Cytogenetics

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HISTORY OF GENETICS

The **history of genetics** started with the work of the Augustinian friar **Gregor Johann Mendel.** His work on pea plants, published in 1866, described what came to be known as Mendelian Inheritance. In the centuries before—and for several decades after Mendel's work, a wide variety of theories of heredity proliferated. 1900 marked the "rediscovery of Mendel" by Hugo de Vries, Carl Correns and Erich von Tschermak, and by 1915 the basic principles of Mendelian genetics had been applied to a wide variety of organisms—most notably the fruit fly *Drosophila melanogaster*. Led by Thomas Hunt Morgan and his fellow "drosophilists", geneticists developed the Mendelian model, which was widely accepted by 1925. Alongside experimental work, mathematicians developed the statistical framework of population genetics, bringing genetic explanations into the study of evolution. With the basic patterns of genetic inheritance established, many biologists turned to investigations of the physical nature of the gene. In the 1940s and early 1950s, experiments pointed to DNA as the portion of chromosomes (and perhaps other nucleoproteins) that held genes. A focus on new model organisms such as viruses and bacteria, along with the discovery of the double helical structure of DNA in 1953, marked the transition to the eraof molecular genetics.

Gregor Johann Mendel

In the following years, chemists developed techniques for sequencing both nucleic acids and proteins, while others worked out the relationship between the two forms of biological molecules: the genetic code. The regulation of gene expression became

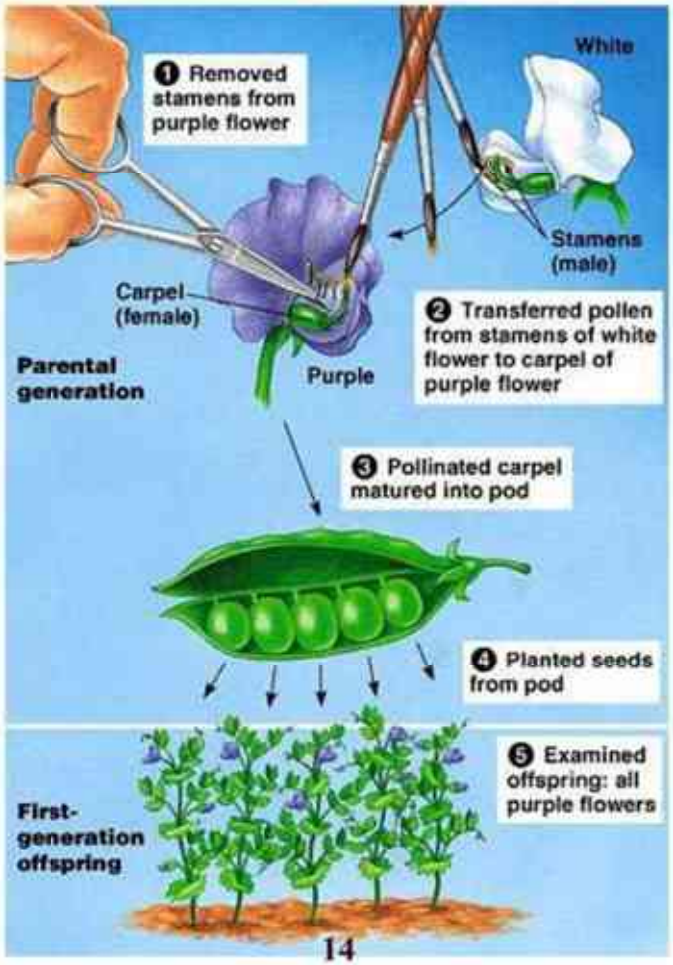
a central issue in the 1960s; by the 1970s gene expression could be controlled and manipulated through genetic engineering. In the last decades of the 20th century, many biologists focused on large-scale genetics projects, sequencing entire genomes.

Mendelian concept of hereditary

The laws of inheritance were derived by Gregor Mendel, a 19th century monk conducting hybridization experiments in garden peas (*Pisum sativum*). Between 1856 and 1863, he cultivated and tested some 29,000 pea plants. From these experiments he deduced two generalizations which later became known as *Mendel's Laws of Heredity* or *Mendelian inheritance*. He described these laws in a two-part paper, "Experiments on Plant Hybridization" that he read to the Natural History Society of Bruno on February 8 and March 8, 1865, and which published in 1866.

Mendel's findings allowed other scientists to predict the expression of traits on the basis of mathematical probabilities. A large contribution to Mendel's success can be traced to his decision to start his crosses only with plants he demonstrated were true breeding. He also measured only absolute (binary) characteristics, such as color, shape, and position of the offspring, rather than quantitative characteristics. He expressed his results numerically and subjected them to statistical analysis. His method of data analysis and his large sample size gave credibility to his data. He also had the foresight to follow several successive generations (F2, F3) of his pea plants and record their variations. Finally, he performed "test crosses" (back-crossing descendants of the initial hybridization to the initial true-breeding lines) to reveal the presence and proportion of recessive characters. Without his careful attention to procedure and detail, Mendel's work could not have had the impact it made on the world of genetics.

INTRODUCTION TO MEDELS LAWS



Mendel discovered that by crossing white flower and purple flower plants, the result was not a hybrid offspring. Rather than being a mix of the two, the offspring was purple flowered. He then conceived the idea of heredity units, which he called "factors", one which is a recessive characteristic and the other dominant. Mendel said that factors, later called genes, normally occur in pairs in ordinary body cells, yet segregate during the formation of sex cells. Each member of the pair becomes part of the separate sex cell. The dominant gene, such as thepurple flower in Mendel's plants, will hide the recessive gene, the white flower. After Mendel self-fertilized the F1 generation and obtained the 3:1 ratio, he correctly theorized that genes can be paired in three different ways for each trait; AA, aa, and Aa. The capital A represents the dominant factor and lowercase a represents the recessive.

Mendel stated that each individual has two factors for each trait, one from each parent. The two factors may or may not contain the same information. If the two factors are identical, the individual is called homozygous for the trait. If the two factors have different information, the individual is called heterozygous. The

alternative forms of a factor are called alleles. The genotype of an individual is made up of the many alleles it possesses. An individual's physical appearance, or phenotype, is determined by its alleles as well as by its environment. An individual possesses two alleles for each trait; one allele is given by the female parent and the other by the male parent. They are passed on when an individual matures and produces gametes: egg and sperm. When gametes form, the paired alleles separate randomly so that each gamete receives a copy of one of the two alleles. The presence of an allele doesn't promise that the trait will be expressed in the individual that possesses it. In heterozygous individuals the only allele that is expressed is the dominant. The recessive allele is present, but its expression is hidden. Mendel summarized his findings in two laws: the Law of Segregation and the Law of Independent Assortment.

Law of Segregation (The "First Law")

The Law of Segregation states that when any individual produces gametes, the copies of a gene separate, so that each gamete receives only one copy. A gamete will receive one allele or the other. The direct proof of this was later found when the process of meiosis came to be known. In meiosis the paternal and maternal chromosomes get separated and the alleles with the characters are segregated into two different gametes.

Law of Independent Assortment (The "Second Law")

The Law of Independent Assortment, also known as "Inheritance Law", states that alleles of different genes assort independently of one another during gamete formation. While Mendel's experiments with mixing one trait always resulted in a 3:1 ratio between dominant and recessive phenotypes, his experiments with mixing two traits (dihybrid cross) showed 9:3:3:1 ratio. But the 9:3:3:1 table shows that each

of the two genes are independently inherited with a 3:1 ratio. Mendel concluded that different traits are inherited independently of each other, so that there is no relation, for example, between a cat's color and tail length. This is actually only true for genes that are not linked to each other.

Independent assortment occurs during meiosis I in eukaryotic organisms, specifically metaphase I of *meiosis*, to produce a gamete with a mixture of the organism's maternal and paternal chromosomes. Along with chromosomal crossover, this process aids in increasing genetic diversity by producing novel genetic combinations.

In independent assortment the chromosomes that end up in a newly formed gamete are randomly sorted from all possible combinations of maternal and paternal chromosomes. Because gametes end up with a random mix instead of a pre-defined "set" from either parent, gametes are therefore considered assorted independently. As such, the gamete can end up with any combination of paternal or maternal chromosomes. Any of the possible combinations of gametes formed from maternal and paternal chromosomes will occur with equal frequency. For human gametes, with 23 pairs of chromosomes, the number of possibilities is 2^23 or 8,388,608 possible combinations. The gametes will normally end up with 23 chromosomes, but the origin of any particular one will be randomly selected from paternal or maternal chromosomes. This contributes to the genetic variability of progeny.

Rediscovery of Mendel's work

Mendel's conclusions were largely ignored. Although they were not completely unknown to biologists of the time, they were not seen as generally applicable, even by Mendel himself, who thought they only applied to certain categories of species or traits. A major block to understanding their significance was the importance attached by 19th century biologists to the apparent blending of inherited traits in the

overall appearance of the progeny, now known to be due to multigene interactions, in contrast to the organ-specific binary characters studied by Mendel. In 1900, however, his work was "re-discovered" by three European scientists, Hugo de Vries, Carl Correns, and Erich von Tschermak. The exact nature of the "re-discovery" has been somewhat debated: De Vries published first on the subject, mentioning Mendel in a footnote, while Correns pointed out Mendel's priority after having read De Vries's paper and realizing that he himself did not have priority. De Vries may not have acknowledged truthfully how much of his knowledge of the laws came from his own work or came only after reading Mendel's paper. Later scholars have accused Von Tschermak of not truly understanding the results at all. Regardless, the "re-discovery" made Mendelism an important but controversial theory. Its most vigorous promoter in Europe was William Bateson, who coined the term "genetics", "gene", and "allele" to describe many of its tenets.

The model of heredity was highly contested by other biologists because it implied that heredity was discontinuous, in opposition to the apparently continuous variation observable for many traits. Many biologists also dismissed the theory because they were not sure it would apply to all species, and there seemed to be very few true Mendelian characters in nature. However, later work by biologists and statisticians such as R.A. Fisher showed that if multiple Mendelian factors were involved in the expression of an individual trait, they could produce the diverse results observed. Thomas Hunt Morgan and his assistants later integrated the theoretical model of Mendel with the chromosome theory of inheritance, in which the chromosomes of cells were thought to hold the actual hereditary material, and create what is now known as classical genetics, which was extremely successful and cemented Mendel's place in history.

Mendel's Laws of Inheritance

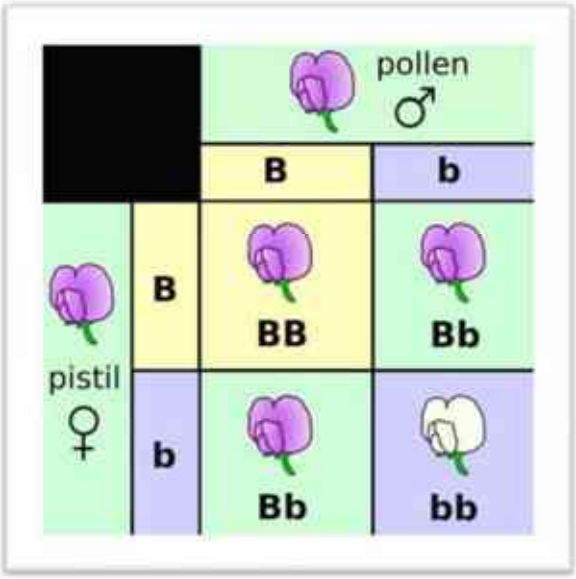
Mendel postulated three laws, which are now called after his name as Mendel's laws of heredity. These are:

- Law of dominance and recessive
- Law of segregation
- Law of independent assortment

1. Law of Dominance

Definition: The suppression of the expressions of one trait of a character by another traitof the same character is called dominance.

When two homozygous individuals with one or more sets of contrasting characters are crossed, the characters that appear in the F1 bybrids are dominant characters and those do not appear in F1 are recessive characters.



Explanation: The dominance and recessive of genes can be explained on the basis of enzymatic functions of genes. The dominant genes - can synthesize active polypeptides or proteins that form functional enzymes, whereas the recessive genes (mutant genes) code for incomplete or non-functional polypeptides. Therefore, the dominant genes produce a specific phenotype while the recessive genes fail to do so. In the heterozygous condition also, the dominant gene is able to express itself, so that the heterozygous and homozygous individuals have similar phenotype.

Types of dominance:

(1) Complete dominance

If the phenotypes of the heterozygotes as well as homozygote dominant individuals are identical then the concerned dominant allele is said to have complete dominance. (eg.,) In garden pea, the homozygote (YY) and heterozygote (Yy) individuals produce only yellow color seeds. (Yy–YY)

(2) Incomplete dominance

Mendel always observed complete dominance of one allele over the other for all the seven characters, which he studied, in garden pea. Later on cases of incomplete dominance were reported. For example, in four ëoí clock plant (*Mirabilis jalapa*) there are two types of flowers viz., red and white. A cross between red and white flowered plants produced plants with intermediate flower color i.e. pink color in F1 and a modified ratio of 1 red: 2 pink: 1 White in F2.

Parents	Red flower	x	White flowerRR	
	RR	x	rr	
F1	Rr pink flower			
F2	1 Red (Rr) :	2 Pink (RR)	: 1 White (rr)	

(3) Codominance

Expression of phenotypic trait of both homozygotes in the heterozygote condition is called co-dominance. In Co-dominance, both alleles of gene have the full expression in heterozygous individuals.

(eg.) Coat color in shorthorn cattle or Blood group in human beings.

In shorthorn cattle, a pair of gene controls, red and white coat color. Crosses between red (CRCR) and white (CW Cw) cattle produce F1 offspring of reddish gray or roan.

Superficially this would seem to be a case of incomplete dominance, but close examination of roan animal reveals that the coat color is composed of a mixture of red hairs and white hairs. The coat color of the roan is not intermediate between red and white but due to the phenotypic expression of both homozygotes. Genotypic and phenotypic ratios are identical in incomplete dominance and Co-dominance. The difference lies in the operating ways of the gene.

