phenotypes of many organisms are affected by changes in the number of chromosomes in their cells. These numerical changes are usually described as variations in the *ploidy* of the organism (*from the Greek word meaning "fold"*). Chromosomal aberrations that change the number of chromosomes in an individual are divided into two categories: *euploidy* and *aneuploidy*.

Aberrations that result in individuals having different numbers of complete sets of chromosomes are called changes in ploidy or *euploidy* (*from the Greek words meaning "true" and "fold"*).

Aberrations that result in individuals having one or more extra chromosomes or losing one or more chromosomes are called *aneuploid* (*for Greek words meaning "not", "true", and "fold") changes.

#### 3.6.1 Euploidy

Individuals that contain one or more complete sets of chromosomes are called *euploid*. Organisms that carry extra sets of chromosomes are said to be *polyploid* (*from the Greek words meaning "many" and "fold"*), and the level of polyploidy is described by referring to a basic chromosome number, usually denoted “x”.

*x* is defined as the number of chromosomes in a set. All species have a normal, or standard, set of chromosomes that contains one copy of each gene normally found in that species. This set is called the *monoploid* set. Most animals and some plants species are *diploid*, which means they have two sets (2x) of chromosomes in their somatic cells and premeiotic germ cells. Humans, for example, have a monoploid chromosome number of 23 (x = 23), and normal human cells contains 2x = 46 chromosomes.

If individuals have three, four, or more complete sets, they are called polyploid individuals. Individuals with three sets (3x) are called *triploids*, individuals with four sets (4x) are *tetraploids*, individuals with five sets (5x) are *pentaploids*, and so on (Table 3.3).
In all sexually reproducing individuals, the first meiotic division (the reduction division) reduces the number of sets of chromosomes in the cell by one half. The chromosome set present in a germ cell or gamete, after a normal first meiotic division, is called the haploid set and is designated by the letter “n”. In diploid individuals, the monoploid and the haploid sets of chromosomes are the same (x = n). For example, the tomato is 2n = 2x = 24, and tomato pollen cells are n = x = 12. In polyploids after the first meiotic division, the germ cells will contain more than one monoploid chromosomes. Thus, the haploid and monoploid chromosome sets will not be the same. For example, in a tertaploid tomato, 4x = 48, cells that have completed the reduction division of meiosis will contain two monoploid chromosome sets (n = 2x = 24).

### 3.6.1.1 Monoploid

Monoploids carry only complete set of chromosomes. Monoploidy is rare in animal (the male honeybee is an outstanding exception), but common in plants. In most sexually reproducing algae and fungi and in all bryophytes, the monoploid phase represents the dominant part of the life cycle. In vascular plants this stage is short-lived and microscopic, though occasionally adult monoploid vascular plants may be recognized in natural populations. These are ordinarily weak, small, and highly sterile. There is good evidence that monoploids developed from unfertilised eggs. Sterility in monoploids is due to extreme irregularity of meiosis because of the impossible of chromosomal pairing and the very low probability of their distribution in complete sets to daughter nuclei. Thus viable gametes are rarely formed; their occurrence depends on the chance movement of the whole monoploid set to one pole at meiosis. This is a highly improbable event.
3.6.1.2 Polyploid
Polyploidy, the presence of extra chromosome sets, is fairly common in plants but very rare in animals. One half of all known plants genera contain polyploid species, and about two-thirds of all grasses are polyploids. Many of these species reproduce sexually. In animals, where reproduction is primarily by sexual means, polyploidy is rare, probably because it interferes with the sex-determination mechanism.

One general effect of polyploidy is that cell size is increased, presumably because there are more chromosomes in the nucleus. Often this increase in size is correlated with an overall increase in the size of the organism. Polyploid species tend to be larger and more robust than their diploid counterparts. These characteristics have a practical significance for human beings, who depend on many polyploid plant species for food. These species tend to produce larger seeds and fruits, and therefore provide greater yields in agriculture. Wheat, coffee, potatoes, bananas, strawberries, and garden plants, including roses, chrysanthemums, and tulip, are also polyploid.

