GENETICS

Key words

Genetics is the study of how hereditary characters are transferred from one individual to another. Let's review some basic concepts which are fundamental for a better understanding of the unit.

NUCLEIC ACIDS

Nucleic acids are macromolecules composed of monomers called **nucleotides.** (Composed of C, H, O, N and P) There are two types of nucleic acids: **ribonucleic acid (RNA)** and **deoxyribonucleic acid (DNA)**. All living organisms contain both types of nucleic acids. Viruses (which as you should remember are not considered to be living organisms) only contain one type of nucleic acid.

Nucleotides:

A nucleotide is composed of three parts:

1. A **phosphate group** (P)
2. A pentose (a five-carbon monosaccharide), which can be: **ribose (R)** or **deoxyribose (D).** Nucleotides which contain a ribose are called **ribonucleotides**, and those which contain a deoxyribose are called **deoxyribonucleotides.**
3. A nitrogenous base: **adenine (A), guanine (G), cytosine (C), thymine (T) and uracil (U).** The first three bases are common to both types of nucleotides. In ribonucleotides, the fourth base is always uracil (never thymine); while in deoxyrybonucleotides the fourth base is always thymine (never uracil).

The bond between the sugar molecule and the nitrogenous base is called a **nucleoside.**

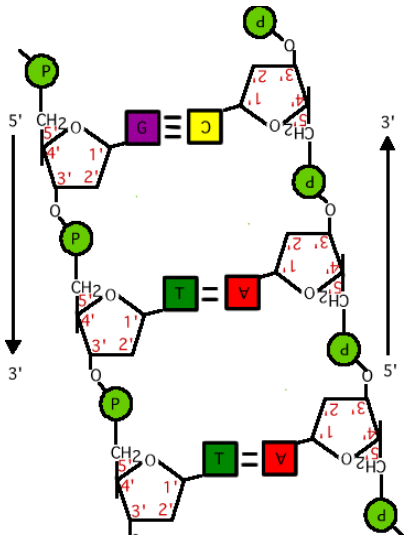
Within cells there are other types of nucleotides which do not make up nucleic acids. Among these types of nucleotides ATP (adenosine-triphosphate) stands out.

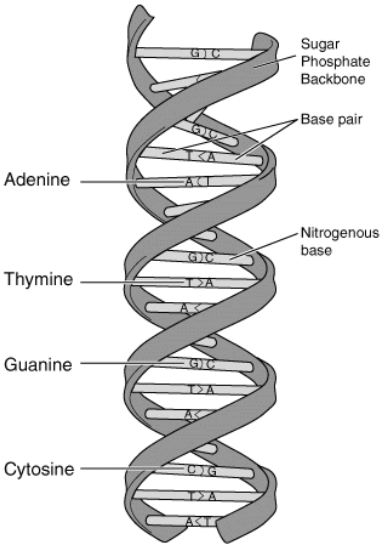
Two nucleotides joined together gives rise to a dinucleotide. Many nucleotides joined together form a **polynucleotide**. Nucleic acids are polynucleotides. RNA is a polynucleotide made of ribonucleotides, whilst DNA is a polynucleotide made of deoxyribonucleotides.

DNA

Deoxyribonucleic acid is found in the nucleus of eukaryotic cells, and in the cytoplasm of prokaryotic cells (we will see this later on). It consists of two polynucleotide chains or strands, as they are called, that spiral around an imaginary axis to form a double helix (a spiral staircase shape). The two strands of the double helix are **complementary** to each other. Only certain bases are compatible with each other: Adenine will only fit

next to Thymine and Cytosine will only fit next to Guanine. Therefore, if in one of the strands there is an adenine, in the other strand there will be a thymine, and vice versa. In the same way, when in one strand there is cytosine, in the other there will be guanine, and vice versa.





(Scheme taken from http://www.ageds.iastate.edu/meat/images/dna2.gif)

Additionally, the two strands are **anti parallel** to each other; one is inverted with respect to the other. One of them goes from 5' to 3' while the other from 3' to 5'. This double helix structure described by Watson and Crick is very stable due to the hydrogen bonds between the nitrogenous bases: 2 hydrogen bonds between A and T, and 3 hydrogen bonds between G and C.

Function: DNA is the most important molecule in living organisms since it contains the genetic material of the organism, which will also be transferred to its descendants. DNA is the main component of chromosomes which are long coils of double-stranded DNA, which contain the genes. A gene is a portion of DNA- of chromosome- responsible for a particular hereditary character (the unit of hereditary information); or, as we will see later on, responsible for protein synthesis. Each gene determines the synthesis of a particular protein.

RNA

Ribonucleic acid is a single-stranded polynucleotide molecule. There are three types of RNA in living organisms: ribosomal RNA (rRNA), transfer RNA (tRNA) and messenger RNA (mRNA).

Function: the function of RNA is to aid in protein synthesis, and therefore in the expression of the genetic information encoded in DNA.

THE GENETIC INFORMATION

As we have already said, the genetic information is found in the DNA. But, how? This information is encoded in a particular **sequence** or order of its nucleotides. You could compare it to the order of the letters in a sentence. Every living organism is characterized and defined by a determined order of such nucleotides.

The information encoded in DNA is organized in small units called **genes**. A gene is a portion of DNA that carries the information for a particular character of an individual (e.g. eye color). Genes are located one after another along the filaments of DNA. Each DNA filament is a **chromosome.** In the nucleus of each and every cell of an organism there are a determined number of chromosomes. Each species of organisms has its own number of chromosomes, which will be the same in all of its cells, with the exception of sex cells or gametes. (Gametes contain half the number of chromosomes than the rest of the cells). For example, we humans have 46 chromosomes inside each of our cells (23 pairs). A chimpanzee has 48 chromosomes (24 pairs) inside each of its cells etc. Therefore, all genes a species contains are found in the chromosomes (the entire set of genes of an organism is its **genome**). In humans, each cell contains about sixty thousand genes (60 000), which are located throughout the 23 pairs of chromosomes. The genetic information of those genes is exactly the same in each cell of the individual. However, not all cells in our body are the same nor do they carry out the same functions. That is because not all of these genes are used by any one cell at any one time. Just a few genes will be 'switched on' in any one cell at any one time and the rest of the genes remain 'switched off'. For example, a nerve cell will express a set of genes that will not be expressed in a muscle cell and vice versa.

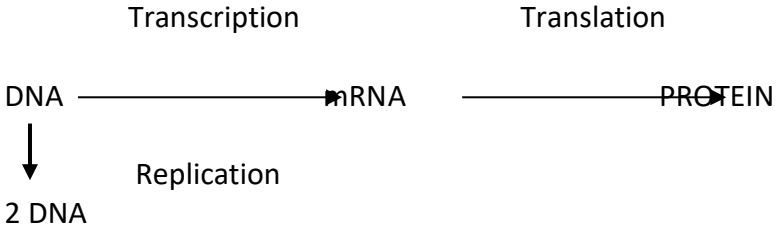
How is the genetic information expressed?

We have said that each gene – portion of DNA- contains the information of a particular character, such as eye color. Now, how can a piece of DNA, with its particular nucleotide sequence, have information to determine that a person will have, for example green eyes? The answer lays in proteins; which are the molecules that carry out cellular functions. What genes really have are chemical instructions for protein synthesis. Each gene determines the synthesis of a particular protein. As we will see later on, the synthesized protein will be responsible for the expression of that particular character, such as the green-colored eyes (refer to protein synthesis).
As we have seen, in order for the genetic information contained in genes (in DNA) to be expressed, such information must be passed down to proteins. Proteins are synthesized in the ribosomes, which are in the cytoplasm of the cell, so the information must somehow get to them. This process, known as protein synthesis, is carried out with the aid of other molecules (mRNA, rRNA and tRNA), and it has two steps (phases):

1st **Transcription**: the information contained in the DNA –in the gene- is transferred to a molecule of mRNA (transcription takes place in the nucleus of the cell). The mRNA leaves the nucleus taking the information to the cytoplasm of the cell.

2nd **Translation**: Once in the cytoplasm the mRNA joins with the organelles known as ribosomes, which will translate the information into a protein. There will be a different protein for each gene and each protein will be responsible for a particular character of the individual- green colored eyes-.

This is the first property of DNA,- transcription and translation- and it is the process by which the genetic code is expressed.



Additionally, DNA presents another property only present in living organisms; it can make copies of itself: **replication.** It is thanks to this property that a cell can divide and make two daughter cells that are identical to each other and identical to the mother cell.

Sometimes, when DNA replicates **mutations** or alterations of the information take place. These mutations are responsible for the introduction of new characters in organisms, which with time, will lead to the evolution of the species.

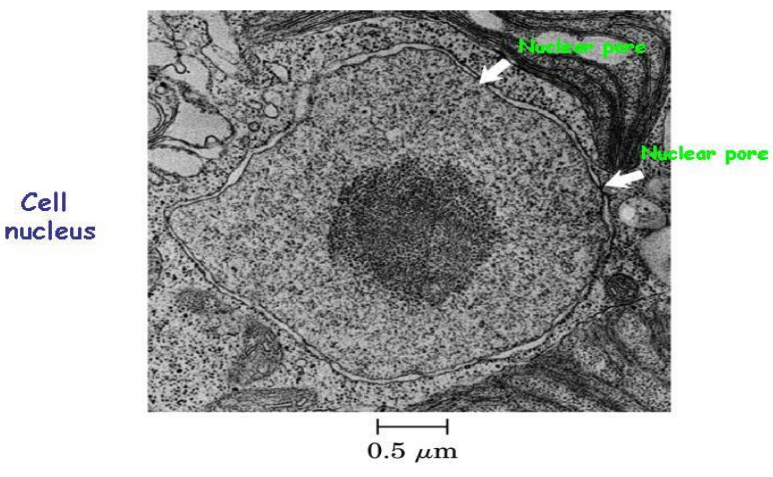
THE NUCLEUS AND THE CHROMOSOMES

Prokaryotic cells do not have a true nucleus, therefore, the genetic material is found floating in the cytoplasm of the cell. Additionally, the DNA of prokaryotes doesn't condense into chromosomes. Therefore, the following information refers only to eukaryotic cells.