(4) Over dominance or Hetero dominance or Super dominance

The phenomenon of expression of phenotype in heterozygote in greater intensity than in the two concerned homozygotes is called over dominance.

The over dominance is not the property of an allele, and it is due to the heterozygous state (inter allelic interaction) of the concerned gene.

(e.g.) Eye color in fruit fly

Dominant allele WW, Ww-Red eye Recessive allele ww-White eye. Eye pigments sepratendine and himmelblaus are present in low concentrations in ww types. WW have relatively higher concentrations of these pigments. However, files heterozygous for this gene Ww have an appreciably higher concentrations of these two pigments than the two homozygotes.

Critical appreciation of Law of Dominance

Scientists conducted crossbreeding experiments to find out the applicability of law of dominance. The experiments were conducted by Correns on peas and maize, Tschermak on peas, by De Vries on maize etc., by Bateson and his collaborators on a variety of organisms, by Davenport on poultry, by Furst on rabbits, by Toyama on silk moth and by many others. These scientists observed that a large number of characters in various organisms are related as dominant and recessive.

Importance of law of dominance:

The phenomenon of dominance is of practical importance as the harmful recessive characters are masked by the normal dominant characters in the hybrids. In Human beings a form of idiocy, diabetes, haemophilia etc. are recessive characters. A person hybrid for all these characteristics appears perfectly normal. Thus harmful recessive genes can exist for several generations without expressing themselves.

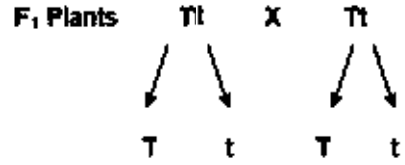
Exceptions to Law of Dominance is the Incomplete Dominance. After Mendel several cases were recorded by scientists, where F1 hybrids exhibited a blending of characters of two parents. These hybrids were found to be midway between the two parents. This is known as incomplete dominance or blending inheritance. It means that two genes of the allelomorphic pair are not related as dominant and recessive, but each of them expresses itself partially. As for example, in four-o'clock plant, Mirabilis jalapa, when plants with red flowers (RR) are crossed with plants having white flowers (rr), the hybrid F1 plants (Rr) bear pink flowers. When these F1 plants with pink flowers are self-pollinated they develop red (RR), pink (Rr) and white (rr) flowered plants in the ratio of 1 : 2 : 1 (F2 generation).

2. Law of Segregation (Purity of Gametes)

Explanation - The law of segregation states that when a pair of contrasting factors or genes or allelomorphs are brought together in a heterozygote (hybrid) the two members of the allelic pair remain together without being contaminated and when gametes are formed from the hybrid, the two separate out from each other and only one enters each gamete.

Example - Pure tall plants are homozygous and, therefore/possess genes (factors) TT; similarly dwarf possess genes tt. The tallness and dwarfness are two independent but contrasting factors or determiners. Pure tall plants produce gametes all of which possess gene T and dwarf plants t type of gametes.

During cross fertilization gametes with T and t unite to produce hybrids of F1 generation. These hybrids possess genotype Tt. It means F1 plants, though tall phenotypically, possess one gene for tallness and one gene for dwarfness. Apparently, the tall and dwarf characters appear to have become contaminated developing only tall character. But at the time of gamete formation, the genes T (for tallness) and t (for dwarfness) separate and are passed on to separate gametes. As a result, two types of gametes are produced from the heterozygote in equal numerosity. 50% of the gametes possess gene T and other 50% possess gene t. Therefore, these gametes are either pure for tallness or for dwarfness. (This is why the law of segregation is also described as Law of purity of gametes).

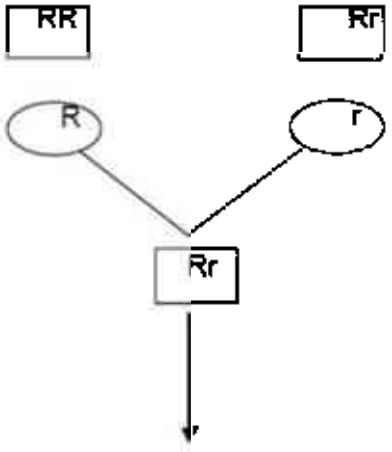


Gametes unite at random and when gametes are numerous all possible combinations can occur, with the result that tall and dwarf appear in the ratio of 3 :1. The results are often represented by Punnett square as follows:

RR have only gene for round

Rr, rR have gene for round and wrinkle

Rr have only wrinkeld gene



	R	r
R	RR	Rr
r	Rr	Rr

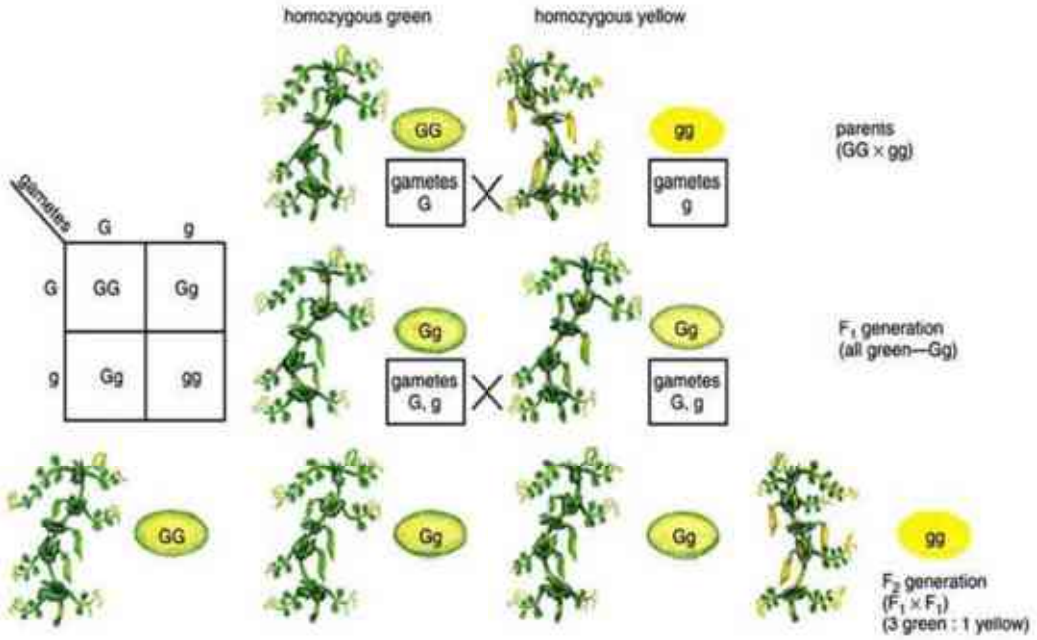
Round, Wrinkled - 3:1 ratio

Critical appreciation of law of segregation

It has been confirmed by cytological studies that dominance or no dominance, the law of segregation holds good to all cases. Its far reaching applicability has made it rare biological generalization.

Monohybrid crosses

A cross is made between two true-breeding parents differing for a single trait, producing an F1 generation. These plants are intercrossed to produce an F2 generation.



Dihybrid Crosses

The following legends were described for peas by Mendel:

T- Tall

tt - dwarf

G - green (pod) gg- yellow

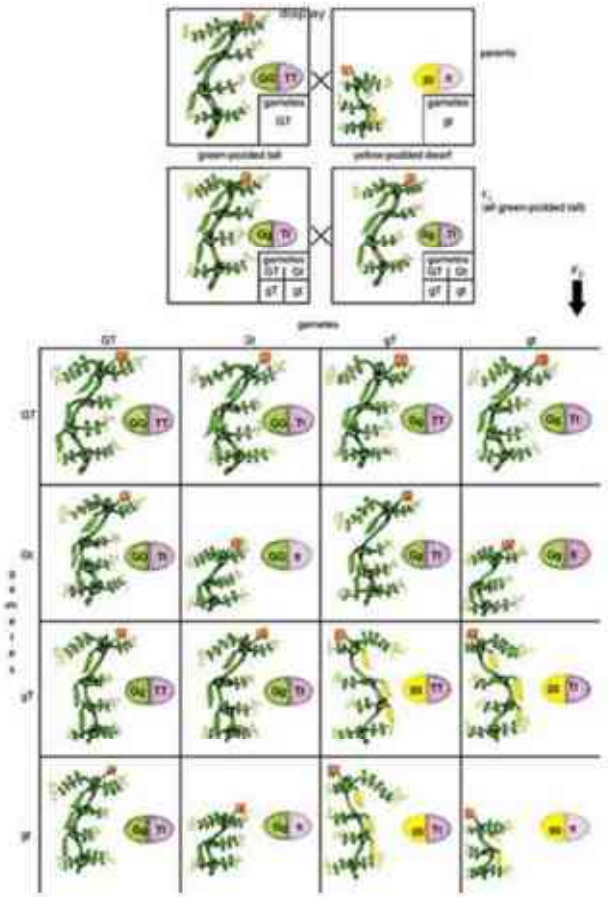
Pure breeding parents can be crossed to produce a dihybrid meaning that 2 genes affecting different traits are heterozygous (segregating) in all the f1 progeny.

Examples:

TT, GG X tt, gg ⟶ Tt, Gg

TT, gg X tt, GG ⟶ Tt, Gg

When the F1 is self-fertilized (plants) or crossed with another Tt, Gg individual, the progeny will show the expected 3 dominant : 1 recessive phenotypic ratio for each trait. If the two traits are independent, the two 3 : 1 ratios will interact to give a ratio based on 16ths.



#	Genotypes	Phenotypes
9	T_, G_	Tall, Green
3	T_, gg	Tall, yellow
3	tt, G_	Dwarf, Green
1	tt, gg	Dwarf, Yellow

3. Law of Independent Assortment

Definition: The inheritance of more than one pair of characters (two pairs or more) is studied simultaneously, the factors or genes for each pair of characters assort out independently of the other pairs. Mendel formulated this law from the results of a dihybrid cross.

Explanation: The cross was made between plants having yellow and round cotyledons and plants having green and wrinkled cotyledons.

The F1 hybrids all had yellow and round seeds. When these F1 plants were self fertilized they produced four types of plants in the following proportion:

Yellow and round

I-	Yellow and round	9
II-	Yellow and wrinkled	3
III-	Green and round	3
IV-	Green and wrinkled	1

The above results indicate that yellow and green seeds appear in the ratio of 9 + 3 : 3 + 1 – 3 : 1. Similarly, the round and wrinkled seeds appear in the ratio of 9 + 3 : 3 +1 – 12:4 or 3 :1. This indicates that each of the two pairs of alternative characters viz. yellow-green cotyledon colour is inherited independent of the round-wrinkled character of the cotyledons. It means at the time of gamete formation the factor for yellow colour enters the gametes independent of R or r, i.e, gene Y can be passed on to the gametes either with gene R or r.

Cytological explanation of the results: In the above experiment yellow and round characters are dominant over green and wrinkled characters which can be represented as follows:

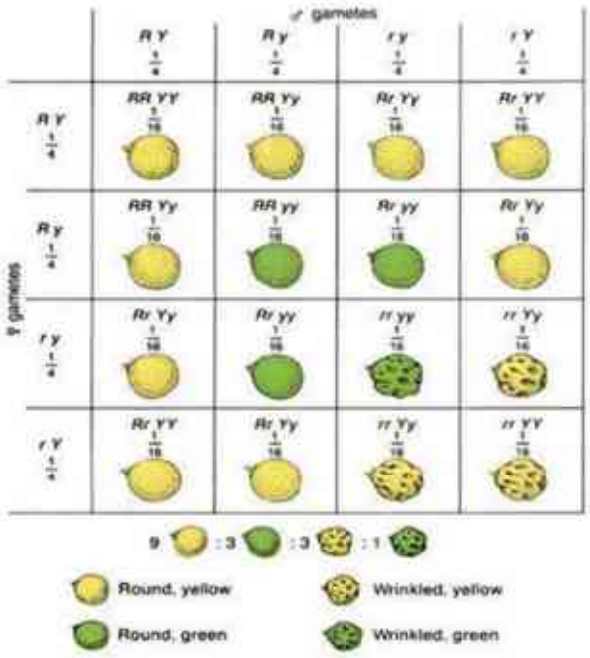
I-	gene for yellow colour of cotyledons	Y
II-	gene for green colour of cotyledons	y
III-	gene for round character of cotyledons	R
IV-	gene for wrinkled character of colyledons	r

Therefore, plants with yellow and round cotyledons will have their genotype YYRR and those with green and wrinkled cotyledons will have a genotype yyrr. These plants will produce gametes with gene YR and yr respectively. When these plants are cross pollinated, the union of these gametes will produce F1 hybrids with YyRr genes. When these produce gametes all the four genes have full freedom to assort independently and, therefore, there are possibilities of four combinations in both male and female gametes.

(i) RY (ii) Ry (iii) rY (iv) ry

This shows an excellent example of independent assortment. These gametes can unite at random producing in all 16 different combinations of genes, but presenting four phenotypes in the ratio of 9: 3: 3: 1.

Dihybrid ratio : RR yy - Round, yellow seeded ; Rr yy - Wrinkled and greed seed



Test cross

F1 Rr Yy x rr yy (recessive)

1:1:1:1

Critical appreciation of law of Independent Assortment-

The law of independent assortment fails to have a universal applicability. Cytological studies have revealed that only those allelomorphs assort independently during meiosis, which are located in different homologous pairs of chromosomes. But, if the allelomorphs for different characters are present in the same homologous pair of chromosomes, these are passed on to the same gamete. Law of independent assortment does not apply to such cases.

The Testcross:

Because some alleles are dominant over others, the phenotype of an organism does not always reflect its genotype. A recessive phenotype (yellow) is only expressed with the organism is homozygous recessive (gg). A pea plant with green pods may be either homozygous dominant (GG) or heterozygous (Gg). To determine whether an organism with a dominant phenotype (e.g. green pod color) is homozygous dominant or heterozygous, you use a testcross.