3.6.1.3 Sterile Polyploids
In spite of their robust physical appearance, many polyploid species are sterile. Extra sets of chromosomes segregate irregularly in meiosis, leading to grossly unbalanced (that is, aneuploid) gametes. If such gametes unite in fertilization, the resulting zygotes almost always die. This inviability among the zygotes explains why many polyploid species are sterile. As an example, let’s consider a triploid species with three identical sets of n chromosomes. The total number of chromosomes is therefore 3n. When meiosis occurs, each chromosome will try to pair with its homologues (Figure 3.10). One possibility is that two homologues will pair completely along their length, leaving the third without a partner; this solitary chromosome is called a univalent. Another possibility is that all three homologues will synapse, forming a trivalent in which each member is partially paired with each of the others. In either case, it is difficult to predict how the chromosomes will move during anaphase of the first meiotic division. The more likely event is that two of the homologues will move to one pole and one homologue will move to the other, yielding gametes with one or two copies of the chromosome. However, all three homologues might move to one pole, producing gametes with zero or three copies of the chromosome. Because this segregational uncertainty applies to each trio of chromosomes in the cell, the total number of chromosomes in a gamete can vary from zero to 3n.
Figure 3.10: Meiosis in a triploid. (a) Univalent formation. Two of the three homologues synapse, leaving a univalent free to move to either pole during anaphase. (b) Trivalent formation. All three homologues synapse, forming a trivalent, which may move as a unit to one pole during anaphase. However, other anaphase disjunctions are possible.

Zygotes formed by fertilization with such gametes are almost certain to die; thus, most triploids are completely sterile. In agriculture and horticulture, this sterility is circumvented by propagating the species asexually. The many methods of asexual propagation include cultivation from cuttings (bananas), grafts (Winesap, Gravenstein, and Baldwin apples), and bulbs (tulips). In nature, polyploid plants can also reproduce asexually. One mechanism is apomixis, which involves a modified meiosis that produces unreduced eggs; these eggs then form seeds that germinate into new plants. The dandelion, a highly successful polyploid weed, reproduces in this way.

3.6.1.4 Fertile Polyploids

The meiotic uncertainties that occur in triploids also occur in tetraploids with four identical chromosome sets. Such tetraploids are therefore also sterile. However, some tetraploids are able to produce viable progeny. Close examination shows that these species contain two distinct sets of chromosomes and that each set has been
duplicated. Thus, fertile tetraploids seem to have arisen by chromosome duplication in a hybrid that was produced by a cross of two different, but related, diploid species; most often these species have the same or very similar chromosome numbers. Figure 3.11 shows a plausible mechanism for the origin of such a tetraploid. Two diploids, denoted A and B, are crossed to produce a hybrid that receives one set of chromosomes from each of the parental species.

Figure 3.11: Origin of a fertile tetraploid by hybridization between two diploids and subsequent doubling of the chromosomes.
Such a hybrid will probably be sterile because the A and B chromosomes cannot pair with each other. However, if the chromosomes in this hybrid are duplicated, meiosis will proceed in reasonably good order. Each of the A and B chromosomes will be able to pair with a perfectly homologous partner. Meiotic segregation can therefore produce gametes with a complete set of A and B chromosomes. In fertilization, these “diploid” gametes will unite to form tetraploid zygotes, which will survive because each of the parental sets of chromosomes will be balanced.

This scenario of hybridization between different but related species followed by chromosome doubling has evidently occurred many times during plant evolution. In some cases, the process has occurred repeatedly, generating complex polyploids with distinct chromosome sets. One of the best examples is modern bread wheat, *Triticum aestivum* (Figure 3.12). This important crop species is a hexaploid containing three different chromosome sets, each of which has been duplicated.

![Figure 3.12](image)

**Figure 3.12:** Origin of hexaploid wheat by sequential hybridization of different species. Each hybridization event is followed by doubling of the chromosomes.
There are seven chromosomes in each set, for a total of 21 in the gametes and 42 in the somatic cells. Thus, modern wheat seems to have been formed by two hybridization events. The first involved two diploid species that combined to form a tetraploid, and the second involved a combination between this tetraploid and another diploid, to produce a hexaploid. Cytogeneticists have identified primitive cereal plants in the Middle East that may have participated in this evolutionary process. In 2010, much of the DNA in the wheat genome was sequenced. This genome is very large, roughly five times the size of the human genome. Analysis of all these DNA sequences will help us to understand wheat’s evolutionary history.