Structure: The genetic material (the DNA) is found in the nucleus. It is composed of: *A **nuclear envelope** which encloses the nucleus, separating its contents from the cytoplasm. It is a double membrane perforated by pores that regulate the entrance and exit of certain large macromolecules and particles (nucleus-cytoplasm). *A liquid known as the **nucleoplasm.** *The **nucleolus**, roughly spherical and which function is the synthesis of ribosomes. *The **chromatin**, long thin fiber of DNA associated to proteins. (Only when the nucleus prepares to divide does the DNA condense into chromosomes).

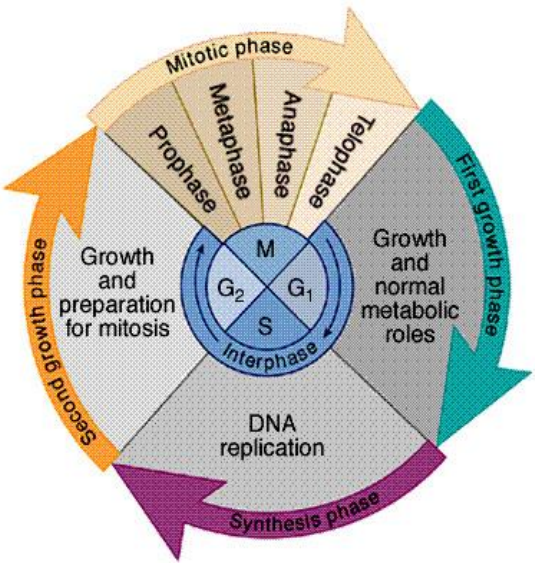
Some cells can have more than one nucleus (muscle cells) and sometimes a nucleus can have more than one nucleolus.

Function: The nucleus controls all cellular



processes, as it contains the DNA with the genetic information of the cell. The nucleus controls protein synthesis in the cytoplasm by sending molecular messengers in the form of RNA. The mRNA is synthesized in the nucleus according to the instructions provided by the DNA (transcription). The mRNA leaves the nucleus via the nuclear pores and once in the cytoplasm it attaches to ribosomes, and the genetic message is translated into proteins. Proteins will carry out the different cellular functions (enzymes that catalyze me-tabolic reactions, transport of substances, etc.).

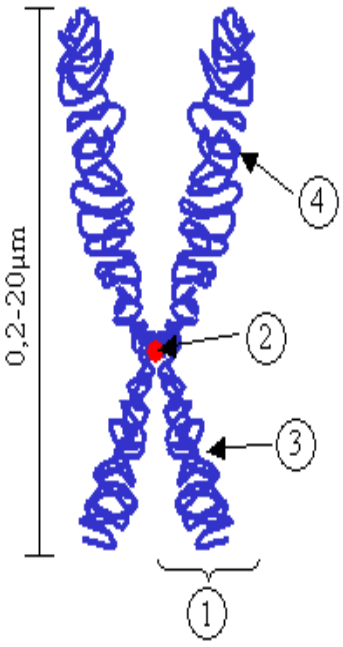
(Scheme taken from http://www.science.org.au/sats2004/images/kobe7.jpg)



Chromosomes and the cell cycle

The cell cycle is the period that goes from the moment the cell has just been formed (from the division of the mother cell into two), to the point where the same cell divides in two daughter cells. The period when the cell is not dividing is called **interphase**. Therefore, the cell cycle consists of two successive **mitotic divisions** alternated with a much longer **interphase** or growth period. Interphase consists of three periods of growth, the first period is called G1, followed by the S phase, during which the chromosomes replicate; and the last part of the interphase is called the G2 phase. This is followed by cellular division (mitosis divides the nucleus and its chromosomes, and cytokinesis divides the cytoplasm, producing two daughter cells).

(Scheme taken from http://bhs.smuhsd.org/bhsnew/academicprog/science/vaughn/Student%20Projects/Paul%20&%20Marcus/cycle.jpg)



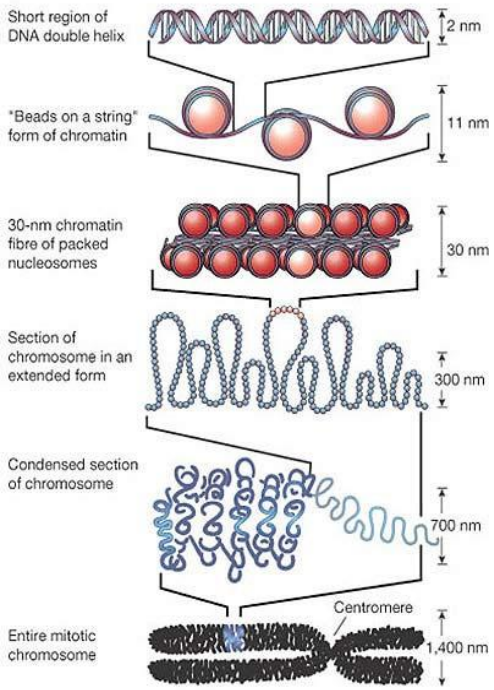


Figure 1: Chromosome. (1) Chromatid. One of the two identical parts of the chromosome after S phase. (2) Centromere. The point where the two chromatids touch, and where the microtubules attach. (3) Short arm. (4) Long arm.

(Schemes taken from http://www.biocrawler.com/encyclopedia/Chromosome and http://home.planet.nl/~gkorthof/images/chromosome_structure.jpg

During the interphase the long filaments of DNA-protein complex called **chromatin** are spread through the nucleus. The proteins associated with the DNA are called **histones.** During all three phases of the interphase the chromatin is transcribing itself (therefore synthesizing RNA, mRNA, t and r). It is an active period. However, when the cell is getting ready to divide, the chromatin condenses into compactly folded and coiled **chromosomes**. These chromosomes now do not transcribe. The cell copies its entire genome by duplicating its chromosomes during the S phase, after replication each chromosome consists of two **sister chromatids** (each a collection of the same genes present in single copy prior to replication). The sister chromatids are held together by a structure called the **centromere**. The end parts of a chromosome are called the **telomeres**.

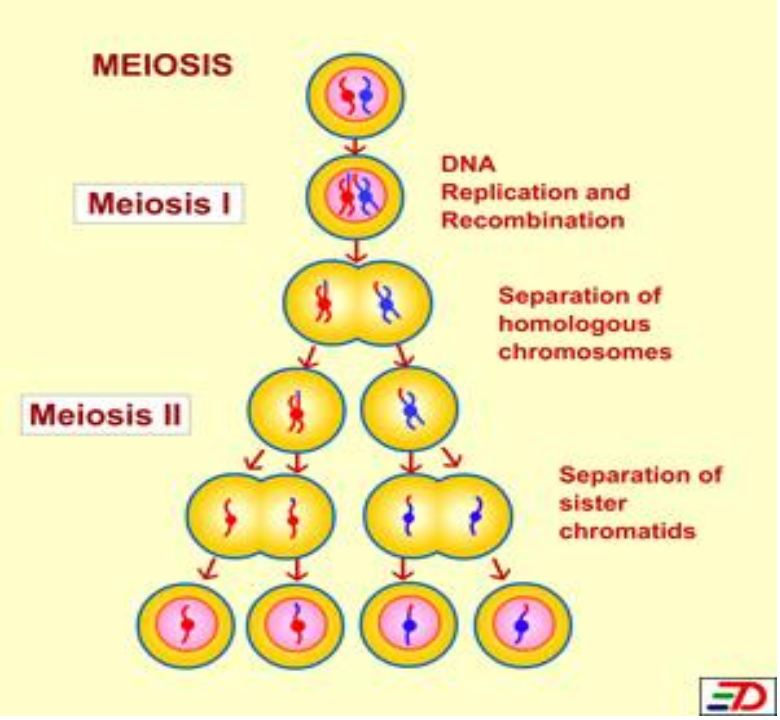
Once cellular division has come to an end, each daughter cell has one sister chromatid from every chromosome (see mitosis later on) so both daughter cells carry identical information. As the interphase starts in each of the new daughter cells, chromosomes start to uncoil going back to the thin fiber chromatin. The chromatin is so thin it can not be seen very well. It starts again to transcribe, then during the S phase it replicates to be ready for the next mitotic division.

The majority of the cells of an organism are **diploid (2n)**; they have two sets of chromosomes. Chromosomes go in pairs (**homologous**), of the same size and shape, and have the same information for the same characters but they are not identical. In a particular place of a chromosome (the same place for both of the pair) we will find the information for hair colour, but in one chromosome we could have the allele for black hair and on the homologous chromosome the allele for blond hair. Each homologous chromosome comes from one of the parents. To summarize, we can say that a diploid cell has **2n chromosomes**, where n indicates the number of one set of chromosomes. This number is characteristic of each species.