The breeding of an organism of unknown genotype with a homozygous recessive. If all the progeny of the testcross have green pods, then the green pod parent was probably homozygous dominant since a GG x gg cross produces Gg progeny. If the progeny of the testcross contains both green and yellow phenotypes, then the green pod parent was heterozygous since a Gg x gg cross produces Gg and gg progeny in a 1:1 ratio. The testcross was devised by Mendel and is still an important tool in genetic studies.

Uses of test cross

(1) Test cross verifies the Mendel's factorial hypothesis.

According to Mendel, a monohybrid tall (Tt) produce two kinds of gametes in equal proportion and recessive parent produce only one kind of gamete't' .Hence this back cross should give Tall and dwarf plants in 1 : 1 ratio. In actual experiment also we get tall and dwarf in '1:1' ratio. Thus Mendel's factorial hypothesis is verified.

(2) Test cross is used for identifying the genotype of an unknown parent.

A tall pea plant may be either homozygous (TT) or heterozygous (Tt). Its genotype may be determined by test cross. If the test cross progeny were tall, then the unknown tall genotype is 'homozygous". If that test cross progeny have tall and dwarf plants in equal proportion, then the unknown genotype is heterozygous.

Dihybrid Test Cross

A dihybrid Yy Rr is crossed with the double recessive parent yyrr. The dihybrid produces four kinds of gametes namely YR, Yr,yR and yr in equal proportions. The green wrinkled produces only one kind of gamete. The expected result is Yellow round, yellow wrinkled, green round and green wrinkled in1:1:1:1 ratio. In actual experiment, the name ratio was obtained.

P	Yellow Round		X	Green	Wrinkled	
	Yy Rr			yy rr		
G	(YR) (Yr) (yR) (yr)			(yr)		
BC_1F_1	Yy Rr	Yy rr		yy Rr	yy rr	
	1	1		1	1	
	Yellow Round	: Yellow Wrinkled	:	Green: Round	Green Wrinkled	:

The Back cross:

If the F1 progeny is mated back to one of their parents, the mating is termed as Back cross.

	Tall xDwarf	(or)	Tall xDwarf	
P	TT tt		TT tt	
G	(T) (t)		(T) (t)	
F_1	Tt (Tall)		Tt (Tall)	
	TtxTT		Ttxtt	
BC_1F_1	Tt:TT	BC_1F_1	Tt:tt	

PEDIGREES

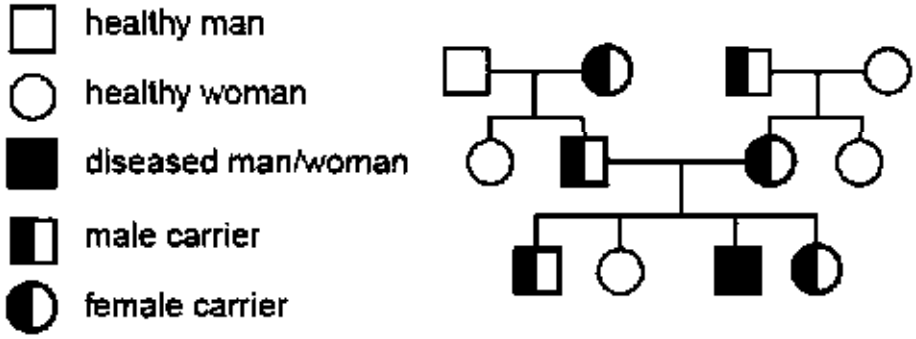
What is a Pedigree?

To understand the process of marker assisted selection (MAS), we first must understand a *pedigree*. A pedigree is the family history of matings and the offspring they produce with reference to specific genetic traits. Animal and plant breeders have long used pedigrees to help select individuals they believed to have desirable traits. In the case of selective breeding, the researchers are interested in the presence or absence of a trait. An organism's pedigree helps researchers determine the inheritance of a trait. Using modern analysis techniques, researchers search for the DNA sequence of the gene(s) that controls the trait. In the process, they may discover other related DNA sequences near to or present in the gene that always accompany the gene of interest. These accompanying sequences, called *molecular markers*, are usually shorter and easier to identify than the larger, more complex gene sequence. The presence of markers for a trait of interest gives researchers a way to determine the presence or absence of desired alleles.

Pedigree Analysis

In a pedigree analysis, information about family members is summarized in a special kind of diagram. Each individual is represented by a symbol, a square for a male and a circle for a female. Individuals who have the trait of interest are represented by black squares (■) or circles (●). Empty squares (□) or circles (○) represent individuals that do not have the trait. The symbols for individuals are arranged in horizontal rows by generation, with each generation denoted by a Roman numeral. Each individual within the generation is numbered. In this manner, it is easy to refer to an individual, such as II-2, which means the second generation, second individual. When two individuals' mate, they are connected by a horizontal line. Their offspring

are arranged together under the connecting parental line. Siblings are arranged in birth order from left to right.



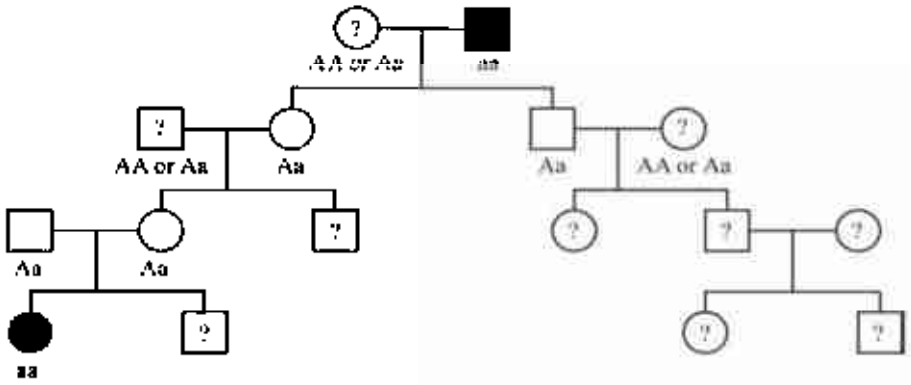
With this information, the use of Mendelian rules, and the rules of probability, it is possible to generate a hypothesis (educated guess) about the alleles that are controlling the trait. The hypothesis from pedigree data usually includes whether an allele is *dominant* or *recessive*, as well as predictions about the genotype of the individuals in the pedigree.

This hypothesis can be used to make predictions about the probable genotypes and phenotypes of future offspring. Traits controlled by recessive or dominant alleles show a definite pattern of inheritance in the pedigree diagram. Traits controlled by a dominant allele appear in all individuals that possess one or more copies of the allele. Individuals with homozygous dominant alleles (AA) or heterozygous alleles (Aa) will express the dominant phenotype. A recessive allele cannot be detected in a heterozygous individual and may stay hidden in a family for many generations until a homozygous recessive (aa) individual appears. The parents of an offspring that expresses a recessive trait (aa) must both be heterozygous (Aa) if they did not express the recessive trait themselves. Another question that often can be answered using pedigree analysis is the probability that future offspring may be heterozygous (carriers) or may be homozygous and have the recessive trait. Pedigree information is used to determine the chance that individuals who both have a family history of a

trait may produce offspring with the trait. We will use Pedigree 1 below as an example of how a pedigree can be used to determine if a trait is dominant or recessive and predict the individuals' genotype and phenotype. The use of Punnett squares also can be very helpful in determining the genotype of the parents and offspring.

Example: In Pedigree below, an original parent (I-2) has the trait of interest. The absence of individuals in generations II and III with the trait of interest indicates that the trait is controlled by a recessive allele. If the individuals with the trait of interest are homozygous recessive, you can make predictions of the genotypes of the other individuals. I-2 and IV-1 have the trait, so their genotypes would be aa.

The recessive allele has traveled from the first generation to the fourth without being expressed. In order for an individual to have the trait, it must have been inherited through a recessive allele from each parent. An individual who is a carrier (heterozygous) would not have the trait. This is the case of the parents of IV-1. Individuals III-1 and III-2 have to be heterozygous (Aa) to have the progeny IV-1 with the trait. Since individual I-2 is homozygous recessive (aa), his offspring II-2 and II-3 must be heterozygous. The exact genotypes of I-1, II-1, II-4, III-3 through III-6, and IV-2 through IV-4 are impossible to determine, except that they must have either the homozygous dominant (AA) or heterozygous (Aa) genotype. The pedigree of additional offspring would be needed to determine their genotypes.



DEVIATION FROM MENDELANIAN RATIO

In Mendel's dihybrid cross, each pair of allelic gene influences one character. Two or more pairs of genes may influence sometimes a single character. Depending upon the form of interaction the 9:3:3:1 ratio is modified in various ways. The phenomenon of two or more genes affecting the expression of each other in various ways in the development of a single character of an organism is shown as gene interaction.

What is Gene Interaction?

Gene interaction is the process by which the expression of two or more genes influences one another in different ways as an organism develops a single characteristic. Most of the traits that comprise living beings are coordinated by various genes.

Types of Gene Interaction

Gene interactions are divided into two categories:

1. **Allelic or Non-epistatic Gene Interaction:** This gene interaction occurs between the alleles of a single gene. When phenotypic ratios diverge from Mendelian ratios, it is difficult for Mendelian genetics to explain some types of inheritance. This is because specific alleles can often be equally or partially dominant to each other or due to the lethal alleles. Allelic, non-epistatic or intra-allelic interactions are the terms used to describe genetic interactions between alleles of a single gene.
2. **Non-allelic or Epistatic Gene Interaction:** This gene interaction involves interactions between genes on identical or distinct chromosomes. When two or more genes affect each other's expression in various ways, non-allelic or epistatic or inter-allelic interaction takes place, resulting in the development of a single character.

ALLELIC OR NON-EPISTATIC GENE INTERACTION

LETHAL GENES

A lethal gene causes the death of all the individuals carrying it before these individuals reach the adulthood.

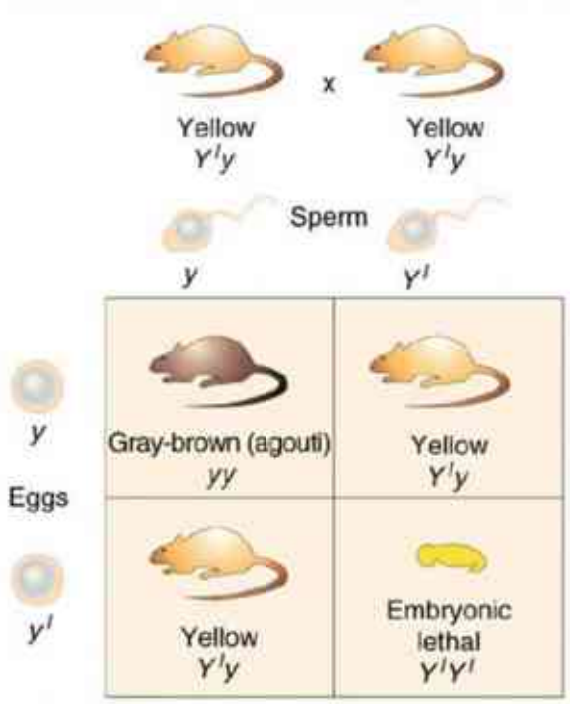
The lethal genes are classified into following types:

a. Recessive lethal

The lethal effect is expressed in the individuals only when the alleles are in homozygous state. This condition is known as recessive lethal.

French geneticist Cuenot (1905) discovered a classic example for recessive lethal affecting coat color in mouse. He found that yellow coat color in mouse is produced by dominant gene Y, while its recessive allele y produces gray / agouti color and yellow is dominant over gray. Further he also observed that all the mouse with yellow coat color were heterozygous (Yy) and no mouse was there in the population with homozygous for Y allele. Cuenot supposed that the sperm carrying yellow (Y allele) could not penetrate egg carrying Y allele.

But later Castle and Little gave the explanation that yellow homozygotes were formed but died in embryonic stage. According to them, yellow had a dominant phenotypic effect on coat color but had at the same time a recessive effect on lethality, so that homozygotes for yellow were in viable. So, a cross of yellow x yellow therefore always produced offspring in the ration 2/3 yellow: 1/3 agouti instead of ¾ yellow: ¼ agouti. From the above experiment it was evident that whether the lethal gene has a dominant or recessive phenotypic effect, it is called recessive lethal as long as its lethality depends upon its presence in homozygous condition.



b. Dominant lethal

The lethal gene whose lethal effects occur in heterozygous individuals is known as dominant lethal. An example of a dominant lethal is the epiloia gene in human beings, this gene causes abnormal skin growth, severe mental defects, and multiple tumors in the heterozygotes so that they die before reaching adulthood. Therefore, dominant lethal cannot be maintained in the population, while recessive lethal are maintained in heterozygous state. Thus, the dominant lethal have to be produced in every generation through mutation.

c. Sex-Linked Lethal

This is a system in which the lethal gene is carried on the sex chromosome, usually X. In human being's lethal effects among the progeny may be caused accidentally by radiation (X-ray) treatment of the reproductive organs of the parents. According to a study by R. Turpin in France, when women receive X-ray exposures in the

abdominal region, recessive lethal mutations are induced in the X chromosome present in the ovum. Such a woman produces more females and very few males in the progeny. If the male parent is exposed to X-rays and dominant lethal mutations are induced on his X chromosome, there will be more boys in the progeny and few females. This is because the single X chromosome is passed to the daughters resulting in their death. Muscular dystrophy is due to an X-linked recessive gene which shows a visible phenotype many years after birth. Boys having this gene are normal for about 10 years after which there is failure of muscular control and death results.

d. Conditional Lethal

Sometimes an organism lives normally under one set of conditions, but when certain changes are introduced in its environment, lethality results. One of the first conditional lethal known was recognized by Dobzhansky in *Drosophila pseudoobscura*. The flies live normally at a temperature of 16.5°C, but at 25.5°C the flies die.