Because chromosomes from different species are less likely to interfere with each other’s segregation during meiosis, polyploids arising from hybridizations between different species have a much greater chance of being fertile than do polyploids arising from the duplication of chromosomes in a single species.

Polyploids created by hybridization between different species are called \textit{allopolyploids} (from the Greek prefix for “other”); in these polyploids, the contributing genomes are qualitatively different. Polyploids created by chromosome duplication within a species are called \textit{autopolyploids} (from the Greek prefix for “self”); in these polyploids, a single genome has been multiplied to create extra chromosome sets.

Chromosome doubling is a key event in the formation of polyploids.

(1) One possible mechanism for this event is for a cell to go through mitosis without going through cytokinesis. Such a cell will have twice the usual number of chromosomes. Through subsequent divisions, it could then give rise to a polyploid clone of cells, which might contribute either to the asexual propagation of the organism or to the formation of gametes. In plants it must be remembered that the germ line is not set aside early in development, as it is in animals. Rather, the reproductive tissues differentiate only after many cycles of cell division. If the chromosomes were accidentally doubled during one of these cell divisions, the reproductive tissues that would ultimately develop might be polyploid.

(2) Another possibility is for meiosis to be altered in such a way that unreduced gametes (with twice the normal number of chromosomes) are produced. If such gametes participate in fertilization, polyploid zygotes will be formed. These
zygotes may then develop into mature organisms, which, depending on the nature of the polyploidy, may be able to produce gametes themselves.

(3) In laboratory, polyploidy can be artificially generated by treatment of cells with colchicine. Colchicine is an alkaloid derivative of the autumn crocus *Colchicum autumnale*. Colchicine blocks spindle fibre formation, which results in a mitotic cell cycle that includes chromosome replication without cell division. After one such cycle, the cell will have twice as many chromosomes. For example, a diploid cell that normally has $2x = 10$ chromosomes will have $4x = 20$ chromosomes. Such cell would be an autotetraploid.

### 3.6.1.5 Tissue-Specific Polyploidy and Polyteny

In some organisms, certain tissues become polyploid during development. This polyploidization is probably a response to the need for multiple copies of each chromosome and the genes it carries. The process that produces such polyploid cells, called *endomitosis*, involves chromosome duplication, followed by separation of the resulting sister chromatids. However, because there is no accompanying cell division, extra chromosome sets accumulate within a single nucleus. In the human liver and kidney, for example, one round of *endomitosis* produces tetraploid cells.

Sometimes polyploidization occurs without the separation of sister chromatids. In these cases, the duplicated chromosomes pile up next to each other, forming a bundle of strands that are aligned in parallel. The resulting chromosomes are said to be *polytene*, from the Greek words meaning “many threads.” The most spectacular examples of polytene chromosomes are found in the salivary glands of *Drosophila* larvae. Each chromosome undergoes about nine rounds of replication, producing a total of about 500 copies in each cell. All the copies pair tightly, forming a thick bundle of chromatin fibers. This bundle is so large that it can be seen under low magnification with a dissecting microscope. Differential coiling along the length of the bundle causes variation in the density of the chromatin. When dyes are applied to these chromosomes, the denser chromatin stains more deeply, creating a pattern of dark and light bands (*Figure 3.13*). This pattern is highly reproducible, permitting detailed analysis of chromosome structure.
The polytene chromosomes of *Drosophila* show two additional features:

1. **Homologous Polytene Chromosomes Pair:** Ordinarily, we think of pairing as a property of meiotic chromosomes; however, in many insect species the somatic chromosomes also pair—probably as a way of organizing the chromosomes within the nucleus. When *Drosophila* polytene chromosomes pair, the large chromatin bundles become even larger. Because this pairing is precise—point-for-point along the length of the chromosome—the two homologues come into perfect alignment. Thus, the banding patterns of each are exactly in register, so much so that it is almost impossible to distinguish the individual members of a pair.