Let's use humans as an example. In all normal body cells (somatic cells) we have 2n chromosomes as these cells are diploid (2n is 46, therefore, n is 23). However, the number of chromosomes in a **gamete** – sperm and ovum- is the **haploid number n.** Cells that are haploid only have one set of chromosomes. When fertilization takes place during sexual reproduction, two haploid gametes fuse together to restore the diploid number in the zygote (46 in humans).

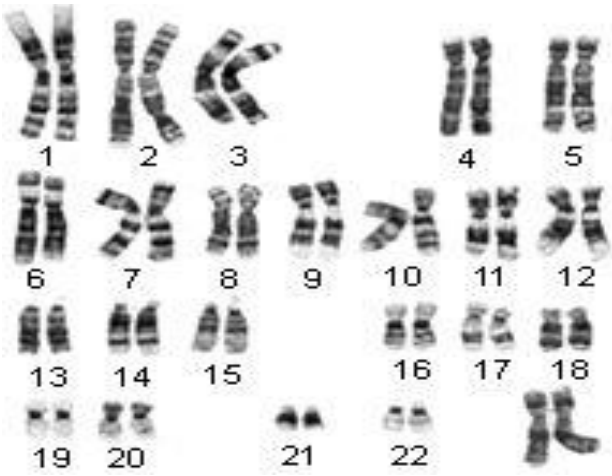
When normal body cells – somatic cells- divide, they do it through a process known as **mitosis**. First of all, cells will replicate their DNA, their chromosomes. Therefore, they will have 4n chromosomes (92 in humans) and then 23 homologous pairs will go to each new daughter cell. Therefore, daughter cells are identical to each other and to the mother cell (all diploid cells).

However, sex cells, those that make gametes, divide through a process known as **meiosis**. Again they will first replicate their DNA, having 4n chromosomes, but they undergo two divisions. From the first division 2 cells are formed each having 2n chromosomes, which again divide resulting in a total of four haploid cells (n), each different from the other and different from the mother cell. When gametes fuse during fertilization, the characteristic 2n of the species is restored.



(scheme taken from http://www.moe.gov.sg/edsoftware/ir/files/bio-meiosis/images/introduction/image3a.jpg)

In mammals and other living organisms there is a chromosome pair that determines the sexual characteristic of the individual. These are called **sex chromosomes X and Y.** Females have two X chromosomes and males have an X and a Y chromosome. The rest of the 44 chromosomes (in humans) are called **autosomes (autosomal chromosomes).** The group of chromosomes of a cell is the karyotype. Chromosomes can be classified by their homologous pair, and ordered by size and shape. The order obtained is called an **idiogram**. Using specific staining techniques, **banding** of chromosomes is obtained which allows us to pair the homologous chromosomes, as well as to group them by decreasing size. This also allows us to determine some genetic diseases.



(scheme taken from http://www.colblindor.com/wp-content/images/karyotype.jpg)

CELLULAR REPRODUCTION

Cells reproduce by **cellular division**. This process is called **mitosis** in eukaryotes, and **binary fission** in prokaryotes. This process gives rise to two daughter cells that are genetically identical to each other and to the mother cell. (Refer to the **cell cycle**).

For unicellular organisms, the cell cycle represents their life cycle, therefore, when the cell divides a new organism is produced. On the other hand, in multicellular organisms, the division of individual cells allows for growth of the organism, repair of damaged tissues, etc, but in order for the organism to reproduce it needs to make gametes; special cells that are produced through a division process called **meiosis**.

As we have already seen in the cell cycle, in order for the cell to divide it needs to replicate its genetic material (DNA), which happens during the S phase.

Reproduction in prokaryotes

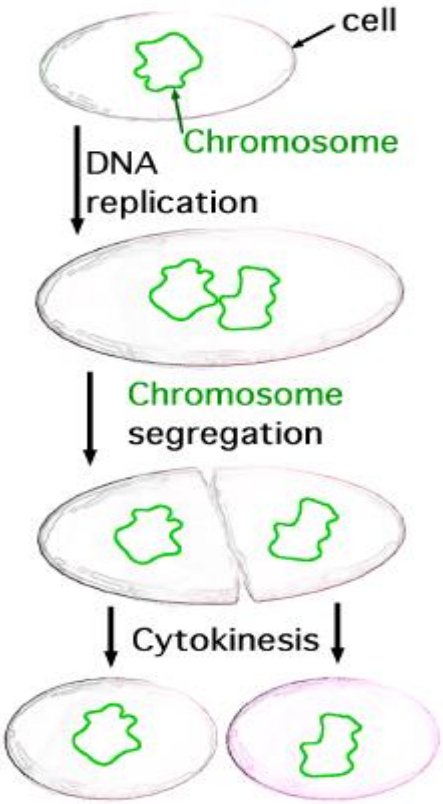
A scheme of reproduction by binary fission:

1. Bacterial chromosome or DNA **replication.**
(Each circular strand of DNA then attaches to the plasma membrane).

2. The cell elongates causing the two **chromosomes** to separate to opposite sides of the cell.

3. The **plasma membrane pinches inward** (invaginates) to divide the cell in two.

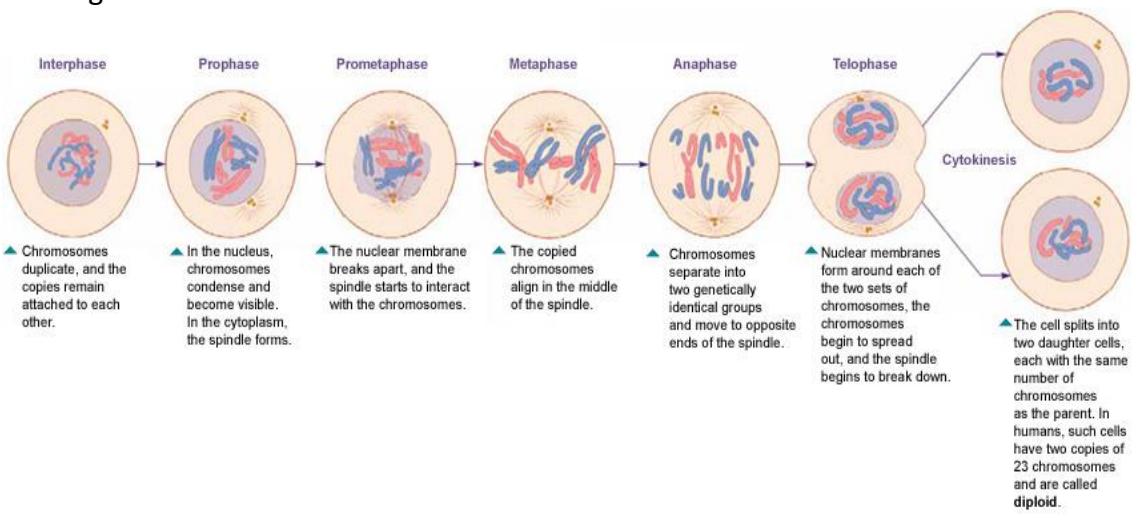
4. Two **daughter cells** are formed that start to grow starting a new cycle.



(scheme taken from http://www.biocrawler.com/w/images/0/00/Binary_fission.png)

Cellular division in eukaryotic cells: Mitosis

Cellular division in eukaryotic cells consists of two phases: first the nucleus divides (**mitosis**) and then the cytoplasm divides (**cytokinesis**). The following scheme shows the stages of mitotic cell division in an animal cell.



(scheme taken from http://images.google.es/imgres**)**

Differences with plant cells:

a. There are no centrioles in plant cells.

b. Cytokinesis, in animal cells occurs by a process known as cleavage, where the formation of a cleavage furrow pinches the cell in two. However, cytokinesis in plant cells, which have walls, is very different. A structure called the cell plate made of cellulose will separate both daughter cells. The cell plate will later give rise to the new cell wall.

SUMMARY: mitosis is a cell reproduction process by which multicellular organisms regenerate lost or damaged cells, or simply make new cells. In the case of unicellular organisms it can be considered as asexual reproduction. **It does not generate genetic variability,** as the new daughter cells are identical to each other and to the mother cell. This is how all somatic cells divide (epithelial cells, liver cells, etc. All but sex cells).

Meiosis

Concept: it is a type of cellular division **needed** in organisms with sexual reproduction. In sexual reproduction, there is **fertilization**, which is the fusion of haploid gametes to restore the diploid number in the zygote. The zygote, by successive mitotic divisions gives rise to the multi-cellular organism, which cells are therefore diploid, all containing identical genetic information.