MULTIPLE ALLELES

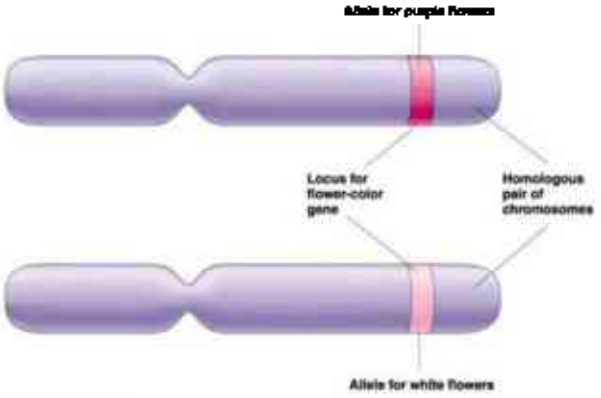
Allele is a shorter term than allelomorph (another form) is the alternate form of gene. Many genes have two alternate forms but several other have more than two alternate forms. More than two alleles at the same locus give rise to a multiple allelic series. Multiple alleles can be defined as a series of forms of a gene situated at the same locus of homologous chromosomes. According to Mendel, each gene had two alternate forms or allele morphs are being dominant and the other being recessive. Dominant being the wild type from which recessive mutant was evolved through mutation. Likewise, a wild type can mutate in many ways and produce many mutant forms and a mutant can again undergo another mutation and give rise to a new mutant. Hence, a gene can exist in more than two allelomorphs. Usually, wild type allele is dominant over its recessive allele. wild allele is represented as +.

Multiple alleles can be defined as a:

- Series of forms of a gene.
- Situated at the same locus of homologous chromosomes.
- Affecting same character.

Multiple alleles are:

- Different forms of the same gene
- That is the sequence of the bases is slightly different in the genes located on the same place of the chromosome.



Multiple alleles are alternative states at the same locus. Remember: each individual will only have two alleles for a trait but there are several alleles to choose from.) The classical example for multiple alleles is human blood group self-incompatibility in tobacco, coat color in rabbit, self-incompatibility genes in brassica.

The number of possible genotypes in a series of multiple alleles is ½ n (n+1)

n = no of alleles

- Di-allelic genes can generate 3 genotypes.
- Genes with 3 alleles can generate 6 genotypes.
- Genes with 4 alleles can generate 10 genotypes.
- Genes with 8 alleles can generate 36 genotypes.

Important features of multiple alleles:

I- Multiple alleles always belong to the same locus and one allele is present at a locus at a time in a chromosome.

II- Multiple alleles always control the same character of an individual.

III- Wild type allele is dominant over other alleles.

IV- There is no crossing over in the multiple alleles.

V- In a series of multiple alleles wild type is always dominant.

VI- When two mutant types are crossed wild form cannot be recovered.

VII- The cross between two mutant alleles will always produce mutant phenotype.

Examples of multiple alleles are:

1) Fur color in a rabbit,

2) ABO blood group in man

3) Wing type in drosophila

4) Eye color in drosophila etc.

1- Fur color in rabbit

In rabbits, four kinds of skin color are known.

Possible genotypes	CC, Cc^{ch}, Cc^{h}, Cc	$c^{ch}c^{ch}$	$c^{ch}c^{h}, c^{ch}c$	$c^{h}c^{h}, c^{h}c$	cc
Phenotype	Dark gray	Chinchilla	Light gray	Himalayan	Albino

CC, Ccch, Cch, Cc	Agouti (wild type)
cchch, cchc,	Chinchilla (salivary grey hair)
ch ch, ch c	Himalayan (white except black feet nose ear tail)
cc	Albino (complete white)

Agouti

This has full color and is also known as wild type. This color is dominant over all the remaining color and produces agouti color in F1 and 3:1 ratio in F2 when crossed with any of the other three colors in rabbits. C represents this color.

Chinchilla

This is lighter than agouti. This color is dominant over Himalayan and albino and produces chinchilla in F1 and 3:1 ratio in F2 when crossed either Himalayan or albino. This is represented by cch.

Himalayan

The main body is white while the tips of ear, feet, tail and snout are colored. This color is dominant over albino and produces 3:1 ratio in F2 when crossed with albino. This is represented by ch .

Albino

This has pure white fur color and is recessive to all other types. This is represented by c. Thus the order of dominance for fur color in rabbits can be represented as follows.

Agouti	Chinchilla	Himalayan	Albino
(C)	(cch)	(ch)	(c)

2-ABO Blood group in man.

Antibody

Antibody is a type of protein, which is commonly referred to as immunoglobin. It is usually found in the serum or plasma. The presence of antibody can be demonstrated by its specific reaction with an antigen.

Antigen

An antigen refers to a substance or agent, which when introduced into the system of vertebrate animal like cow, goat, man etc. induces the production of specific antibody, which binds specifically to this (Antigen) substance Antigen are located in the red blood corpuscles (RBC). If a person has a particular antigen in his RBCs, his serum has usually antibodies against the other antigen. In human RBC two types of antigens viz A and B are present. Depending upon the presence or absence of antigen A and B the blood group in man is of four types viz A, B, AB and O. A person with blood group A has antigen A on the surface of RBCs: protein with blood group B will have antigen B those with blood group AB have antigens A and B; and those with blood group O have no antigen on the surface of their RBCs.

BloodGroup	Genotype	Antigenfound	Antibody present	Compatible blood group
A	I^AI^A, I^Ai	A	B	A and O
B	I^BI^B, I^Bi	B	A	B and O
AB	I^AI^B	AB	None	A,B, AB,O
O	ii	None	AB	O

Recent studies shows that antigen is galactosamine and B is galactose Antibodies A, B, AB and None and are naturally present in the serum of individuals having A,B,AB, and O blood group respectively. The agglutination or coagulation of RBCs

leads to clotting of blood due to interaction between antigen antibodies. The blood group B cannot be transferred to an individual having blood group A because the recipient has antibody against antigen B which is present on the RBCs of blood group B. Similarly, the reverse transfusion is not possible. The blood group AB does not have antibody A and B. Hence individuals with AB blood group can accept all types of blood, viz., A, B, AB, and O. Such individuals are known as universal acceptors or recipients. The O blood group does not have any antigen and has antibody against antigen A and B, it cannot accept blood group other than O. Individuals with blood group O are known as universal donors, because transfusion of blood group O is possible with all the four blood types. The consideration of Rh (rhesus) type is important in blood transfusion. Each blood group has generally two types of Rh group, viz positive and negative. The same type of Rh is compatible for blood transfusion Opposite type lead to reaction resulting in death of the recipient. These are few examples of multiple alleles Now it is believed that multiple alleles are present almost for all genes.

Medical applications of blood group inheritance

It is necessary to match the donor and recipient before a blood transfusion is made. If A group blood is transfused into a B group man, the 'A antigen' of the door reacts with 'A antibody' of the recipient and agglutination occurs. This agglutination reaction may be severe or even fatal. In blood transfusion, the antigen of the donor and antibody of the recipient must be considered and matched.

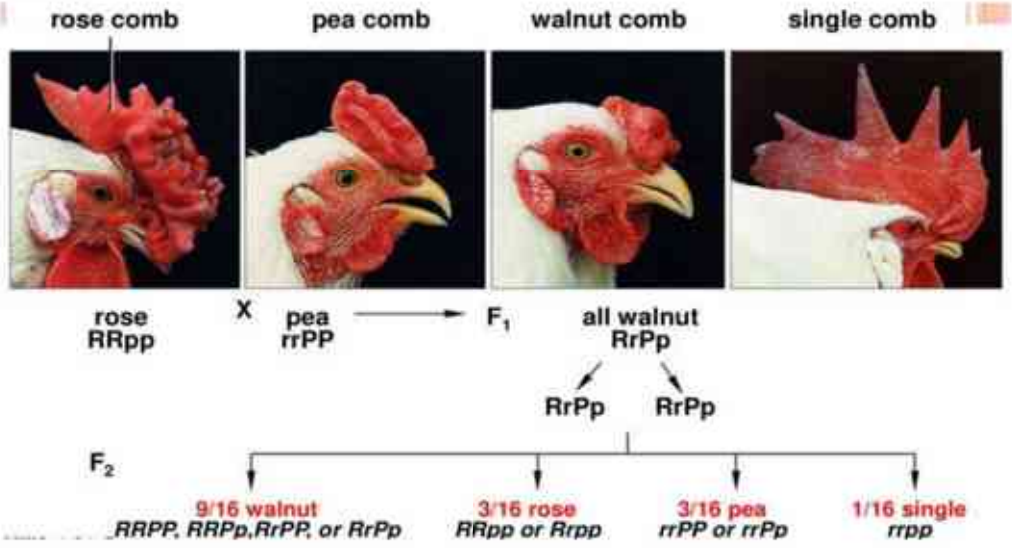
NON-ALLELIC OR EPISTATIC GENE INTERACTION

Simple Interaction (9:3:3:1)

Inheritance of comb pattern in fowls (without modification of 9:3:3:1 ratio)

This was reported by W.Bateson and R.C. Punnett. Domestic breeds of chickens have different comb shapes. Rose comb is found in Wyandotte breed, pea comb in Brahmas and single comb in leghorns. Each of these types breeds true. When Rose comb fowl is crossed with Pea comb, the F1 walnut combed birds are crossed together, four kinds of combs appear in the F2 generation in the ratio of 9 wainut:3 rose: 3 Pea:1 single. In this cross neither single comb nor walnut was expressed in the original parent lines. These two phenotypes were explained as the result of gene product interaction.

The F2 ratio of 9:3:3:1 is expected only in dihybrid cross. The number of Walnut in F2 generation (9) indicates that they are double dominants. The number of single comb in F2 generation (1) indicates that they are double recessives. The Walnut comb depends on the presence of two dominant genes R and P, R alone produces rose comb and P alone produces pea cob. The absence of both R and P produces single comb.



Parents	Rose	x	Pea
	RRpp	↓	rrPP
Gametes	(Rp)		(rP)
F_1	RrPp x Rr Pp		
	Walnut		
Gametes	(RP) (Rp) (rP) (rp)		

F2 generation

	(RP)	**(Rp)**	**(rP)**	**(rp)**
(RP)	RR PP Walnut	RR Pp Walnut	Rr PP Walnut	Rr Pp Walnut
(Rp)	RR Pp Walnut	RR pp Rose	Rr Pp Walnut	Rr pp Rose
(rP)	Rr PP Walnut	Rr Pp Walnut	rr PP Pea	rr Pp Pea
(rp)	Rr Pp Walnut	Rr pp Rose	rr Pp Pea	rr pp Single

Although the usual 9:3:3:1 ratio was obtained, the result from this cross was unusual in three important respects.

i. The F1 resembles neither parent-a new character appears in the F1 – Walnut.
ii. Two phenotypes (Walnut and single) not expressed in the original parents appeared in F2.
iii. The genes 'R' and 'P' were non-allelic, and the comb pattern is influenced by two different genes.

Epistasis

Epistasis is a phenomenon in which the expression of one gene is masked or prevented by another non-allelic gene. The gene which prevents the expression of another gene is called epistatic gene, the gene whose expression is masked is called hypostatic gene. Epistasis should not be confused with dominance. Epistasis is the interaction between different genes (non-alleles) whereas dominance is the interaction between different alleles of the same gene.

The term epistasis was coined by Bateson in 1909. Various types of epistatic gene interaction are:

(1) Dominant epistasis (12:3:1)

(2) Recessive epitasis (9:3:4)

(3) Duplicate dominant epistasis (15:1)

(4) Duplicate recessive epistasis (9:7)

(5) Polymeric gene interaction (9:6:1).

(6) Dominant and recessive (inhibitory) epistasis (13:3)

(1) Dominant Epistasis (12:3:1)

In dominant epistasis, a dominant allele at one locus can mask the expression of both alleles (dominant and recessive) at another locus, it is known as dominant epistasis. When the dominant allele at one locus, for example A allele, produces a certain phenotype regardless of the allelic condition of the other locus, then the 'A' locus is said to be epistatic to the B-locus. Furthermore, the dominant allele A can express itself in the presence of either B or b, then this epistasis is said to be dominant epistasis. Only when the genotype of the individual is homozygous recessive at the epistatic locus (aa) can the alleles of the hypostatic locus (B or b) be expressed. Thus, the genotypes A-B- and A-bb produces the same phenotype, whereas aaB- and aabb produce two additional phenotypes. The classical 9:3:3:1 ratio becomes 12:3:1 ratio.

Example: An example of dominant epistasis is found for fruit colour viz white, yellow and green. White colour is controlled by dominant gene W and yellow colour by dominant genes G. White is codominant over both yellow and green. The green fruits are produced in recessive condition (wwgg). A cross between plants having white and yellow fruits produced F1 with white fruits. Intermating of F1 plants produced plants with white, yellow and green coloured fruits in F2 was 12:3:1 ratio. Here W is dominant to w and epistatic to alleles G and g. Hence it will mask the expression of G.g alleles. Hence in F2 plants with W-G- (9:16) and W-gg (3:16) genotypes will produce white fruits; plants with wwG-3/16 will produce yellow fruits and those with wwgg 1/16 genotype will produce green fruits. Thus the normal dihybrid ration 9:3:3:1 is modified to 12:3:1 ratio in 1:2 generation. Similar type of gene interaction has been reported for skin colour in mice and seed coat colour in barley.