2. **All the Centromeres of Drosophila Polytene Chromosomes Congeal into a Body Called the Chromocenter:** Material flanking the centromeres is also drawn into this mass. The result is that the chromosome arms seem to emanate out of the chromocenter. These arms, which are banded, consist of euchromatin, that portion of the chromosome that contains most of the genes; the chromocenter consists of heterochromatin, a gene-poor material that surrounds the centromere. Unlike the euchromatic chromosome arms, this centric heterochromatin does not become polytene. Thus, compared to the euchromatin, it is vastly underreplicated.
In the 1930s CB Bridges published detailed drawings of the polytene chromosomes (Figure 3.14). Bridges arbitrarily divided each of the chromosomes into sections, which he numbered; each section was then divided into subsections, which were designated by the letters A to F. Within each subsection, Bridges enumerated all the dark bands, creating an alphanumeric directory of sites along the length of each chromosome. Bridges’ alphanumeric system is still used today to describe the features of these remarkable chromosomes.

Figure 3.14: Bridges’ polytene chromosome maps. (Top) Banding pattern of the polytene X chromosome. The chromosome is divided into 20 numbered sections. (Bottom) Detailed view of the left end of the polytene X chromosome showing Bridges’ system for denoting individual bands.

The polytene chromosomes of *Drosophila* are trapped in the interphase of the cell cycle. Thus, although most cytological analyses are performed on mitotic chromosomes, the most thorough and detailed analyses are performed on polytenized interphase chromosomes. Such chromosomes are found in many species within the insect order Diptera, including flies and mosquitoes. Unfortunately, humans do not have polytene chromosomes; thus, the high-resolution cytological analysis that is possible for *Drosophila* is not possible for our own species.

### 3.6.2 Aneuploidy

#### 3.6.2.1 Types of Aneuploidy

Individuals that have gained or lost one or more chromosomes are called **aneuploids** (Table 3.4). Aneuploid is a general term that refers to any loss or gain
of a chromosome, thus special terminology has been devised to convey more specific information.

Table 3.4: Summary of variation in chromosome number (Heteroploidy)

<table>
<thead>
<tr>
<th>Type</th>
<th>Designation</th>
<th>Chromosome complement (where one set consists of four chromosomes, numbered 1, 2, 3, and 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euploids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoploid</td>
<td>x</td>
<td>1-2-3-4</td>
</tr>
<tr>
<td>Diploid</td>
<td>2x</td>
<td>1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Triploid</td>
<td>3x</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Autotetraploid</td>
<td>4x</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Allotetraploid</td>
<td>4x</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Aneuploids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trisomic</td>
<td>2x + 1</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Monosomic</td>
<td>2x – 1</td>
<td>1-2-3-4 2-3-4</td>
</tr>
<tr>
<td>Double trisomic</td>
<td>2x + 1 + 1</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Double monosomic</td>
<td>2x – 1 – 1</td>
<td>1-2-3-4 3-4</td>
</tr>
<tr>
<td>Tetrasomic</td>
<td>2x + 2</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Double tetrasomic</td>
<td>2x + 2 + 2</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
<tr>
<td>Triploid tetrasomic</td>
<td>3x + 1</td>
<td>1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4 1-2-3-4</td>
</tr>
</tbody>
</table>

**Disomic:** A normal diploid individual can be said to be disomic (to have two copies) for each chromosomes.

**Trisomic:** Individuals who are diploid but have an extra chromosome are said to be trisomic for the chromosome. The chromosome number is then written 2x + 1. For example, a trisomic tomato would have two normal sets 2n = 2x = (24 + 1) = 25 chromosomes.

**Monosomic:** Diploid individuals that lose a single chromosome are said to be monosomic for that chromosome and are consequently 2x – 1. A monosomic tomato would have two normal sets 2n = 2x = (24 – 1) = 23 chromosomes.