If the gametes were also produced by mitosis, these would be diploid and genetically identical. During fertilization, the fusion of these diploid gametes would produce a tetraploid (4n) zygote, which would give rise to 4n organisms. In the same line, these

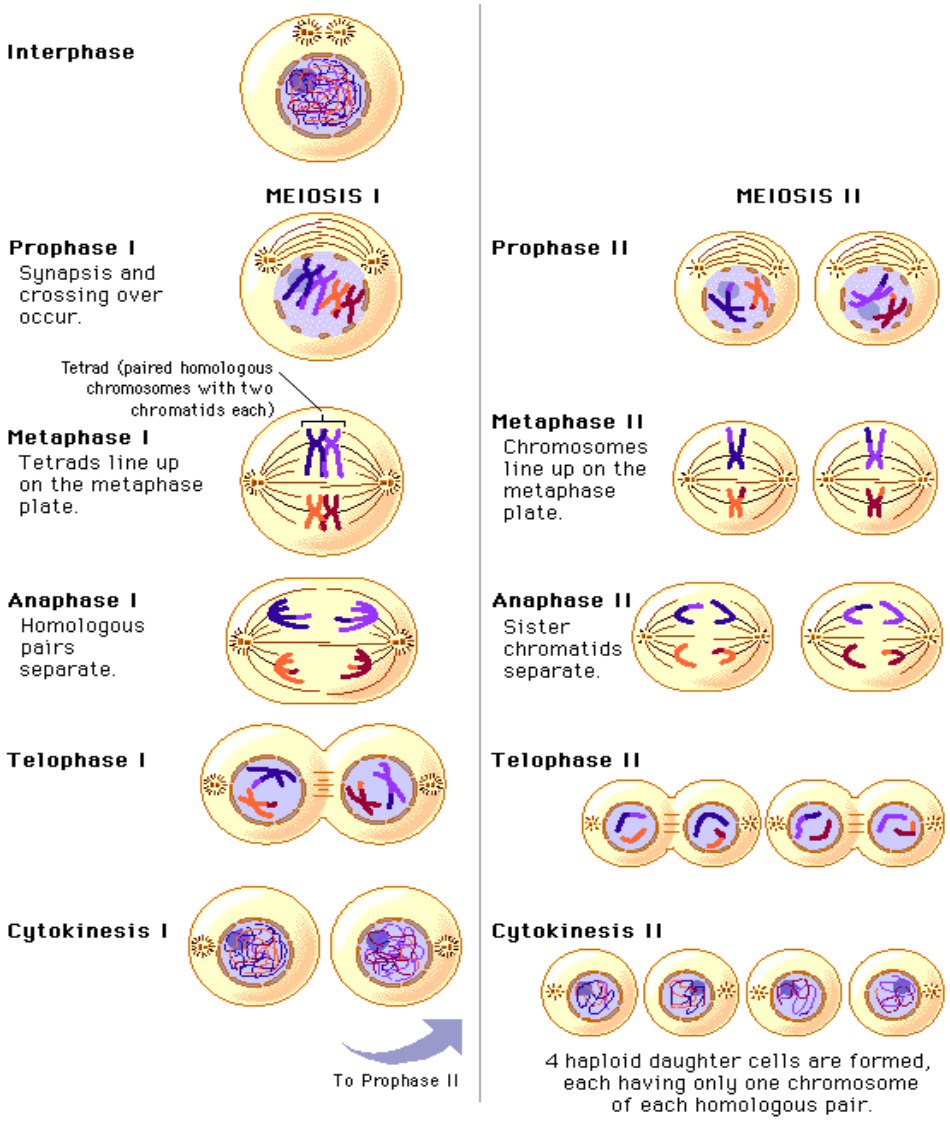
4n organisms would produce 4n gametes…. and so on. In each generation the number of chromosomes of the species would be doubled. Therefore a mechanism of cell division is needed where the number of chromosomes is reduced (halved): going from 2n cells to n cells. This process is meiosis.

Besides being necessary, meiosis is very beneficial, as it generates **genetic variability**: the daughter cells are different from each other and also different from the mother cell.

Process: meiosis (like mitosis) is preceded by the replication of chromosomes or DNA. However, this single replication is followed by **two** consecutive cell divisions, called meiosis I and meiosis II. These divisions result in four daughter cells (rather than the two daughter cells of mitosis), each with only half as many chromosomes as the parent.

Meiosis I: consists of prophase I, metaphase I, anaphase I and telophase I.

During **prophase I** homologous chromosomes, each made up of two chromatids, come together as pairs (forming a tetrad, a complex of four chromatids). At numerous places along their length, nonsister chromatids (chromatids belonging to homologous chromosomes, in contrast to sister chromatids belonging to the same chromosome) are **criss-crossed** and **recombined**. As a result of these crossings, mixed chromatids are formed with fragments from the mother and the father chromosomes (this is the first source of variability in meiosis).



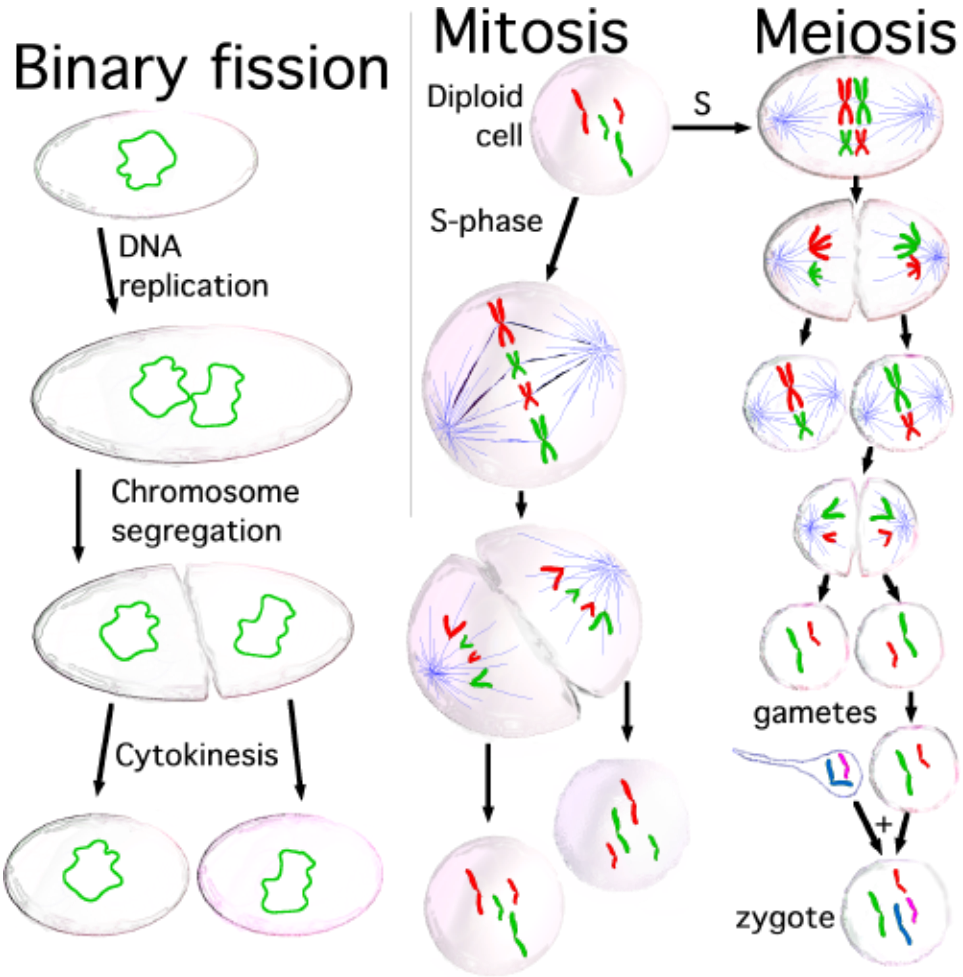
(scheme taken from http://www.phschool.com/science/biology_place/labbench/lab3/images/stages2.gif)

During **metaphase I**, the homologous pairs are randomly arranged on the metaphase plate: sometimes the paternal chromosome is on the right and the maternal on the left and it could also be the other way around. This way many different and diverse combinations can happen (this is the second variability source of meiosis: for example, a new daughter cell could have chromosomes 1, 2', 3, 4, 5' etc, while the other would have 1', 2, 3', 4', 5 etc).

In **anaphase I** and **telophase I** the homologous chromosomes migrate toward the opposite poles of the cells. Segregation of chromosomes (each pole now has a haploid chromosome set, but each chromosome still has two chromatids) and finally cytokinesis, usually occurring simultaneously with telophase I forms two daughter cells each with only one of the homologous chromosomes.

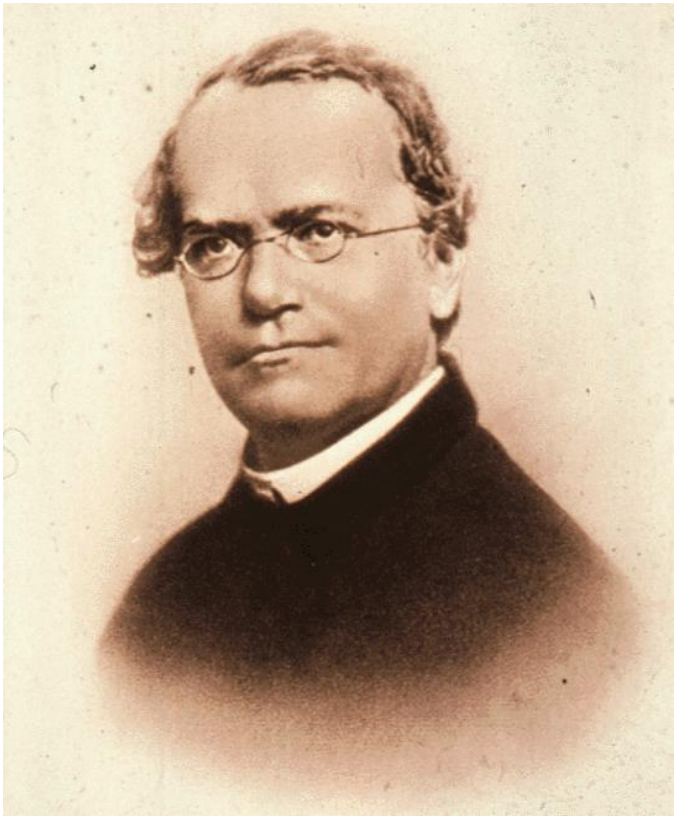
There is no further replication of the genetic material prior to the second division of meiosis II.