Parents White fruit x Yellow fruit

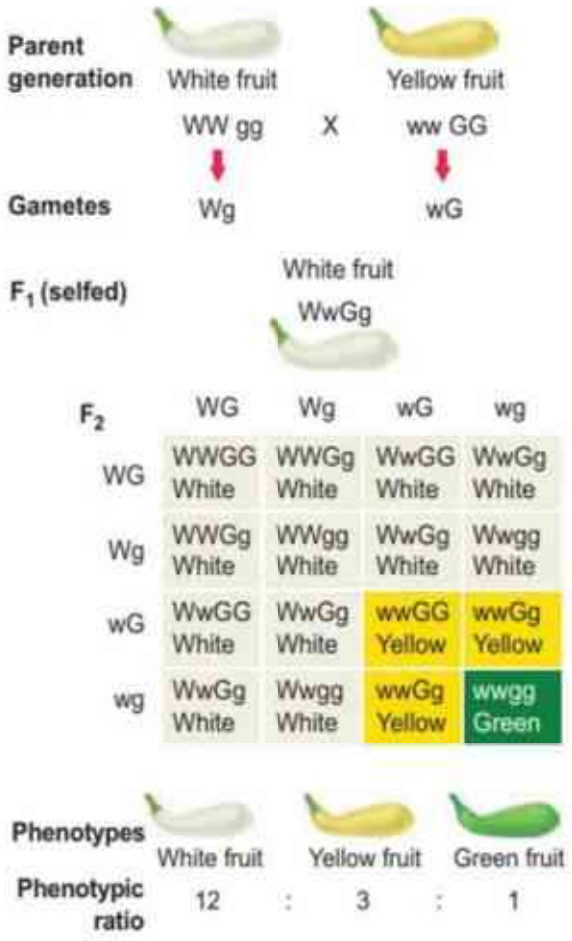
WWgg x wwGG

WwGg

White fruit

	WG	**Wg**	**wG**	**wg**
Wg	WWGG (W)	WWGg (W)	WwGG (W)	WwGG (W)
Wg	WWGg (W)	WWgg (W)	WwGg (W)	Wwgg (W)
WG	WwGG (W)	WwGg (W)	wwGG (Y)	WwGg (Y)
wg	WwGg (W)	Wwgg (W)	wwGg (Y)	wwgg (G)

Ratio = 12 White: 3 Yellow: 1 Green



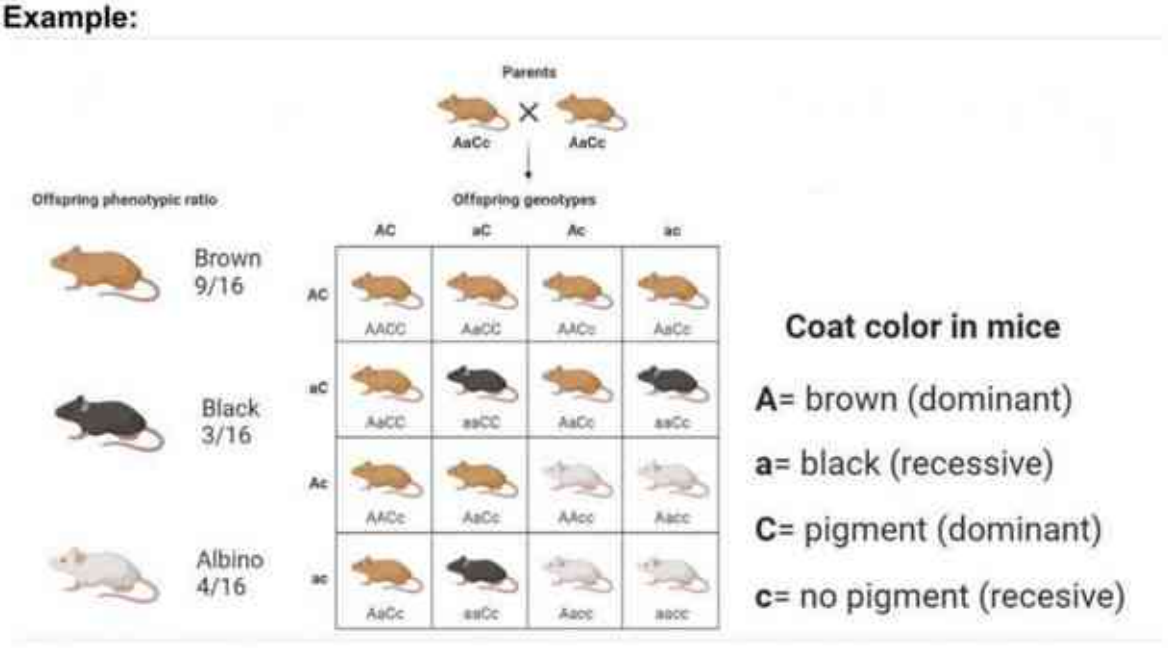
(2) Recessive Epistasis (Supplementary gene action) 9:3:4

Recessive epistasis: The recessive allele of a locus masks the expression of both dominant and recessive alleles at another locus. It is known as recessive epistasis.
Supplementary gene: Gene which by itself has no effect but qualitatively alters the effect of another gene is the supplementary gene.

If the recessive genotype at one locus (aa) suppresses the expression of alleles at the B-locus, the A-locus is said to exhibit recessive epistasis over the B locus. Only if the dominant allele is present at the 'A' locus can the alleles of the hypostatic B-locus be expressed. The genotypes A-B- and A-bb produce two additional phenotypes. The 9:3:3:1 ratio becomes a 9:3:4 ratio.

Here one dominant gene has its own phenotypic effect and other dominant gene has no effect of its own but its presence with the first gene modified the phenotypic expression. Thus in supplementary gene action the dominant allele of one gene is necessary for the development of the concerned phenotype, while the other gene modifies the expression of the first gene.

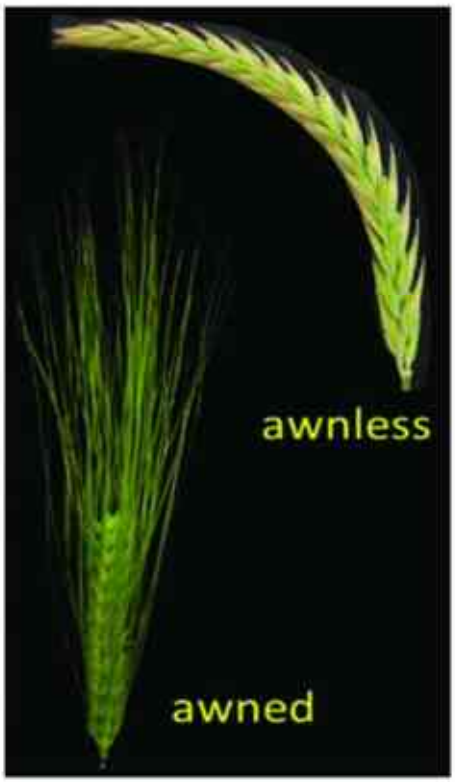
Example:



(3) Duplicate dominant epistasis (15:1)

Duplicate genes are two pairs of alleles either alone or together produce the same effect. They are identical genes but are situated on two different pairs of chromosomes. Each gene is dominant to its allele but does not add to the effect of the other. For more explanation, when a dominant allele at either of two loci can mask the expression of recessive alleles at the two loci, it is known as duplicate dominant epistasis.

Example: In rice awn character is controlled by two dominant duplicate genes (A and B). Presence of any of these two alleles can produce awn. The awnless condition develops only when both these genes are in homozygous recessive state (aabb). A cross between awned and awnless strains produced awned plants in F1. Intermating of F1 plants produced awned and awnless plants in 15:1 ratio in F2 generation. The allele A is epistatic to a/b alleles and all plants having allele A will develop awn. Another dominant allele B is epistatic to alleles a/b. An individual with these alleles also develop awn character.



Parents Awned rice x Awnless rice

AAbb x aaBB

AaBb

Awned rice

	AB	**Ab**	**aB**	**ab**
AB	AABB (A)	AABb (A)	AaBB (A)	AaBb (A)
Ab	AABb (A)	AAbb (A)	AaBb (A)	Aabb (A)
aB	AaBB (A)	AaBb (A)	aaBB (A)	aaBb (A)
ab	AaBb (A)	Aabb (A)	AaBb (A)	aabb (a)

Ratio = 15 awned: 1 awnless

(4) Duplicate recessive epistasis (Complimentary gene action) 9:7

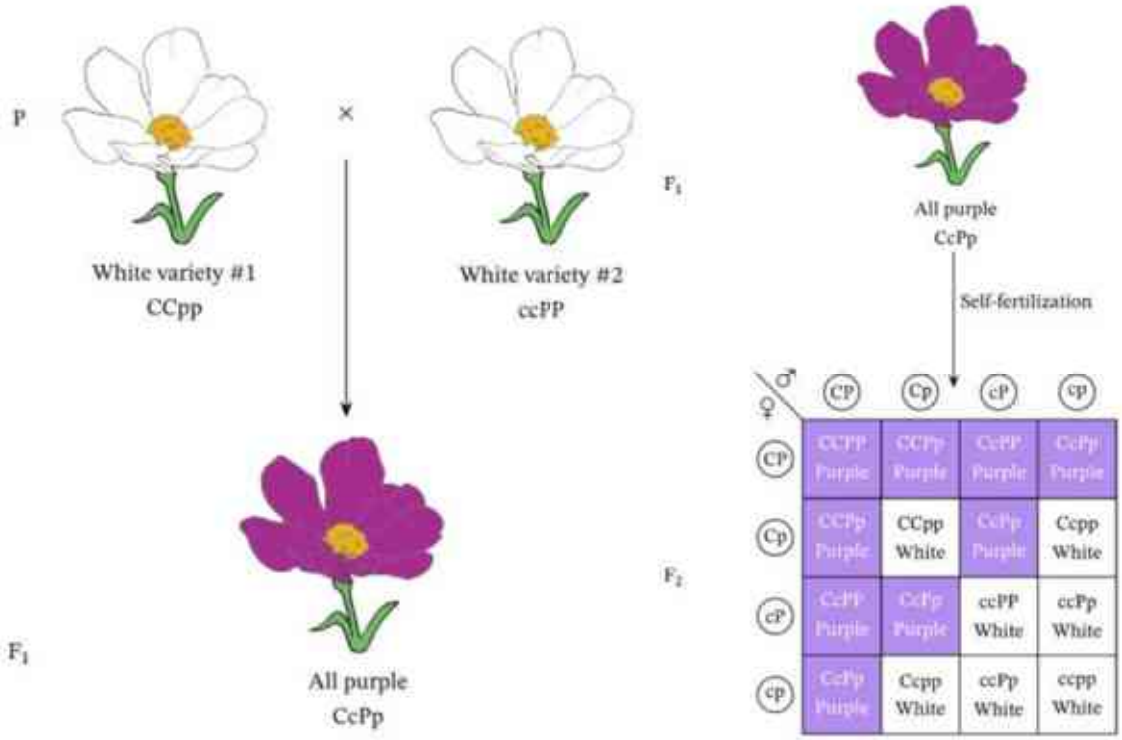
Non alletic genes that act together to produce a phenotype different from that produced by either alone. When recessive alleles at either of the two loci can mask the expression of dominant alleles at the two loci, it is called duplicate recessive epistasis. This is also known as complementary epistasis.

Example for duplicate recessive epistasis the flower color in sweet pea. The purple color of flower in sweet pea is governed by two dominant gene say C and P when these genes are in separate individuals (Ccpp or ccPP) and white (ccpp) they produce white flower. C cross between purple flower (CCPP) and white flower (ccpp) strains produced purple color in F1 intermating of F1 plants produced purple and white flower plants in 9:7 ratio in F2 generation. Here the recessive allele.a. is epistatic to B/b alleles and mask the expression of these alleles, another recessive allele b is epistatic to A/a alleles and mask their expression.

Parents	purple	x	White
	CCPP	x	ccpp
	CP		cp
		CcPp	
		Purple	

	CP	**Cp**	**cP**	**cp**
CP	CCPP (P)	CCPp (P)	CcPP (P)	CcPp (P)
Cp	CCPp (P)	CCpp (W)	CcPp (P)	Ccpp (W)
cP	CcPP (P)	CcPp (P)	ccPP (W)	ccPp (W)
cp	CcPp (P)	Ccpp (W)	ccPp (W)	ccpp (W)

Ratio = 9 Purple: 7 white



(5) Duplicate genes with cumulative effects or Additive gene interaction (9:6:1) (Polymeric gene action)

Two non-allelic genes have similar effect when they are separate but produced enhanced effect when they come together. Such gene interaction is known as duplicate genes with cumulative effect.

If the dominant condition (either homozygous or heterozygous) at either locus (but not both) produces the same phenotype, the F2 ratio becomes 9: 6: 1. For example, where the epistatic genes are involved in producing various amounts of substance such as pigment, the dominant genotypes of each locus may be considered to produce one unit of pigment independently. Thus, genotypes A-bb and aaB- produce one unit of pigment each and therefore have the same phenotype. The genotype aabb produces no pigment, but in the genotype. A-B- the effect is cumulative and two units of pigments are produced. The 9 : 3 :3 :1 ratio is modified into 9 : 6 : 1 ratio.

Example Squash fruit shape: Two completely dominant genes A and B affect the shape of the fruit, genes A and B alone (e.g. Aabb and aaBB give gives rise disc shape fruit, the effect of A is the same as that of B. But when both the genes A and B are present together they produce sphere shape fruit indicating the effect of A and B genes of fruit shape are added together. Individual homozygous recessive for both these genes are long shape fruit.