**Double Trisomic:** Individuals that have two different extra chromosomes are double trisomic (2x + 1 + 1). A doubly trisomic tomato would have 2n = 2x = (24 + 1 + 1) = 26 chromosomes.

**Double Monosomic:** Individuals that have lost one copy of two different chromosomes are double monosomic (2x – 1 – 1). A doubly monosomic tomato would have 2n = 2x = (24 – 1 – 1) = 22 chromosomes.
**Tetrasomic:** Individuals that have two extra copies of a single chromosome are said to be tetrasomic. A tetrasomic tomato would have \(2n = 2x = (24 + 2) = 26\) chromosomes.

**Nullisomic:** Individuals that have lost both copies of one chromosome are said to be nullisomic. A nullisomic tomato would have \(2n = 2x = (24 - 2) = 22\) chromosomes.

### 3.6.2.2 Aneuploidy in Human Beings

The chromosome content of an aneuploid human is designated by using a special notation that gives the total number of chromosomes present and a description of the abnormality.

**Down Syndrome:** The best-known and most common chromosome abnormality in humans is Down syndrome, a condition associated with extra chromosome 21 (trisomy-21). This syndrome was first described in 1866 by a British physician, Langdon Down, but its chromosomal basis was not clearly understood until 1959. People with Down syndrome are typically short in stature and loose-joints, particularly in ankles; they have broad skulls, wide nostrils, large tongues with a distinctive furrowing, a specific peculiarity of the upper eyelid (epicanthal fold) that suggests Oriental eyes, and stubby hands with a cease on palm.

Trisomy-21 can be caused by chromosome disjunction in one of the meiotic cell division. The nondisjunction event can occur in either parent, but it seems to be more likely in females. In addition, the frequency of nondisjunction increases with maternal age. Thus, among mothers younger than 25 years old, the risk of having a child with Down syndrome is about 1 in 1500, whereas among mothers 40 years old, it is 1 in 100. This increased risk is due to factors that adversely affect meiotic chromosome behaviour as a woman ages.

**Trisomy for Other Chromosome:** Trisomy for chromosome 13 (Patau’s syndrome) and 18 (Edwards’ syndrome) have also been reported. However, these are rare, and the affected individuals show serious phenotypic abnormalities and are short-lived, usually dying within the first few weeks after birth. Another viable trisomy that has been observed in human beings is the triplo-X karyotype (47,XXX). These individuals survive because two of the three X chromosomes are inactivated, effectively reducing the dosage of the X chromosome to the normal level of one. Triplo-X individuals are female and are phenotypically normal, or nearly so; sometimes they exhibit a slight mental impairment and reduced fertility.
**Turner Syndrome:** In human beings, there is only one viable monosomy, the 45,X karyotype. These individuals have a single X chromosome as well as a diploid complement of autosomes. Phenotypically, they are female, but because their ovaries are rudimentary, they are almost always sterile. 45,X individuals are usually short in stature; they have webbed necks, hearing deficiencies, and significant cardiovascular abnormalities. Henry H. Turner first described the condition in 1938; thus, it is now called Turner syndrome.

**Klinefelter Syndrome:** The 47,XXY karyotype is also a viable trisomy in human beings. These individuals have three sex chromosomes, two X’s and one Y. Phenotypically, they are male, but they can show some female secondary sexual characteristics and are usually sterile. In 1942 H.F. Klinefelter described the abnormalities associated with this condition, now called Klinefelter syndrome; these include small testes, enlarged breasts, long limbs, knock-knees, and underdeveloped body hair. The XXY karyotype can originate by fertilization of an exceptional XX egg with a Y-bearing sperm, or by fertilization of an X-bearing egg with an exceptional XY sperm. The XXY karyotype accounts for about three-fourths of all cases of Klinefelter syndrome. Other cases involve more complex karyotypes such as XYY, XXXY, XXXXY, XXXYYY, and XXXXXX.