During the 2nd meiotic division, the two chromatids of each chromosome separate into the daughter cells in a very similar way as mitosis. At the end of meiosis II there will be four daughter cells, each with the haploid number (n) of chromosomes and genetically different from one another and from the mother cell (genetic variation).
SUMMARY: meiosis is a cellular division necessary for organisms with sexual reproduction. Meiosis reduces the number of chromosomes by half (which will be restored during fertilization) and allows for genetic variation (the daughter cells are genetically different from each other, and also from the mother cell).



CONCEPT: Genetics is the branch of biology which studies not only how hereditary traits (such as physiological, anatomical, behavioral, etc) are transferred, but also, the mechanisms responsible for their transmission. It studies the hereditary information in living beings and how the traits of a living being are transferred to the next generation.

MENDELIAN GENETICS



Gregor Mendel, the father of genetics, was an Austrian monk that lived in the XIX century. He worked on the transmission of the characters of pea plants through successive generations. Gregor Mendel discovered the basic principles of heredity by breeding garden peas in carefully planned experiments. Mendel spoke of *heritable factors.* The concepts of gene and chromosome came later. Walter Sutton and Theodore Boveri in 1903 proposed the *chromosome theory of inheritance.* And thanks to the works of Watson and Crick about the nature of DNA, it was proven that the heritable factors (the genes) were in fact DNA fragments.

http://www.jic.ac.uk/germplas/pisum/zgs4f1.gif

These are the main concepts that you should know:
GENE: there are different ways to define a gene. If we are talking about classic or Mendelian genetics, we will define a gene as a sequence of nucleotides (usually a DNA fragment, but in viruses composed of RNA it is an RNA fragment) that contains information for a particular character, e.g. the gene that determines eye colour. (Geneticists use the term character for a heritable feature, such as eye colour, that varies among individuals. Each variant for a character, such as brown or blue, is called a trait).

A more complete definition of a gene is:
A sequence of nucleotides to which a specific function can be assigned. Examples of such functions: a) control of the expression of a particular character; b) coding of a specific polypeptide chain (the transcription of itself into mRNA and the following translation into a polypeptide chain in the ribosomal unit); that it transcribes to tRNA; d) transcription to rRNA.

Each gene occupies a specific position on a chromosome called its **locus** (loci –plural). Genes are passed down from parents to offspring (via the gametes) during sexual reproduction. Each gamete has one set of chromosomes (they are haploid). Fertilization between a male and a female gamete gives rise to a zygote, with two sets of chromosomes (diploid). The individual from that zygote will also have two sets of chromosomes (also diploid). E.g. Humans have 23 chromosomes in their gametes or sex cells (ovum and sperm). The rest of the cells of our body have 23 pairs (46) of chromosomes.

HOMOLOGOUS CHROMOSOMES are a pair of chromosomes having the same structural features. Each member of the pair of chromosomes has the same number and pattern of genes. The genes found in the same locus on both chromosomes carry information for the same character, but may have different alleles.

ALLELE (OR ALLELOMORPH): An allele is an alternative form that a gene can have due to successive mutations. They are found in the same locus in each homologous and carry information for the same character, e.g. the gene that determines straight hair and that which determines curly hair. A gene can have multiple alleles, but diploid organisms can only have two of those, as we have our chromosomes in pairs.

HOMOZYGOUS (TRUE-BREED): An organism which has a pair of identical alleles for a certain character is said to be homozygous for that character. Normally genes are represented by letters, so a homozygous organism will have the same letters (AA, aa, BB, etc)

HETEROZYGOUS (HYBRID): Organisms having different alleles for a character. E.g. Aa, Bb, etc.

COMPLETE DOMINANCE (DOMINANT HEREDITY): In all hybrid individuals an allele (the dominant allele) for a particular character, is fully expressed, and the other allele or recessive allele has no noticeable effect on the organisms appearance.

CODOMINACE: Neither allele is dominant or recessive. Instead both alleles are separately (equally) manifested in the phenotype. E.g. human blood type group AB.

INCOMPLETE DOMINANCE: It is characterized by an intermediate phenotype. For example the pink flowers of snapdragon hybrids.

GENOTYPE: It is the genetic information of a particular organism as specified by its alleles. The genotype is hereditary, as progenitors pass it down to their offspring, e.g. AaBb, etc.

PHENOTYPE: It is the observable characteristics of an organism produced by the interaction of its genes and the environment which surrounds its development. E.g. Black hair, blue eyes, etc. e.g. how the environment influences the phenotype of an individual: in the Himalayan rabbits, the genotype determines the presence of an

enzyme which, at low temperatures, makes a dark pigment that affects certain body parts (nose, legs, tail etc) If the animal moves to a warmer place, the pigmentation in such places disappears.

MENDEL'S LAWS

MENDEL'S FIRST LAW

Experiment

Mendel chose garden pea plants for his experiments (*Pisum sativum).* He observed and followed seven characteristics (which he could easily control as each characteristic only had two possibilities: tall and dwarf plants (stem length), green or yellow seed, round or wrinkle seed shape, etc).

Mendel also made sure that he started his experiments with varieties that were true-breeding (which means that when the plants self-pollinate, all their offspring are of the same variety). In a typical breeding experiment, he would cross-pollinate between two contrasting, true -breeding pea varieties: for example between tall and dwarf plants. This mating or crossing of two varieties is called hybridization. He observed that in the F1 generation (hybrids) all the offspring were tall plants. The character for dwarf plants did not show up. Mendel called the **dominant allele** the feature fully expressed in the hybrids and the **recessive allele** the feature that did not show up in the hybrids. From this experiment he derived (came up with) his first law:

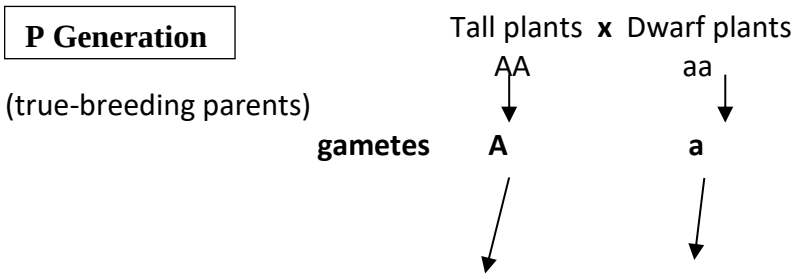
Law of Uniformity of the first filial generation

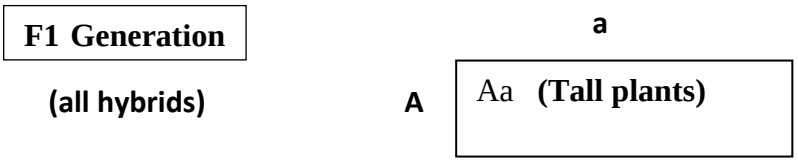
If two homozygous individuals (P generation) for a single pair of alleles but with different expression, cross themselves, all the descendants from the first generation, (which will be denominated by hybrids F1), will be identical (both, in their genotype and phenotype).

In other words: when the crossover between individuals pertaining to true-breeding of the same species is made, all the hybrids of the first filial generation are alike.

Interpreting the experiment

Let's call A the allele that determines tall plants and a the allele that determines dwarf plants. As this cross is carried out between two contrasting, true-breeding pea varieties, the P generation will be AA and aa. Homologous chromosomes segregate (separate) during gamete formation. All gametes produced by tall plants will carry the allele A, and all gametes produced by dwarf plants will carry the allele a. After fertilization, alleles A and a will join in the zygote and the new plant will carry alleles Aa. Therefore, all of the F1 offspring will be hybrids. Since all plants in F1 were tall plants, that means that allele A (tall plant) was dominant to allele a (dwarf plants), which is the recessive allele.





Expected genotypic proportions: 100% Aa; expected phenotypic proportions: 100% tall plants.

Extending Mendelian Genetics: In this century, geneticists have extended Mendelian principles to patterns of inheritance more complex than Mendel actually described. It was either brilliant or lucky that Mendel chose pea plant characters that turned out to have a relatively simple genetic basis. Each character is determined by one gene, for which there are only two alleles, one completely dominant to the other recessive. However this is not always the case, these conditions are not met by all heritable characters. So we will extend Mendelian genetics to patterns of inheritance that were not reported by Mendel.

It was later demonstrated that although complete dominance is fairly common, there are other possibilities. The range of relationship between alleles includes complete dominance, codominance and different degrees of incomplete dominance. In incomplete dominance, the F1 hybrids have an appearance somewhere in between the phenotypes of the two parental varieties. For example when red snapdragons are crossed with white snapdragons, all the F1 hybrids have pink flowers.