Parents AA BB x aa bb

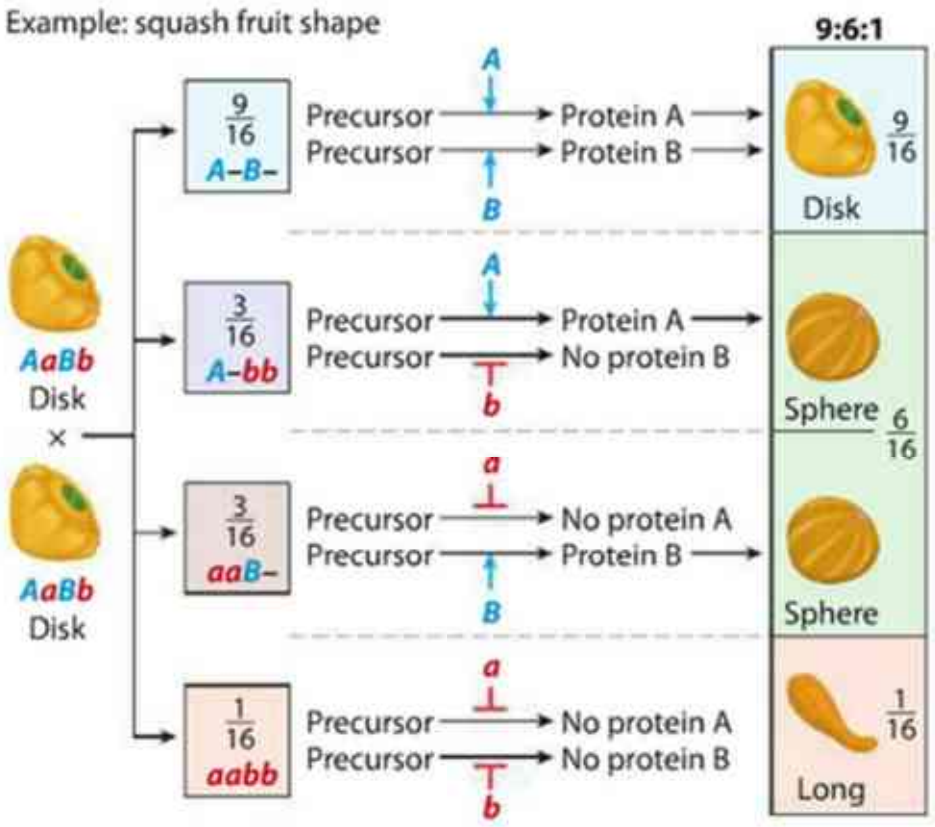
Disc x Long

Aa Bb

Long awned

	AB	**Ab**	**aB**	**ab**
AB	AABB (D)	AABb (D)	AaBB (D)	AaBB (D)
Ab	AABb (D)	AAbb (S)	AaBb (D)	Aabb (S)
aB	AaBB (D)	AaBb (D)	aaBB (S)	aaBb (S)
ab	AaBb (D)	Aabb (S)	aaBb (S)	aabb (L)

Ratio = 9 Disc: 6 Sphere: 1 Long



(6) Dominant and Recessive interaction Inhibitory gene action (13:3)

In this type of epistasis, a dominant allele at one locus can mask the expression of both (dominant and recessive) alleles at second locus. This is also known as inhibitory gene interaction.

Example of this type of gene interaction is found for anthocyanin pigmentation in rice. The green colour of plants is governed by the gene I which is dominant over purple colour. The purple colour is controlled by a dominant gene P. when a cross was made between green (IIpp) and (iiPP) colour plants, the F1 was green. Intimating of F1 plants produced green and purple plants in 13:3 ratio in F2.

Parents Green x Purple

IIpp x iiPP

IiPp

Green rice

	IP	**Ip**	**iP**	**ip**
IP	IIPP (G)	IIPp (G)	IiPP (G)	IiPP (G)
Ip	IIPp (G)	IIpp (G)	IiPp (G)	Iipp (G)
IP	IiPP (G)	IiPp (G)	IiPP (P)	iiPp (P)
ip	IiPp (G)	Iipp (G)	IiPp (P)	Iipp (G)

Ratio = 13 Green: 3 Purple

The summary of all six epistatic ratios are given in the table:

	A-B-	A-bb	aaB-	aabb
Classical ratio	**9**	**3**	**3**	**1**
Dominant epistasis/ Epistatic gene interaction	**12**			**1**
Recessive epistasis / Supplementary gene interaction				
Duplicate genes with cumulative effect / Additive gene interaction				**1**
Duplicate dominant genes / Duplicate gene interaction	**15**			
Duplicate recessive genes / Complementary gene action	**9**			
Dominant and recessive interaction/ Inhibitory gene action	**13**			

Ratio	Description	Interaction
9:3:3:1	Complete dominance at both gene pairs; new phenotypes result from interaction between dominant alleles, as well as from interaction between both homozygous recessives	**None (Independent Assortment)**
12:3:1	Complete dominance at both gene pairs; however, when one gene is dominant, it masks the phenotype of the other gene	**Dominant epistasis**
9:4:3	Complete dominance at both gene pairs; however, when one gene is homozygous recessive, it masks the phenotype of the other gene	**Recessive epistasis**
15:1	Complete dominance at both gene pairs; however, when either gene is dominant, it masks the effects of the other gene	**Duplicate dominant epistasis**
9:7	Complete dominance at both gene pairs; however, when either gene is homozygous recessive, it masks the effect of the other gene	**Duplicate recessive epistasis**
9:6:1	Complete dominance at both gene pairs; however, when either gene is dominant, it masks the effects of the other gene	**Duplicate interaction**
13:3	Complete dominance at both gene pairs; however, when either gene is dominant, it masks the effects of the other gene	**Dominant and recessive epistasis**

MULTIPLE FACTOR

It is quite natural that small differences exist among individuals of similar genotype due to the effect of environment on genotype. On the other hand, there are some heritable differences also exist with continuous variation. Most of the economical traits show continuous variation and they are measurable or quantifiable.

Quantitative characters:

Quantitative characters are traits which show continuous variation and governed by a large number of genes called multiple genes or multiple factors or polymeric genes or polygenes. Their inheritance follows same mendelian principles.

Qualitative characters:

Qualitative characters showdiscontinuous variation and are governed by one or two major genes or oligognes.

- **Quantitative genetics (Inheritance of Multiple Genes)**

The phenotypic traits of the different organisms may be of two kinds, viz., qualitative, and quantitative. The qualitative traits are the classical Mendelian traits of kinds such as form (e.g., round or wrinkle seeds of pea); structure (e.g., horned, or hornless condition in cattles); pigments (e.g., black, or white coat of guinea pigs); and antigens and antibodies (e.g., blood group types of man) and so on. We have already discussed that each qualitative traitmay be under genetic control of two or many alleles of a single gene with little or no environmental modifications to obscure the gene effects. The organisms possessing qualitative traits have distinct (separate) phenotypic classes and are said to exhibit discontinuous variations.

The quantitative traits, however, are economically important measurable phenotypic traits of degree such as height, weight, skin pigmentation, susceptibility

to pathological diseases or intelligence in man; amount of flowers, fruits, seeds, milk, meat or egg produced by plants or animals, etc. The quantitative traits are also called metric traits. They do not show clear cut differences between individuals and forms a spectrum of phenotypes which blend imperceptively from one type to another to cause continuous variations. In contrast to qualitative traits, the quantitative traits may be modified variously by the environmental conditions and are usually governed by many factors or genes (perhaps 10 or 100 or more), each contributing such a small amount of phenotype that their individual effects cannot be detected by Mendelian methods but by only statistical methods.

Such genes which are non-allelic and effect the phenotype of a single quantitative trait, are called polygenes or cumulative genes. The inheritance of poly genes or quantitative traits is called quantitative inheritance, multiple factor inheritance, multiple gene inheritance or polygenic inheritance. The genetical studies of qualitative traits are called qualitative genetics.

Certain Characteristics of Quantitative Inheritance

The quantitative inheritance has following characteristics:

(1) The segregation phenomenon occurs at an indefinitely large number of gene loci.

(2) If a substitution of a allele occurs in a gene locus then such allelic substitutions havetrivial effects.

(3) The genes for a multiple trait have different biochemical functions but similar phenotypic effects, therefore, the phenotypic effects of gene substitutions are interchangeable.

(4) Blocks of genes are bound together by inversions and transmitted as units from inversion heterozygotes to their progeny, but such blocks are broken up by crossing overin insertion homozygotes.

(5) The polygenes have pleiotropic effects; that is, one gene may modify or suppress more than one phenotypic trait. A single allele may do only one thing chemically but may ultimately affect many characters.

(6) The environmental conditions nave considerable effect the phenotypic expression of poly genes for the quantitative traits. For example, height in many plants (e.g., corn, tomato, pea, marigold) is genetically controlled quantitative trait, but some environmental factors as soil, fertility, texture, and water, the temperature, the duration and wavelength of incident light, the occurrence of parasites, etc., also affect the height. Similarly, identical twins with identical genotypes, if grow up in different kinds of environments, show different intelligence quotients.

Example of Quantitative trait (Skin Color in Man)

Another classical example of polygenic inheritance was given by Davenport (1913) in Jamaica. He found that two pairs of genes, A-a and B-b cause the difference in skin pigmentation between Negro and Caucasian people. These genes were found to affect the character in additive fashion. Thus, a true Negro has four dominant genes, AABB, and a white has four recessive genes aabb. The F_1 offspring of mating of aabb with AABB, are all AaBb and have an intermediate skin color termed mulatto. A mating of two such mulattoes produce a wide variety of skin color in the offspring, ranging from skins as dark as the original Negro parent to as white as the original white parent. The results of this cross are as follows:

Parents:	Negro		White
	AABB	x	aabb
Gametes:		↓	
F_1:	Mulatto		Mulatto
	AaBb	x	AaBb

↓

F_2 results:

Phenotypes	Genotypes	Genotypic Frequency	Phenotypic Ratio
Black (Negro)	AABB	1	1
Dark	AaBB, AA Bb	2 2	4
Intermediate	AaBb aaBB AA bb	4 1 1	6
Light	Aabb Aa Bb	2 2	4
White	aa bb	1	1

These results are clearly showing that A and B genes produce about the same amount of darkening of the skin; and therefore, the increase or decrease of A and B genes cause variable phenotypes in F_2 in the ratio of 1 Negro: 4 dark: 6 intermediate: 4 light : 1 white.

- **Qualitative characters**

The easiest characters, or traits, to deal with are those involving discontinuous, or qualitative, differences that are governed by one or a few major genes. Many such inherited differences exist, and they frequently have profound effects on plant value and utilization. Examples are starchy versus sugary kernels (characteristic of field and sweet corn, respectively) and determinant versus indeterminant habit of growth in green beans (determinant varieties are adapted to mechanical harvesting). Such differences can be seen easily and evaluated quickly, and the expression of the traits remains the same regardless of the environment in which the plant grows. Traits of this type are termed highly heritable.

A qualitative trait is expressed qualitatively, which means that the phenotype falls into different categories. These categories do not necessarily have a certain order. The pattern of inheritance for a qualitative trait is typically monogenetic, which means that the trait is only influenced by a single gene. Inherited diseases caused by single mutations are good examples of qualitative traits. Another is blood type. The environment has very little influence on the phenotype of these traits.

The major differences between the two are following:

Qualitative genetics	Quantitative genetics
It deals with the inheritance of traits of kind, viz., form, structure, colour, etc.	It deals with the inheritance of traits of degree, viz., heights of length, weight, number, etc.
Discrete phenotypic classes occur which display discontinuous variations	A spectrum of phenotypic classes occur which contain continuous variations.
Each qualitative trait is governed by two or many alleles of a single gene.	Each quantitative trait is governed by many non-allelic genes or polygenes.
The phenotypic expression of a gene is not influenced by environment.	Environmental conditions effect the phenotypic expression of polygenes variously.
It concerns with individual mattings and their progeny.	It concerns with a population of organisms consisting of all possible kinds of matings.
In it analysis is made by counts and ratios.	In it analysis is made by statistical method

MODIFYING GENES

These are group of genes, which enhances or reduce the phenotypic effect of a major gene. Such genes have small and cumulative effect on the expression of the major genes. As a result, continuous variation is generated in the phenotype governed by a single major gene, which converts qualitative character into a quantitative one. In rats, guinea pigs and rabbits, piebald spotting is produced by recessive genes when present in a homozygous state (ss). The degree of spotting depends upon the modifying factors, designed as S1, S2, S3 etc. which enhances or reduces the expression of this spotting gene with cumulative on spotting. Most quantitative characters of crop plants may be determined in a similar fashion. Some modifying genes affect more than one character.

- **Major and minor genes**

In the pie bald spotting the modifying factors produce some spotting even in the absence of the spotting genes but their effect is much more pronounced in the presence of s, Obviously the spotting gene s is a major gene controlling spotting, while the modifying genes are minor genes affecting this trait

Inheritance of quantitative characters Concept of polygenes

Colour, sex etc which shows distinct categories are known as qualitative characters. They are usually governed by one or major genes or oligogenes. Characters like length of ear in corn, yield of grain, yield of milk, stature etc do not fall into clear cut classes and shown more or less continuous variation and are governed by a large number of minor genes called multiple genes or polygenes. The characteristic feature of quantitative characters is 1) continuous variation and 2) a marked influence of the environment on their expression.

▪ Transgressive segregation

The appearance in F2 individuals with higher or lower intensity of characters than the parents is called as transgressive segregation. It is produced when the parents have positive alleles of different genes affecting a quantitative traits and segregation of these genes produce two extreme homozygotes in F2, which transgress the parental limit for the character. The reappearance of ancestor is called atavism, throw back or reversion.

▪ Expressivity

The degree of phenotypic expression of a penetrant gene is called expressivity. In other words, the ability of a gene to produce identical phenotypes in all the individuals carrying it in the appropriate genotype is known as incomplete expressivity. Many genes have incomplete expressivity, while the wild type (normal) alleles are buffered against such variations.