**47,XYY Karyotype:** The 47,XYY karyotype is another viable trisomy in human beings. These individuals are male, and except for a tendency to be taller than 46,XY men, they do not show a consistent syndrome of characteristics. This kind of individual first came to notice when Jacobs and others (1965) reported a high incidence of XYY males (9 of 315 persons) housed in the maximum-security section of a Scottish criminal institution. Many similar reports followed during the latter of the 1960s leading to an initial notion the XYY males are more aggressive and more likely than XY male to commit crimes of violence. A possible connection between XYY karyotype and antisocial behaviour has not been studied thoroughly enough to draw a firm conclusion. All the other trisomies in human beings are embryonic lethals, demonstrating the importance of correct gene dosage. Unlike Darura, in which each of the possible trisomies is viable, human beings do not tolerate many types of chromosomal imbalance.
3.7 Changes in Chromosome Structure

Chromosome rearrangements, mutations that change the structure of chromosomes, are the second major category of chromosomal aberrations. These rearrangements usually result from chromosomes that break into fragments that subsequently rejoin improperly. There are four types of chromosomal rearrangements (Table 3.5):
1. Deletion or Deficiency (lost portions of chromosome),
2. Duplication (added chromosomal material),
3. Inversion (changes in the order of genes on a chromosome), and
4. Translocation (exchanges between chromosomes that are not homologous).

Table 3.5: Changes in chromosome structure by chromosome breaks

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Gene Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>ABCDEFGH</td>
<td>None</td>
</tr>
<tr>
<td>Deletion</td>
<td>No rejoining, chromosomal segment lost</td>
<td>AB.FGH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>.CDEFGH</td>
</tr>
<tr>
<td>Duplication</td>
<td>Broken segment becomes attached to homolog that has experienced a break; homolog then bears one block of genes in duplicate</td>
<td>ABCDEFGHEFGH</td>
</tr>
<tr>
<td>Inversion</td>
<td>Broken segment reattached to original chromosome in reverse order</td>
<td>ABCFEDGH</td>
</tr>
<tr>
<td>Translocation</td>
<td>Broken segment becomes attached to a non-homolog resulting in new linkage relations</td>
<td>LMNOPQRCDSEFGH</td>
</tr>
</tbody>
</table>

3.7.1 Deletion

3.7.1.1 Mechanism of Deletion

Mutations that remove a portion of a chromosome are called deletions, or deficiencies. Deletions may be as small as a single nucleotide pair, or they may be almost as large as an entire chromosome. Large deletions can be detected cytologically, but small ones cannot. In a diploid organism, the deletion of a chromosome segment makes part of the genome hypoploid. This hypoploidy may be associated with a phenotypic effect, especially if the deletion is large. A classic example is the *cri-du-chat syndrome* (from French words for “cry of the cat”) in human beings. This condition is caused by a conspicuous deletion in the short arm of chromosome 5; about half of the arm appears to be missing. Individuals heterozygous for this deletion and a normal chromosome have the karyotype 46 (5p−), where the term in parentheses indicates that part of the short arm (p) of one
of the chromosomes 5 in missing. These individuals are severely impaired, mentally as well as physically; their plaintive cat-like crying gives the syndrome its name.

When a chromosomal fragment is missing at one end of the chromosome, it is called **terminal deficiency**. Very rarely, deletions occur through loss of the telomere at the tip of the chromosome. These terminal deficiencies are rare because the telomere is needed for proper chromosome replication and possesses bound proteins and looped nucleic acids that prevent binding to other chromosome. When a chromosome is broken into three segments and the two terminal fragments join, such a deficiency is called an **interstitial** (or intercalary) deficiency (**Figure 3.15**).

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**Figure 3.15**: Terminal and interstitial deficiencies.

### 3.7.1.2 Breakpoint Effects and Position Effects

Deficiencies may also produce a mutant phenotype because of **breakpoint effects**. For example, a chromosome break may occur within a gene, eliminating part of the gene and producing an altered gene product. Also, when a chromosome loses a segment, subsequent joining of the two ends may bring close together two regions of the chromosome and alter gene expression. Such a change is called a **position effect**. Position effects are known to occur when chromosome aberrations shift a gene to a new location, particularly when genes are moved adjacent to a region of heterochromatin. Position effects may give a mutant phenotype without altering the base sequence of the gene itself. A third type of breakpoint effect occurs when a deficiency is generated with breakpoints in two different genes. When the two ends are joined, a hybrid gene is generated with the 5’ region of one gene attached to the 3’ region of another. The hybrid gene may have novel properties that produce a mutant phenotype.
3.7.2 Duplication

Mutations that produce extra copy of a portion of a chromosome are called duplications. Like deletions, duplications may be as small as a single base pair or as large as most of a chromosome. Duplications are classified according to the location and arrangement of the extra material in the chromosome (Figure 3.16).

