SUMMING-UP

1 The human genome

- An individual's set of genes constitutes their **genome**. In humans it is organised into 23 pairs of chromosomes and is present in all somatic cells.
- The image of the chromosomes obtained during the mitosis metaphase, when the DNA is compacted, is called a **karyotype**. The first karyotype was obtained in 1956 and today karyotyping is the first step in any analysis regarding the genetic heritage of an individual.
- The human genome has been the subject of a research project that led to the determination of the entire sequence of bases that make up our DNA.
- The comparison of the human genome with that of other species has revealed that the species genetically closest to ours is that of the chimpanzee.

2 Point mutations

- Although the process of DNA replication is a very precise mechanism, it may encounter errors that cause a change in the nucleotide sequence, called a **mutation**.
- Depending on whether this involves a body's germ cells or somatic cells, these mutations are distinguished as **germline** or **somatic** mutations.
- Mutations can involve highly variable portions of the genome: when an error involves only a single nitrogenous base in a DNA sequence, and therefore only one gene, it is called a **point mutation**.
- Point mutations may include the replacement, deletion or insertion of a nitrogenous base in the nucleotide sequence.

3 Chromosomal abnormalities

- Chromosomal alterations involve long portions of DNA and are of two types:
  a) chromosomal mutations; and
  b) genomic mutations.
- **Chromosomal mutations** are alterations of a segment of DNA that may be deleted, duplicated or undergo a change of position. There are four forms of chromosomal changes:
  – deletion;
  – duplication;
  – inversion;
  – translocation.
- **Genomic mutations** consist of a variation in the number of chromosomes compared to the norm: a body's karyotype is composed of more or less chromosomes than the typical number for the species. Genomic alterations are the basis of some diseases that affect humans, such as Down syndrome.

4 Autosomal genetic diseases

- There are many diseases of genetic origin caused by DNA mutations.
- In general, an error in DNA replication causes a change in the encoded protein, which is then unable to function. The following situations are possible.
  – If the **allele** is **recessive**, it is manifested in the phenotype of homozygotes that have been affected by the disease. Some diseases also occur in the heterozygote when the protein produced by a single allele is not quantitatively sufficient to ensure a normal situation. There are also cases in which heterozygotes are not affected by the disease. However, since they have a copy of the mutant allele, they can be transmitted to offspring, and for this reason are called **carriers**. Some examples of such diseases are: phenylketonuria, albinism, cystic fibrosis and sickle cell anaemia.
  – If the **allele** is **dominant** it is manifested in the phenotype of all individuals who possess it (both heterozygous and homozygous). Huntington's disease, achondroplasia dwarfism, and hypercholesterolemia are diseases of this type.

5 Genetic diseases related to sex chromosomes

- Genes carried on sex chromosomes (X and Y) determine characters called **sex-linked characters**.
- A particularly important aspect of the transmission of characters carried on sex chromosomes concerns genetic diseases caused by *recessive alleles carried by the X chromosome*, such as colour blindness and haemophilia.
- These types of disease have a different frequency depending on the individual's gender; males in particular are more prone to phenotype disease.

6 Spontaneous and induced mutations

- DNA mutations can occur spontaneously, i.e. without the intervention of external causes, or may be determined by factors external to the cell, called **mutagens**.
- Mutagens are chemical substances, radioactive materials, X-rays, ultraviolet rays from the sun, etc.
- Spontaneous mutations are events that occur very rarely: on average, in eukaryotic cells, a mutation occurs once in every 10^4 to 10^9 duplicated base pairs. Generally, these point mutations, involve the replacement, addition or elimination of a nucleotide during the synthesis of a new DNA strand.
- When a cell is exposed to mutagenic agents the frequency of mutations greatly increases.