▪ Penetrance

The frequency with which a gene produces a phenotypic or visible effect in the individuals, which carry it, is known as penetrance. In other words, penetrance refers to the proportion of individuals which exhibit phenotypic effect of a specific gene carried by them. In general, genes express themselves in all the individuals in which they represent in the appropriate genotype, this is known as complete penetrance. But many genes do produce the concerned phenotype in all the individuals which carry them in the appropriate genotype. Such a situation is known as incomplete penetrance. When a gene is present in the appropriate genotype, the per cent of individuals in which it can express itself is a measure of its penetrance. Thus, the chlorophyll deficiency gene in lima beans has a penetrance of 10 %. Almost all the genes showing incomplete penetrance exhibit incomplete expressivity as well. Thus

incomplete penetrance is in fact an expression of incomplete expressivity in that some individuals show such a small expression of the gene that the trait is not detectable.

- **Pleiotropism**

In general, one gene affects a single character. But many genes are known to affect more than one character such genes are known as pleiotropic genes and the condition is termed as pleiotropy. An example of a pleiotropic gene in human beings is the recessive gene (s) which produces sickle cell anemia in the (ss) homozygotes. These gene causes changes in two or more parts of characters, which are not related, then the gene is said to be pleiotropic gene.

E.g., In cotton the Punjab hairy lintless gene lic produces seeds without lint. This gene also causes incomplete lancinations of the leaf, reduction in boll size and fertility. In a plant a gene may produce red pigment in several organs, such as flowers stem, leaves but still it is not correct to say that the gene is pleiotropic because the gene has only one general effect, the production of pigment. A gene for wing may be vestigial gene can be called as bristle gene or a fecundity gene. A number of other recessive genes produce marked and often detrimental effect in human beings. They are referred as syndromes.

- **Phenocopy**

The phenomenon of multiple phenotypic expression of a single gene is called pleiotropism. It is an environmentally induced change with resembles the effect a gene mutation is called phenocopy. The term "phenocopy" was first proposed by Richard Goldschmidth. He subjected pupae of Drosophila to a high temperature (35°C) for a short time at different periods in their development. Several phenotypes appeared which were similar to the phenotypes produced by certain mutant genes.

Goldschmidth found that the genes had not been changed by the heat treatment, and the descendants of the phenocopies were normal in their phenotypes when they were grown at normal temperature.

In human, the gene for disease phenylketonuria has pleiotropic effect and produces various abnormal phenotypic traits, collectively called syndrome. For example, the affected individuals have excess quantity of amino acid phenylalanine in their urine, cerebrospinal fluid and blood. They have short stature, mental retardation, widely spaced incisors, pigmented patches on skin, excessive sweating and non-pigmented hairs and eyes.

- **Polydactyly**

Polydactyly is a condition with extra fingers and toe or toes in man is due to the presence of dominant gene P. The normal condition is produced by the genotype PP. The genotype and pp produce polydactyly. Some heterozygous individuals are not polydactyly. (Pp). Therefore, the gene has penetrance of less than 100 percent and said to be incompletely penetrant. A gene though penetrant, may be quite variable in its expression. The degree of expression produced by a penetrant genotype is termed expressivity. The polydactylous condition may be penetrant in the left hand and not in the right hand or may be penetrant in the feet and not in hands.

- **Iso-alleles**

These alleles, which are similar but on testing it proves to be a different one. Blood group A person have three slightly different types such as IA1, IA2, IA3 which are similar but found to be different after testing.

a. **Mutant isoalleles**: Such alleles act within the phenotypic range of a mutant character.
b. **Normal isoalleles**: such alleles act within the phenotypic range of a wild character.

- **Pseudo-alleles**

The genes that are so closely linked can be separatable only by rare crossing over. Such genes are called pseudo-alleles.

Pseudo-alleles are closely linked genes that have similar functions. Their proximity on the chromosome makes their distinction by the complementation tests traditionally used by geneticists difficult. For this reason, and because they have similar functions, they were initially often considered as allelic forms of the same gene, hence their name. The Hox cluster is an emblematic example of a pseudo-allelic gene complex.

The first observations were made very early but remained puzzling until a simple model explaining their formation and characteristics emerged in the middle of the 1930s: pseudo-alleles originated by gene duplication, the two copies of the gene remaining closely associated on the chromosome, but progressively diverging in structure and function. This model did not prevent the active discussion of new observations on pseudo-alleles in the following years. There is an additional, more important reason for a historian to be interested in this system. The study of pseudo-alleles was an unsuccessful attempt to bridge the gap between genes and genomes, and to find in the structural organization of the genome clues to how genes function. As Edward B. Lewis put it in 1955: The phenomenon of pseudo-allelism promises to contribute much to our understanding of the gene – how it functions, how it mutates, how it evolvesl (Lewis 1955). The history of pseudo-allelism illustrates the difficulty of demonstrating that genomes are more than the addition of individual genes.

NON-MENDELENIAN INHERITANCE

But some characters in several organisms do not show Mendelian inheritance or they show a non-Mendelian inheritance pattern. In such cases, the following characteristic featuresare observed.

(1)There is consistent difference between the results from reciprocal crosses; generally,only the trait from female parent is transmitted.

(2)In most cases, there is no segregation in the F2 and subsequent generations. Characters showing non-Mendelian inheritance may be grouped under three broadcategories:

- Those related to cellular structures and patterns,
- Those produced by intracellular parasites, symbionts, and viruses.
- Those associated with DNA containing cell organelles viz., mitochondria and chloroplasts.

CYTOPLASMIC INHERITANCE

Besides chromosomes, various organelles of cytoplasm also contain DNA. The mitochondria and plastids have their own DNA and carry their genetic characters themselves. The mechanism in which cytoplasmic inclusions (e.g., alpha, beta, sigma and kappa particles) and organelles (plastids, mitochondria, centriole, etc) take part in transmission of characters from generation to generation is called cytoplasmic inheritance. Since cytoplasmic inheritance is based on cytoplasmic DNA molecules, itis also called extra chromosomal inheritance.

The smaller inheritable extra chromosomal unit is called as **plasma gene** and all the plasma genes of a cell constitute the **Plasmon** (like the genome). Cytoplasmic inheritance is due to the plasma genes located in cell organelles that are integral constituents of normal cells.

Characteristics of cytoplasmic inheritance:

(1) **Reciprocal differences:** Reciprocal crosses show marked differences for the characters governed by plasma genes. In most cases, plasma genes from only one parent, generally the female parent are transmitted, this phenomenon is known as uniparental inheritance.

(2) **Lack of segregation:** In general, F2 F3 and the subsequent generations do not show segregation for a cytoplasmically inherited trait. This is because the f1 individuals generally receive plasma genes from one parent only.

(3) **Irregular segregation in biparental inheritance:** In some cases, plasma genes from both the parents are transmitted to the progeny, this is known as biparental inheritance.

(4) **Somatic segregation:** Plasma genes generally show somatic segregation during mitosis, a feature of rare occurrence in the case of nuclear genes.

(5) **Association with organelle DNA:** Several plasma genes have been shown to be associated with cp-DNA or mt-DNA.

(6) **Nuclear transplantation:** If nuclear transplantation revealas a trait to be governed by the genotype of cytoplasm and not by that of nucleus, cytoplasmic inheritance of the trait is strongly indicated. In nuclear transplantation, nucleus of a cell is removed and replaced by a nucleus of another genotype from a different cell. Generally, nuclei of somatic cells are transplanted into zygotes before the first mitotic division is initiated.

(7) **Transfer of nuclear genome through back crosses:** The nucleus of a variety or species may be transferred into the cytoplasm of another species or variety through repeated back crossing with the former, which is used as the recurrent male parent. Lines produced in this way are known as alloplasmic lines since they have nuclei and cytoplasm from two different species. A comparison of

the various characters of alloplasmic lines with those of the corresponding euplasmic line (lines having nuclei and cytoplasm from the same species) demonstrates cytoplasmic effects, if any on these traits. This technique is time consuming, but extremely powerful; it has been extensively used to study the cytoplasmic differentiation during evolution.

(8) **Mutagenesis:** Some mutagens e.g.: Ethidium bromide are highly specific mutagens for plasma genes while nuclear genes are not affected by them. Induction of mutation by such agents in a gene indicates it to be a plasma gene.

(9) **Lack of chromosomal location:** In many organisms, extensive linkage maps of nuclear genes are available. If a gene is shown to be located in one of these linkage groups, it cannotbe a plasma gene. Failure to demonstrate the location of a gene in one of the linkage groups of an organism is indicative of its cytoplasmic location, but this is highly tentative.

(10) **Lack of association with a parasite, symbiont, or virus:** In many cases, a cytoplasmically inherited character is associated with a parasite, symbiont or virus present in the cytoplasm ofthe organism. Such cases cannot be regarded as cases of cytoplasmic inheritance. Only those cytoplasmically inherited characters which are not associated with parasites, symbionts or viruses can be regarded as governed by plasma genes.

The known cases of true cytoplasmic inheritance are concerned with either chloroplast or mitochondrial traits and are usually associated with their DNA. Such cases are therefore often referred to as organellar inheritance, plastid inheritance and mitochondrial inheritance.

Mitochondria (mt DNA)

Mitochondria are present in living organisms arise from preexisting mitochondria. They are small cytoplasmic organelles present in animal and plant cells but not

present in bacteria and viruses. Mitochondria provide cellular energy through oxidative phosphorylation. Mitochondria contain a small circular DNA molecule code for limited number of structures and functions. The size of mtDNA ranges from about 16 kb in mammals up to several hundred kilo base pairs in higher plants (e.g. 570 kb in maize) and mt DNA usually found in multiple copies per organelle. The mtDNAplay a significant role in crop improvement. Recent evidence showed that the cytoplasmic genetic male sterility system in crop plants is due to the interaction of mitochondrial genome to the nuclear genome.

In addition to these cases of non-Mendelian inheritance, some characters in several organisms exhibit a Mendelian inheritance pattern but the development of these characters in an individual is markedly affected by the genotype of the maternal parent of the concerned individual; such cases are classified as maternal effects.

The evidence for cytoplasmic inheritance was first presented by Correns in Mirabilis jalapa and by Baur in Pelargonium zonale in 1908. In case of cytoplasmic inheritance generally the character of only one of the two parents (usually the female parent) is transmitted to the progeny. As a result, reciprocal crosses exhibit consistent differences for such characters and there is a lack of segregation in the F2 and the subsequent generations. Such inheritance is also referred as extra nuclear inheritance, extrachromosomal inheritance, and maternal inheritance.

Genes governing the traits showing cytoplasmic inheritance are located outside the nucleus and in the cytoplasm; hence they are referred to as plasma genes, cytoplasmic genes, cytogenes, extranuclear genes or extra chromosomal genes. The sum of all the genes present in the cytoplasm of a cell is known as Plasmon, while all the genes present in a plastid constitute a plastron.

CHROMOSOMES

History: W. Hofmeister in 1848, discovered nuclear filaments in the nuclei of pollen mother cells of *Tradescantia*. First accurate count of chromosomes was made by W. Flemming in 1882, in the nucleus of a cell. In 1884, W. Flemming, Evan Beneden and E. Strasburger demonstrated that the chromosomes double in number by longitudinal division during mitosis. Beneden in 1887 found that the number of chromosomes for each species was constant. The term "Chromosomes" was coined in 1888 by W. Waldeyer for the nuclear filaments. W.S. Sutton and T. Boveri suggested role of chromosomes in heredity in 1902, confirmed by Morgan in 1933.

- **The structure of chromosomes varies in viruses, prokaryotes and eukaryotes :**

A. **Viral chromosome-** In viruses there is a single chromosome bearing a single nucleic acid molecule (DNA or RNA) surrounded by a protein coat called Capsid. It may be linear or circular. The viruses having DNA as genetic material are called DNA viruses and those having RNA as genetic material are known as RNA viruses. A limited amount of genetic information is present in the viral chromosome which codes for little more than the production of more virus particles of the same kind in the host cell. In RNA viruses, often the RNA directs the synthesis of DNA complementary to itself by reverse transcription in the host. The RNA is then transcribed by the DNA for the formation of new virus particles. Such ribovirus is called retrovirus. The AIDS causing virus is a retrovirus.

B. **Prokaryotic chromosomes-** Prokaryotic chromosome (e.g., bacteria) has a single and circular two-stranded DNA molecule which is not enveloped by any membrane. It lacks proteins and is in direct contact with the cytoplasm. The bacterial chromosome is packed into the nucleoid by some RNA that appears to

form a core. It is attached to plasma membrane permanently at least at one point. In addition to the main chromosome some extra-chromosomal DNA molecules may also be present in most of the bacterial cells they are also double stranded and circular but are much smaller in size. They are known as plasmids. The plasmid may occur independently in the cytoplasm of calls or may also be found in association of main chromosomal DNA and called as episome.

C. **Eukaryotic chromosomes-** The eukaryotic chromosomes are present in nucleus and in certain other organelles, like mitochondria and plastids. These chromosomes are called nuclear and extra nuclear chromosomes respectively. Nuclear chromosomes are double stranded long DNA molecules of linear form. Proteins are associated with them. They are surrounded by nuclear envelope. More DNA is involved in coding far more proteins than the prokaryotic chromosomes. Extra nuclear chromosomes are present in mitochondria and plastids. They are double stranded short DNA molecules of circular form. They lack protein association. Less genetic information is available for the synthesis of only some particles of proteins for the organelles containing them. Other proteins are received from the cytoplasm where they are synthesized under the direction of nuclear chromosomes.

➢ **Material of Chromosomes**

The chromatin material of the eukaryotic chromosomes according to its percentage of DNA, RNA and proteins and consequently due to its, staining property has been classified into following by classical cytologists:

a) Euchromatin

The euchromatin is the extended form of chromatin and it forms the major, portion of chromosomes. The euchromatin has special affinity for basic stains and is

genetically active because its component DNA molecule synthesizes RNA molecules only in the extended formof chromatin.