![Tandem, reversed, and displaced duplications](image)

Figure 3.16: Tandem, reversed, and displaced duplications.

When the duplicated segment of the chromosome is in the same sequence and adjacent to the original copy, it is referred to as a tandem duplication. However, if the extra chromosomal material is reversed in orientation, it is called a reverse tandem duplication. A dispersed duplication is an extra copy of genetic material in another location on the chromosome. Finally, a duplication may also exist as a small, free chromosome, but it must possess a centromere to be retained cell division.

3.7.3 Inversion

Inversions are changes in the order of genes in a chromosome. They result from a chromosome being broken at two locations, generating three fragments, and the internal fragment being reinserted to reverse order. Inversions are divided into two general classes, depending upon whether the centromere is included in the inverted region. If the centromere is included in the inverted region, an inversion is called a pericentric inversion. If the centromere is not included in the inverted region, an inversion is called a paracentric inversion (Figure 3.17). Both types of inversions change the order of genes in a chromosome. Because the genes in the inversion are
not lost, inversions usually affect only those genes at or very near the breakpoints. Inversion breakpoints may cause position effects.

![Diagram of Pericentric inversion and Paracentric inversion](image)

**Figure 3.17:** Pericentric and paracentric inversions. The chromosome has been broken at two points, and the segment between them has been inverted. A pericentric inversion (a) changes the size of the chromosome arms because the centromere is included within the inversion. By contrast, a paracentric inversion (b) does not because it excludes the centromere.

### 3.7.4 Translocation

When chromosome breaks occur in different chromosomes at the same time, the fragments may rejoin in the wrong combinations. Such exchanges of material between two nonhomologous chromosomes are called **translocations**. Two common types of translocations are **reciprocal translocations**, an exchange of the distal portions of two chromosomes, and **transpositions** (or interstitial transposition), which are the insertion of a portion of one chromosome into another (**Figure 3.18**). Translocation can produce mutant phenotypes by breakpoint effects and position effects similar to duplications or inversions. In addition, translocations alter the genetic linkage groups. For example, if two genes on one chromosome are normally linked and one gene is translocated to a new chromosome, the two genes will no longer be linked but will now show independent assortment.
The breakpoint/rejoin positions in translocations have been found to be the cause of a number of important human diseases, especially cancers. For example, chronic myeloid leukaemia is fundamentally a genetic disorder that is caused by a specific type of translocation in blood stem cells. This translocation is called the Philadelphia chromosome because it was first discovered in cases studied in Philadelphia. It involves a translocation between chromosome 11 (breakpoint q25) and 22 (breakpoint q13). This translocation is believed to be caused by exposure to mutagenic agents such as irradiation or benzene. The fact that only translocations between chromosomes 11 and 22 at these specific breakpoints cause chronic myeloid leukaemia indicates that the cancer results from a breakpoint effect that changes the activity of a gene or group of genes located at these positions.

**Normal Chromosomes**

\[ \begin{array}{cccccccc}
  a & b & c & d & e & f \\
  u & v & w & x & y & z \\
\end{array} \]

**Reciprocal Translocation**

\[ \begin{array}{cccccccc}
  a & b & c & d & y & z \\
  u & v & w & x & e & f \\
\end{array} \]

**Transposition**

\[ \begin{array}{cccccccc}
  a & b & y & c & d & e & f \\
  u & v & w & x & z \\
\end{array} \]

**Figure 3.18:** Reciprocal translocation and transposition.

**References**

3.8 Review Questions

1. How do the XX/XY sex determination mechanisms differ between humans and Drosophila? How are they similar?

2. Describe briefly how organisms with XX/XY or XX/XO sex-determination system solve the problem of equalizing the activity of X-linked genes in the male and female sexes.