MENDEL'S SECOND LAW

Experiment

Mendel took the plants from the F1 and self-pollinated them producing an F2 generation. He observed that all the traits that were lost in the F1 reappeared in the F2 generation. So in the F2 generation he observed both, tall and dwarf plants (Mendel observed the same pattern of inheritance in the other characters with which he experimented). He therefore derived his second law:

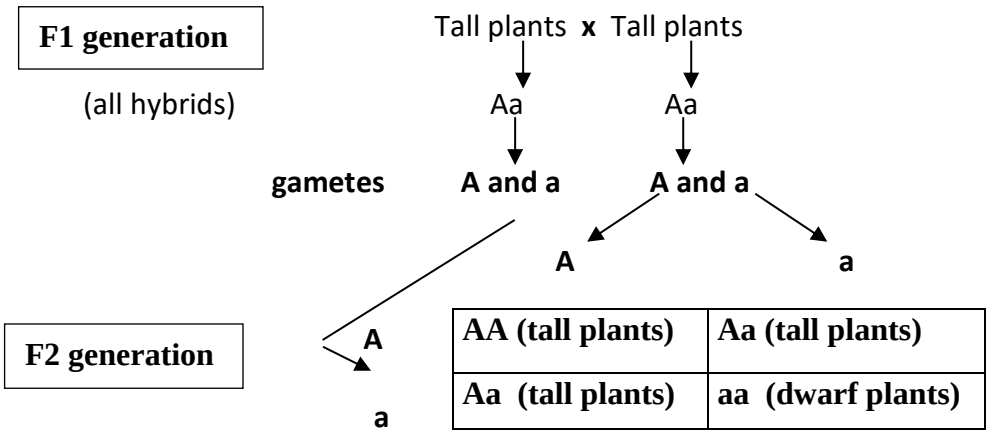
Mendel's law of segregation

When two hybrids are crossed for a particular character, the two genes (alleles) for the character segregate (separate) during gamete production (alleles are independent of each other). Therefore combining randomly in all possible mathematical combinations, giving rise to a non-homogeneous descendency.

Interpreting the experiment (we will refer to the same cross as before)

The tall plants from the F1 hybrids (Aa) will make two different types of gametes with the same probability. Some gametes will carry the allele A for tall plants, and others the allele a for dwarf plants. When the F1 hybrids are allowed to self-pollinate the gametes will combine randomly with all possible phenotypes appearing in the F2 generation: tall and dwarf plants. The mathematical proportions expected will be maintained (there will be more plants with the dominant phenotype).

(Continuing with the same cross as before)



AA (tall plants)	**Aa (tall plants)**
Aa (tall plants)	**aa (dwarf plants)**

Expected genotypic proportions: ¼ AA; ½ Aa; ¼ aa; expected phenotypic proportions: ¾ tall plants; ¼ dwarf plants.

In the case of incomplete dominance such as with the snapdragon flowers, in the F2 generation we can see pink, red and white flowers, so the law of segregation is also valid for incomplete dominance. The segregation of the red and white alleles in the gametes produced by the pink-flowered plants confirms that the genes for flower color are heritable factors that maintain their identity in the hybrids.

MENDEL'S THIRD LAW

Mendel derived the law of segregation by carrying out monohybrid crosses (breeding experiments using parental varieties that differ in a single character, such as stem length) But what would happen if he mated parental varieties differing in two characters – a dihybrid cross?

Experiment

Now Mendel chose a dihybrid cross (stem length, tall or dwarf plants; and pod colour, green or yellow pod). He crossed a true-breeding tall plant with greed pod with a true-breeding dwarf plant with yellow pod. All of the F1 was homogeneous: All of the F1 generation were tall plants with green pod. When he self-pollinated the F1 he obtained the following F2: 9/16 tall plants with green pod; 3/16 tall plants with yellow pod; 3/16 dwarf plants with green pod; and 1/16 dwarf plants with yellow pod. He derived his third law as follows:

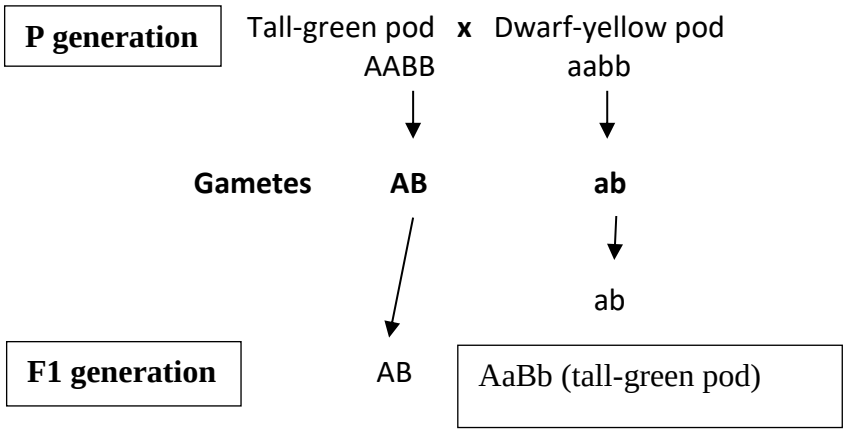
Mendel's law of independent assortment

Two pairs of genes (alleles) segregate independently of each other. Each character is independently inherited, and such characters combine randomly in all possible mathematical proportions.

Interpreting the experiment

If we study two characters such as stem length and pod color we can observe the following: The dominant allele A determines tall plants; the recessive a determines dwarf plants. The dominant allele B determines green pods; and the recessive b determines yellow pod. If we cross homozygous tall green-colored pod plants (AABB) with dwarf yellow-colored pod plants (aabb), all of the F1 generation is tall green-colored pod (AaBb). As those hybrids are allowed to self-pollinate (if the two

characters segregate independently the gametes produced are: AB, Ab, aB, ab), the phenotypic ratio of the F2 generation is a 9:3:3:1.



AaBb x AaBb

Gametes for both: AA, Ab, aB, ab

	AB	Ab	aB	ab
AB	AABB (tall-green)	AABb (tall-green)	AaBB (tall-gree)	AaBb (tall-green)
Ab	AABb (tall-green)	AAbb (tall-yellow)	AaBb (tall-green)	Aabb (tall-yellow)
aB	AaBB (tall-green)	AaBb (tall-green)	aaBB (short-green)	aaBb (short-green)
ab	AaBb (tall-green)	Aabb (tall-yellow)	aaBb (short-green)	aabb (short-yellow)

EXTENDING MENDELIAN GENETICS

Mendel's laws have been tested over and over again. Additionally, as we have already mentioned Mendelian genetics have been extended as scientists have acquired more knowledge on how heredity works. Let's have a look at some of those:

1. **Lethal genes (recessively inherited disorders):** These could alter mendelian ratios. Lethal genes are generally recessive genes (there could be some lethal dominant genes, however, the majority of those are eliminated as they kill the individual who carries them and therefore are not passed down to any offspring). In disorders classified as recessive, heterozygotes are normal in phenotype, because one copy of the "normal" allele is present. Heterozygotes will be carriers passing them down to offspring, becoming more or less abundant in a population. These lethal genes cause death to homozygotes. Refer to genetic problems.
2. **Multiple alleles:** Diploid individuals can only have two alleles for each character, but most genes exist in more than two allelic forms (Mendel thought

that each character only had two allelic forms). The ABO blood group in humans are one example of multiple alleles. Blood group is determined by three alleles A=B>O. There are four phenotypes for this character and six different genotypes. The letters indicate the genotype and in parenthesis the phenotype corresponding to the genotype: AA (blood group A); AO (blood group A); BB (blood group B); BO (blood group B); AB (blood group AB) and OO (blood group O). Refer to genetic problems.

3. **The effect of environment on phenotype**: Phenotype depends on the environment as well as on the genes. As we have already mentioned the product of a genotype is generally not a rigidly defined phenotype, but a range of phenotypic possibilities over which there may be variation due to environmental influences. For example, a seed contains in its genes all the necessary information for it to develop as a plant, grow, blossom and produce fruit. However, environmental factors such as light, water, temperature, etc are needed for those processes to take place. Other environmental factors can be pH, ion concentration, hormones, etc. E.g. Hydrangea flowers of the same genetic variety range in color from blue-violet to pink, depending on the acidity of the soil.

THE CHROMOSOME THEORY OF INHERITANCE

It was not until the year 1900 that biology finally caught up with Mendel. From 1865, the year that Mendel finished his experiments, until 1900 a series of important discoveries, particularly in the field of cytology, took place which favoured the understanding of Mendelian heredity. Around the turn of the century cytology and genetics converged (‘came together’) as biologists began to see parallels between the behaviour of chromosomes and the behaviour of Mendel’s heritable factors. The following are the most important of such discoveries:

- Fertilization of an ovum by a sperm is observed for the first time. It therefore confirmed the role of gametes as carriers of the hereditary material.
- It was discovered that the cell nucleus was involved in the transmission of the hereditary material.
- The first chromosomes were seen, as they, every now and then, showed up in the nucleus.
- Cytologists worked out, step by step, the processes of mitosis (1875) and meiosis (1890s). The material in the nucleus that is strongly stained and gives rise to chromosomes is called **chromatin**.
- It was observed that somatic cells of the same species always have **the same number of chromosomes.** Each species has its own specific number of chromosomes.
- During mitosis the chromosomes contained in the mother cell are equally and uniformly distributed between the two daughter cells.
- Sperms and ova of any species must contain half the number of chromosomes than somatic cells.
- When two gametes fuse together the number of chromosomes of that particular species is restored.

- Chromosomes are DNA filaments. Genes are DNA fragments.
- In 1903, Walter S. Sutton and Theodore Boveri, independently suggested that **genes are located on chromosomes in a lineal manner** (much like the pearls in a necklace), and the **chromosome theory of inheritance** began to take form; According to this theory, Mendelian genes are located on chromosomes, and it is the chromosomes that undergo segregation and independent assortment. It is important to understand the following:

- During meiosis I chromosomes that are very similar pair up (homologous chromosomes); each homologous coming from each parent. There are therefore two genes (alleles) for each character, each one coming from each of the parents.
- During meiosis homologous chromosomes undergo segregation and independent assortment. –therefore giving rise to different gametes.
- Each gamete will only have one of the homologous. During fertilization when two gametes fuse the new pair of alleles will be produced.