3. Do males of all species have Y chromosomes? Explain your answer.

4. Briefly define each of the following and explain its significance to the study of genetics.
   (i) Autosome.
   (ii) SRY (Sry)
   (iii) Sxl
   (iv) Pseudoautosomal
   (v) Hemizygous

5. Describe briefly the mechanisms that compensate the numerical differences of x-linked genes in males.

6. What is haemophilia? What is the genetic basis of haemophilia?

7. Describe the genetic basis of colour blindness?

8. What is the molecular nature of a "fragile site" in a chromosome? What are the biological consequences of the fragile X syndrome.

9. Describe three different types of human sex chromosome trisomy. What is the sex in each case? What are the major phenotypic traits in each case?

10. Propose a possible genetic explanation for each of the following:
    (i) A human male with two X chromosomes and no Y chromosome.
    (ii) A human female with one X and one Y chromosome.

11. How does the pattern of inheritance of sex-linked genes differ from that of autosomal genes:
    (i) For recessive alleles?
    (ii) For dominant alleles?

12. How will the following differ in a ZZ/ZW system, compared to an XX/XY system?
    (i) Which will be the homogametic sex in each?
    (ii) Which sex will exhibit hemizygous expression of recessive genes in each?

13. Describe the process of sex determination in human being.

14. Describe the process of sex determination in Drosophila.

15. Describe the major differences between dosage compensation in Drosophila and humans.

16. If a male is heterozygous for a Z-linked trait, how will it be expressed in his female progeny. Describe a comparable phenomenon in an XX/XY system.

17. Distinguish between the following pairs in a manner that makes it clear that you know what each is and how they differ.
    (i) Euploid and aneuploid
    (ii) Triploidy and trisomy
    (iii) Autopolyploid and allopolyploid
    (iv) Breakpoint effect and position effect
    (v) Inversion and translocation

18. Give a brief definition of the following terms:
    (i) Haploidy
    (ii) Disomic
    (iii) Monosomic
    (iv) Trisomic
    (v) Double trisomic
    (vi) Double monosomic
    (vii) Tetrasomic
    (viii) Double tetrasomic
    (ix) Nullisomic
19. Human autosomal aneuploidies tend to cause very severe symptoms.
   (i) What mechanisms are responsible for the generally more severe effects of
       autosomal aneuploidies than are seen with sex chromosome aneuploidies.
   (ii) What is the only human autosomal trisomy that is likely to allow survival into
       adulthood.
   (iii) Identify two other human autosomal trisomies that sometimes result in live births,
       but with severe birth defects.

20. Briefly identify the genetic defect that is responsible for cri-du-chat syndrome.

21. Describe the genetic basis and syndromes of the following genetic disorder:
   (i) Down syndrome
   (ii) Patau’s syndrome
   (iii) Edward’s syndrome
   (iv) Turner syndrome
   (v) Klinefelter syndrome

22. What do you understand by 47,XYY karyotype?

23. Why are allotetraploids more likely to be fully fertile than autotetraploids?

24. Describe a process for the experimental generation of an allotetraploid from a cross-
    species hybrid.

25. Does the chromosome number of an allotetraploid have to be an even multiple of four?
    Explain your answer.

26. What is the agricultural significance of allopolyploids?

27. A fertile allopolyploid plant with a chromosome number of 38 is crossed with one of its
    parent species. Do you expect the progeny to be fertile? Explain your answer.

28. Does the formation of an allotetraploid between two plant species insure that the most
    desirable properties of both will be found in the allotetraploid? Explain the reasoning
    behind your answer.

29. What approach would you use to attempt to construct an allotetraploid from two plant
    species that are not capable of cross pollination? Describe the steps that are involved.

30. What problems stand in the way of fertility of triploid plants?

31. Define the following terms:
   (i) Tandem duplication
   (ii) Pseudodominance
   (iii) Paracentric inversion
   (iv) Reciprocal translocation
   (v) Translocation heterozygote

32. Explain how a deletion mutation can cause partial hemizygosity.