(LINKED GENES AND RECOMBINATION: How these affect Mendel's ratios)

SEX CHROMOSOMES AND SEX-LINKED INHERITANCE

Generally, males produce small motile gametes, and females produce large non-motile gametes. Although the anatomical and physiological differences between male and females are numerous, the chromosomal basis of sex is rather simple. Most frequently, in determining the sex of an individual there are two chromosomes involved. These are known as **heterochromosomes** or **sex chromosomes** (we have already seen that chromosomes which do not determine the sex are called autosomes) In humans and many other species, there are two varieties of sex chromosomes, designated the X and the Y chromosomes. Females have two X chromosomes (genotype XX), and males have an X chromosome and a smaller Y chromosome (genotype XY). When meiosis occurs in the gonads (male testes and female ovaries), the two sex chromosomes segregate, and each gamete receives one. Each ovum contains one X chromosome. In contrast, half the sperm cells contain an X chromosome, and half contain a Y chromosome. If a sperm cell bearing an X chromosome happens to fertilize an ovum, the zygote is XX, a female; if a sperm cell containing a Y chromosome fertilizes an ovum, the zygote is XY, a male. Sex is a matter of chance; a 50% probability for each sex.

In addition to the role of sex chromosomes in determining sex, these chromosomes, especially the X chromosome, have genes for many characters unrelated to sex. Therefore, the heredity of such characters is **sex-linked**. In humans the term sex-linked usually refers to X-linked characters. Fathers pass X-linked alleles to all their daughters, but to none of their sons. On the other hand, mothers can pass sex-linked alleles to both sons and daughters. There are very few but yet some characters which are Y-linked. Fathers pass Y-linked alleles to all their sons.

If a sex-linked (X-linked) trait is due to a recessive allele, a female will express the phenotype only if she is a homozygote. Any males receiving the recessive allele from his mother will express the trait. A heterozygote female for a sex-linked disorder will

show a normal phenotype but as she is carrying the recessive allele is called a carrier. Some sex-linked (X-linked) disorders are the following:

Colour blindness (daltonism) is a mild disorder due to a recessive allele (d), where the person with the disorder can not distinguish red from green. The dominant allele (D) determines normal vision. The different genotypes and corresponding phenotypes possibilities are: X^DX^D (normal female); X^DX^d (normal female but carrier of the disorder); X^dX^d (colour blind female); X^DY (normal male) and X^dY (colour blind male).

Hemophilia is a sex-linked recessive trait where the dominant (H) allele determines a protein required for blood clotting. The recessive allele (h) determines hemophilia; the most seriously afflicted individuals may bleed to death after relatively minor cuts, etc. X^HX^H (normal female); X^HX^h (normal but carrier female); X^hX^h (hemophiliac female); X^HY (normal male) and X^hY (hemophiliac male).

MUTATIONS

A mutation is any change in the genetic makeup of a cell or organism that can be passed down to offspring.

Mutations can happen spontaneously (for example, errors during DNA replication can lead to base-pair substitutions etc.) or can be induced by what are called mutagens. Some examples of mutagens are X-rays, ultraviolet light, some chemicals or even some viruses. Mutations are generally prejudicial to the organism. However, some times they are beneficial, and in such cases they can be important in the evolution of the species, as the mutation can be transmitted to an entire population.

Types of mutations:

1. Genetic mutations: affect just one nucleotide or a few nucleotides in a single gene (of a particular chromosome). For example sickle-cell anemia.
2. Chromosome structure mutations: Those that affect larger or more important sections of a chromosome, changing the structure of the chromosome. For example the Cri du chat syndrome (cat cry syndrome).
3. Chromosome number mutations: This will alter the number of chromosomes in a cell. For example Down syndrome (or trisonomy 21, as the individual will have 3 chromosomes 21 instead of the normal 2).

THE NEW GENETIC OR DNA TECHNOLOGY

Since the 70's there have been great advances in the knowledge of nucleotides, as well as some major developments in DNA technology (known as **recombinant DNA technology or genetic engineering**) that allows the manipulation of genetic material. DNA technology has launched an industrial revolution in biotechnology: specific genes can be isolated, large amounts of pure DNA can be obtained, DNA can be spliced at specific locations, genes from one organism can be transferred to other living organisms where it can be replicated and expressed (**transgenic organisms**), the synthesis of artificial genes etc.

The application of DNA technology is of great importance in different fields such as the medical field, in the diagnosis of diseases and a possible cure of such diseases; in the forensic field, identifying dead people or possible criminals; in the pharmaceutical

industry, in agriculture etc. The old mysteries of Genetics have now become clearer, but the manipulation of the genetic material opens up new unknowns.

GENETIC ENGINEERING

What is genetic engineering?

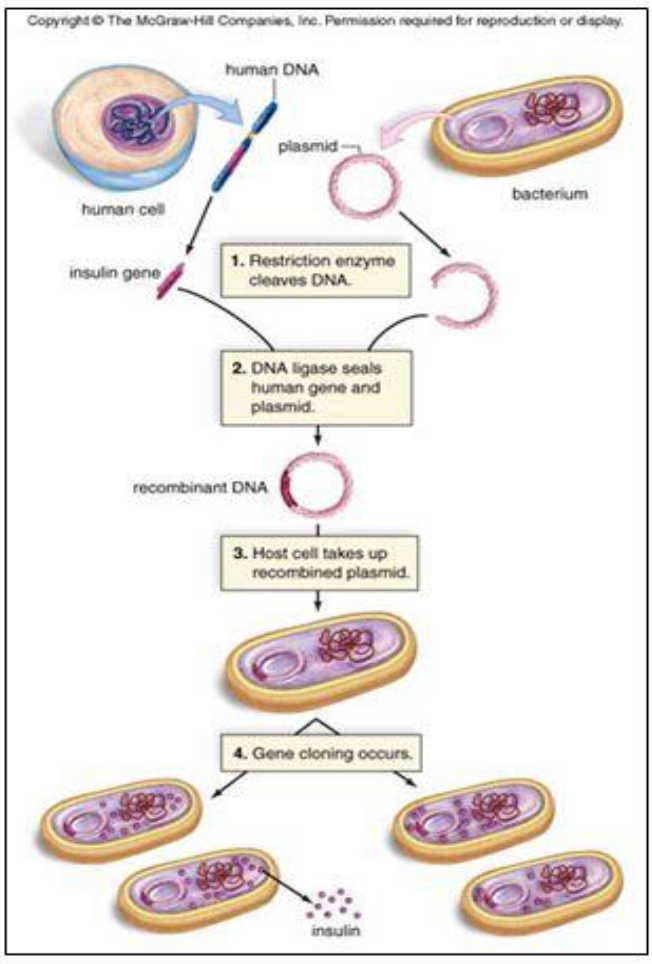
It is a group of techniques which allow the manipulation of the genome of a living organism.

Such genetic manipulation basically consists of the following:

a) Insertion of new genes into a genome (transferring genes).
b) Eliminating existing genes.
c) Modifying the information of a particular gene.

The advances achieved in the field of molecular Genetics, (in reference to the genetic material its replication and transcription), have been the basis for a group of techniques used for manipulating and analyzing DNA used in genetic engineering and known as **recombinant DNA technology.**

The use of genetic engineering in research has allowed the production of valuable products by manipulating the genetic material of microorganisms such as: insulin and the growth hormone, interferons, vaccines, enzymes for industrial use, etc. Additionally, manipulation of the genome of some organisms has allowed the development and production of a number of transgenic organisms (animals and plants) for potential agricultural use.



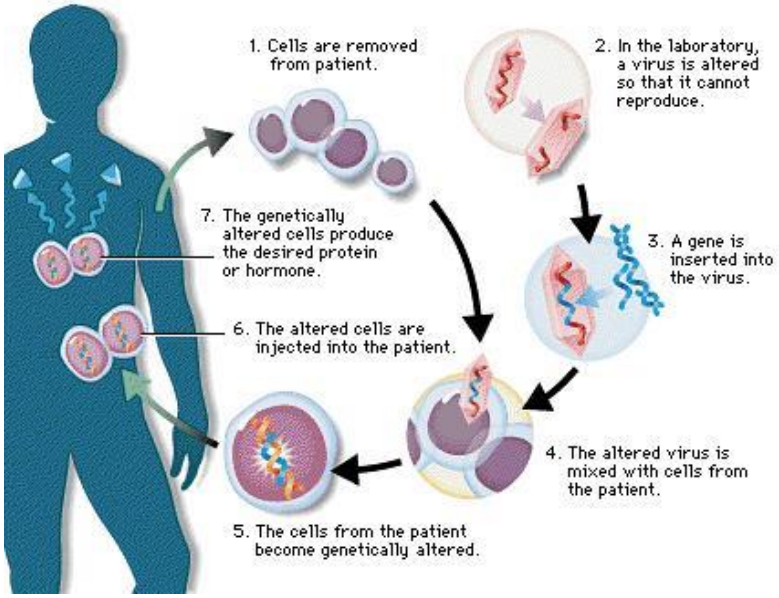
To carry out recombinant DNA technology, the following are needed:

1. **Restriction enzymes,** which are a kind of "genetic scissors" used to cut segments of DNA which contains the gene that we want to transfer. Each type of restriction enzyme cuts at specific sequence of DNA.
2. **DNA ligases**, which are enzymes which join segments of DNA.

3. **Transfer vector**, generally plasmids (small circular molecules of DNA present in many bacteria) and viruses, which act as "vehicles" to transport the DNA to the receptor organism.
4. **Receptor or host cells**, which will receive the gene from another organism. The individuals that have received the new gene are called **transgenic organism.**

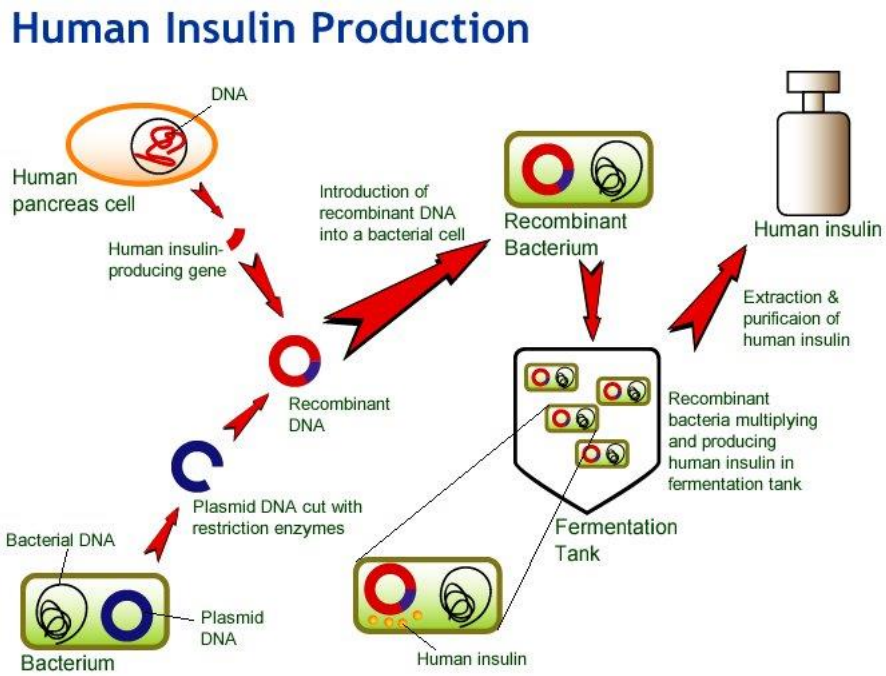
PRACTICAL APPLICATIONS OF GENETIC ENGINEERING

1. Gene therapy. Genetic engineering has the potential to actually correct some genetic disorders in individuals. In the near future, many therapeutic treatments will not be providing the individual with the molecule that he/she is not able to synthesize (insulin, growth hormone etc), but rather supplement the defective gene with a functional, normal gene, so that the individual can again synthesize its own molecule.



2. Making antibiotics. Traditionally specific strains of microorganisms were used for the production of antibiotics. With genetic engineering, the genes responsible for the production of the particular antibiotic are cloned in microorganisms. Modified antibiotics can also be obtained.

3. Producing mammalian proteins. Before genetic engineering a number of proteins of medical interests (insulin, growth hormone, several proteins of the immune system – such as molecules called interferons) were directly obtained from tissues. Nowadays, these are made by recombinant DNA procedures. The genes in charge of a particular protein are cloned in microorganisms for use in treating human patients E.g. Human insulin is produced in bacteria or yeast – *Saccharomyces cerevisiae.*



4. Vaccines. Traditional vaccines for viral diseases are of 2 types: particles of a virulent virus that have been inactivated by a chemical or physical means, and active virus particles of an attenuated (non-pathogenic) viral strain. In both cases some risks are taken as not all the micoorganism is completely inactivated. With genetic engineering, since most **antigens** are proteins, the genes of interest are cloned. (An antigen is a foreign substance that triggers an immune response; some antigens include molecules of viruses, bacteria, fungi, etc). Recombinant DNA techniques can generate large amounts of a specific protein molecule from the protein coat of a particular disease-causing virus, bacterium or other microbe. This avoids the risks mentioned earlier.

5. Production of transgenic organisms (animal and plants). It is possible to produce living organisms which genome has been artificially modified by the insertion of genes. Transgenic animals are produced by injecting foreign DNA into the nuclei of egg cells or early embryos. And transgenic plants are usually obtained by using DNA vectors to move genes from one organism to another in cell cultures.

6. DNA sequencing. The human genome project.

THE HUMAN GENOME PROJECT

The Human Genome Project is perhaps the most ambitious biological research project worldwide to date. This effort to map the entire human genome, is not only very expensive, but it will also take many years to be accomplished. The goal of this project is to locate each and every gene of the 23 pairs of chromosomes that make up the entire human genome, and to study its mechanisms of expression. It has been estimated that human DNA contains about 20 000 – 25 000 genes, though this number is constantly being modified. These genes make up about 5 to 10% of the total content of our DNA: there are lots of duplicated fragments, and other fragments that do not code for proteins. The sequencing of all the nucleotides that make up the human genome has already been accomplished (2003). However, the most difficult task is still under progress: determining all coding genes, localizing each and every gene, studying how they are expressed, etc. In many years, once the project is completely finished,

among many others things we will be able to determine: which parents could have children with particular genetic disorders; there will be some significant advances in gene therapy, we will have a better understanding of some diseases such as cancer and their possible treatments, etc…….But it will also raise significant ethical questions.

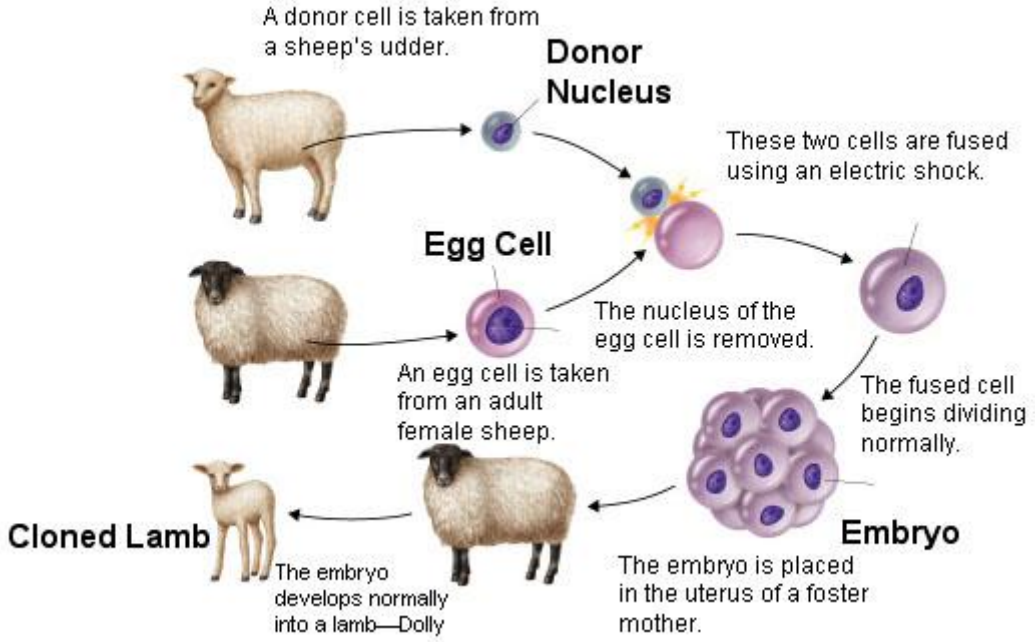
CLONING

A clone is a group of organisms that has been derived asexually from a single progenitor (individual). Unless mutation occurs during the development of the cells in a clone, the resulting descendants are genetically identical among themselves and to the progenitor.

Although many organisms produce clones as a natural form of reproduction, this type of reproduction does not happen among vertebrates (there are some rare exceptions).

Procedure (diagram in the following page): if we extract the nuclei of sheep's ovule, and replace them with diploid nuclei from another sheep's udder, this new cell will develop normally and it will differentiate making a clone. This procedure has been done with other mammals such as mice, etc.

The technical problems that could arise in cloning a human are minimal, and some of the advantages that this could bring about are obvious. However, there are many ethical issues regarding the cloning of humans.



GENETIC ENGINEERING AND BIOETHICS

We have already mentioned the great possibilities that the development of genetic engineering represents. But, the magnitude of such possibilities opens the door to numerous unknowns that should not only be answered by the scientific community, as

they concern our entire society. Over the last few decades, a new discipline that brings together Biology and Ethics – **Bioethics,** has been created. One of the main purposes of Bioethics is to determine precise limits on how far the development of genetic engineering should go, as it raises significant ethical questions. We propose some questions for class discussion:

- Do we have the right to direct or lead the future of a species, including our own?
- UNESCO has declared the human genome Patrimony of Humanity, however, biotechnological research is being carried out mainly by private companies. Therefore, the obtained products have property rights. The sequencing of a human gene could be exploited by the company that identifies it. To what extent can we commercialize the genes of our genome?
- Who should have the right to examine someone else's genes?
- How should the information be used? Should a person's genome be a factor in their suitability for a job? Should insurance companies have the right to examine an applicant's genes?
- Could it be dangerous to consume transgenic foods?
- Would it be fair to use the enormous amount of money needed to sequence and study the 90% of the human genome that never transcribes towards other aims such as food production for a rapidly growing and malnourished population in developing countries?
- Stem cell research is another controversial issue. Do we have the right to stop all research with stem cells knowing that millions of diseased people will benefit from the research? What restrictions should be placed on such research?