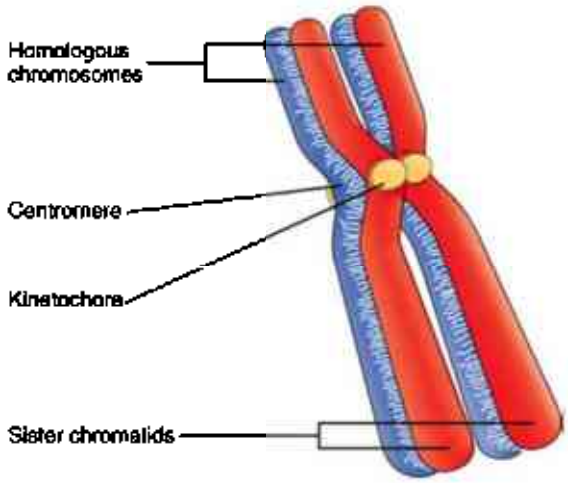
b) Heterochromatin

The heterochromatin is a condensed intercoiled state of chromatin, containing two to three times more DNA than euchromatin. However, it is genetically inert as it does not direct synthesize RNA (i.e., transcription) and protein and is often replicated at a different time fromthe rest of the DNA.

Recent molecular biological studies have identified three kinds of heterochromatins, namely constitutive, facultative, and condensed heterochromatin. The constitutive heterochromatin is present at all times and in the nuclei of virtually all the cells of an organism. In an interphase nucleus, it tends to clump together to form chromocenter or false nucleoli. In Drosophila, for example, most pupal, larval and adult cells contain large blocks of constitutive heterochromatin that lie adjacent to centromeres. Constitutive heterochromatins contain highly repetitive satellite DNA which is late replicating, it fails to replicate until late in the S-phase and is then replicated during a brief period just before the G2. The facultative heterochromatin reflects the existence of a regulatory device designed to adjust the "dosages" of certain genes in the nucleus

➢ **Morphology of Chromosomes**

During the interphase stage, the eukaryotic chromosomes are extended into long and thin chromatin fibers where they lie criss-cross to form the **chromatin reticulum.** They replicate in the S-phase and become double. At this stage they consist of two chromatids that are held together at one point called **centromere.** At the time of cell division, the chromosomes condense and tightly coil up and become distinct at metaphase stage. The eukaryotic chromosomes vary in number, size, shape and position but they have remarkably uniform structure.



A Homologous Pair of Chromosomes with their Attached Sister Chromatids.

➢ Number of Chromosomes

Eukaryotic chromosomes vary in number from two to a few hundred in different species. In a species all the individuals have same number of chromosomesin all of their cells, except the gametes. Since the chromosome number is constant for a species, it is helpful in determining and taxonomic position of thespecies.

➢ Size of Chromosomes

In a **species all the chromosomes are not of the same size.** Their size also varies from species to species. The particular chromosome of a species however has more or less a constant size. The organisms having fewer chromosomes have large sized chromosomes than those having many. Generally, plant chromosomes are larger than animal chromosomes and among plants the monocots have larger chromosomes than the dicots.

➢ Shape of Chromosomes

The chromosomes at metaphase stage look like slender rods that may be straight or curved to form an arc or a letter S. In anaphase stage they may assume J or V shapes, depending upon the position of the centromere.

➢ Position and chemical composition of Chromosomes

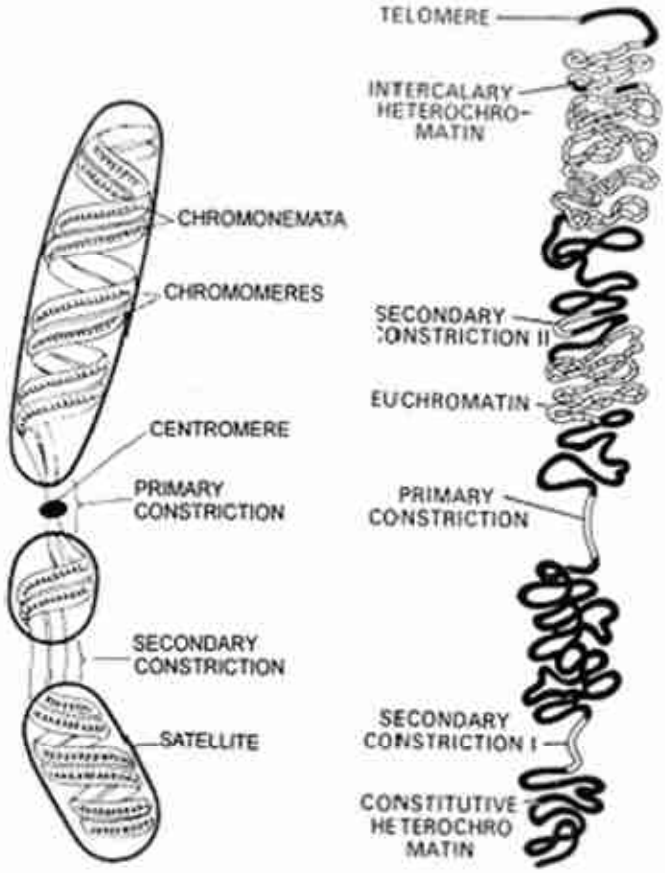
In a nucleus each chromosome is independent of all the other chromosomes in its location. Thus, they may occupy any region of the nucleus. The chromatin in the eukaryotic chromosome consists chemically of about 35% DNA, about 60% proteins, about 5% RNA, some metal ions and certain enzymes.

➢ Structure of Chromosomes

At **metaphase stage**, since the chromosome is a highly condensed nucleoprotein filament, it contains two greatly coiled sister chromatids. These chromatids that lie side by side along their length, are held together at a point called centromere, an area of the narrow region also called **primary constriction** of the metaphase chromosome. At the centromere each chromatid has a darkly staining, disc like, fibrous structure, called **kinetochore**, to which spindle microtubules attach during cell division. Kinetochores are the sites where force is exerted to pull the chromatids towards the poles. One or more chromosomes may have additional narrowregions called the **secondary constrictions**. The part of the chromosome separated by secondary constrictions is termed as **satellite**. A chromosome with a satellite is called **sat chromosome**. The size and the shape of the satellite remain constant for a species.Secondary constrictions are associated with the nucleoli and are known as the **nucleolar organizers**. The chromosomes which have nucleolar organizing regions areknown as the ***nucleolar chromosomes***. ***Ends***- The ends of chromosomes are called **telomeres**. The function of telomere varies from the rest of the chromosome. On exposure to X-rays a chromosome may break and its pieces may rejoin, but no segment connects to the telomere, showing that the telomere has a polarity, and it, somehow "seals" the end.

➢ Ultra-structure of Chromosomes

A chromatid contains a very fine filament called chromonema which is a single, long, double stranded DNA molecule. It is wrapped around histones to form **nucleosomes**. The nucleosome and non-histone proteins together form the chromatin fiber. The chromatin fiber has reactive groups, probably H1 histone molecules, which act as "folders" and crosslink the chromatin fiber changing it into a great coiled, compact metaphase chromatid.



Detailed schematic structure of chromosomes.

➢ Types of Chromosomes

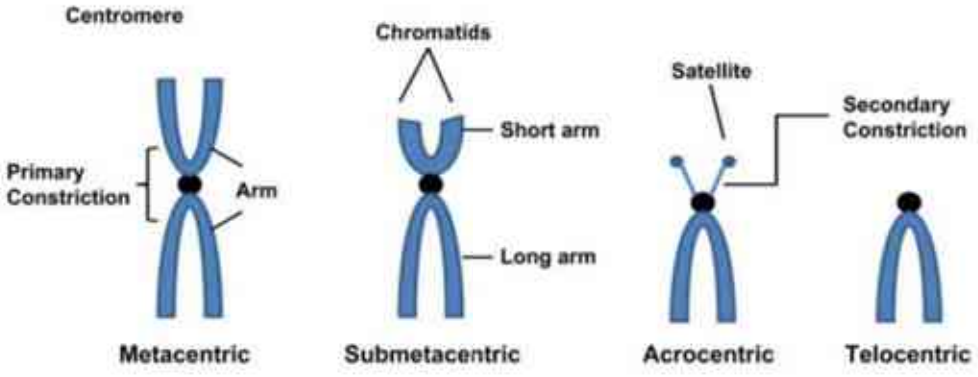
On the basis of the position and number of centromeres, chromosomes are classified:

(i) Metacentric: In metacentric chromosomes the centromere is at the middle of the chromosome, and the arms are equal. In anaphase the chromosome appears V-shaped. For example: human chromosome no. 3

(ii) Submetacentric: In such chromosome, the centromere is near the center of the chromosome, and the arms are slightly unequal and in anaphase the chromosome appears J or L shaped. For example: Human chromosome No. 1.

(iii) Acrocentric: In this type the centromere is near one end of the chromosome, and the arms are very unequal. For example: Human chromosome No. 4 & 5.

(iv) Telocentric: The centromere is at one end in such chromosomes, and the arms are on one side only. The chromosome remains rod shaped in anaphase also



Types of chromosomes based on the position and number of centromeres.

Depending upon the number of centromeres there are three types of chromosomes:

(i) Acentric: The chromosome is without a centromere, which is formed by breakage of the chromosome. It does not attach to spindle microtubules, so it is lost in the cell division.

(ii)Monocentric: It is the chromosome with a single centromere, and it is the most common type.

(i) **Dicentric:** It is the chromosome with two centromeres and is formed by the fusion of two chromosome segments each having a centromere. It is unstable and may break when the two centromeres are pulled to opposite poles in mitosis.

➢ **Functions of Chromosomes**

1- Chromosomes carry hereditary characters from parents to offspring.
2- They direct the synthesis of structural proteins and thus, help cell grow, and divide.
3- By directing the formation of necessary enzymes, they control metabolism.
4- They guide cell differentiation during development.
5- They form nucleoli at nucleolar organizer sites in daughter cells.
6- They produce variations through changes in their genes and contribute to the evolution of the organisms.
7- They play role in sex determination.
8- They maintain the continuity of life by replication.

➢ **Special types of chromosomes**

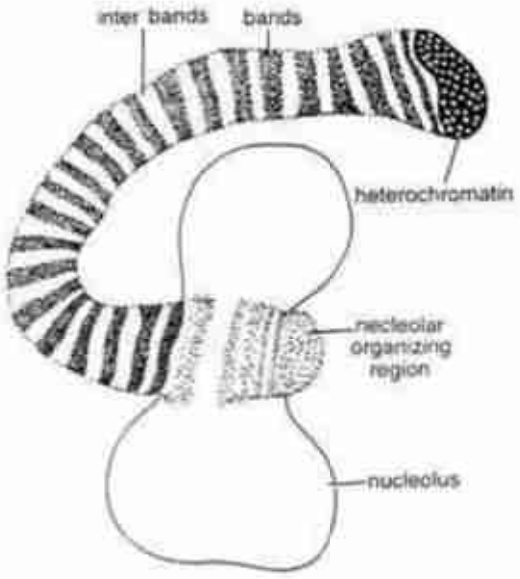
Some tissues of certain organisms contain chromosomes, which differ significantly from normal chromosomes in terms of either morphology or function. Such chromosomes are referred to as special chromosomes.

- **Giant Chromosomes**

Giant chromosomes are special, enormously enlarged chromosomes about 100 times thicker than the ordinary mitotic chromosomes. These are seen in certain tissues of varied groups of animals and plants. They are easily visible under light microscope. The giant chromosomes are of two types: polytene and lampbrush.

(A) Polytene Chromosomes

Polytene chromosomes were first observed by Balbiani (1881) in Chironomus (a dipteran larva). Because of their large size showing numerous strands these are named as polytene chromosomes by Kollar. These banded chromosomes occur in the larval salivary glands (salivary gland chromosomes), midgut epithelium, and rectum and Malpighian tubules of various genera of dipterans.



Structure of polytene chromosome showing nucleolar part.

These chromosomes are about 100-200 times larger than those of somatic chromosomes. They are roughly cylindrical and exhibit a distinct pattern of transverse striated structures consisting of alternate darkly staining band and light staining interbands. Dark bands are rich in DNA along with a small amount of RNA and basic proteins. They are genetically active. The inter-bands contain less of DNA but more acidic proteins and hence they are less active. The polytene chromosomes are formed by repeated replication of DNA without division of chromosome into daughter chromosomes. This amplification without separation is called

polytenization. As a result, a thick bundle of parallel DNA molecules all having the same banding pattern across them is produced. Thus, there can be as many as several thousands of chromonemata in a giant chromosome.

Functions of the Giant Polytene Chromosomes

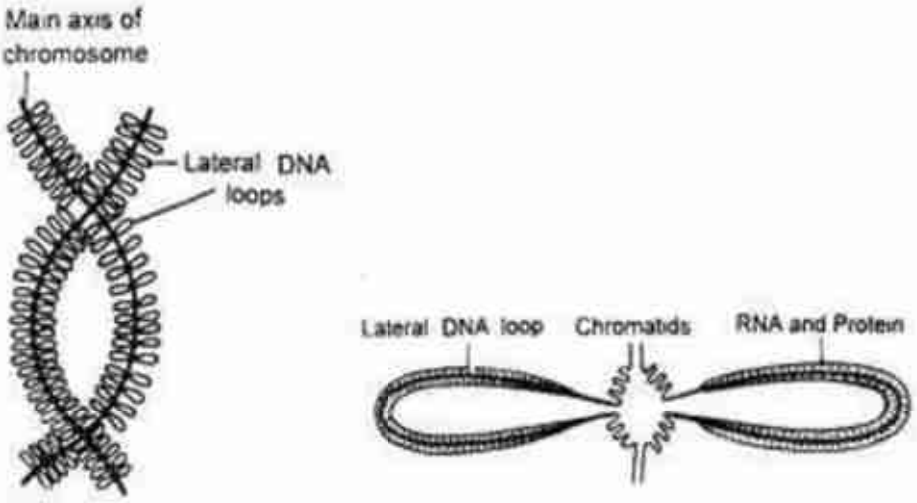
- Polytene chromosomes carry genes which ultimately control physiology of an organism. These genes are formed of DNA molecules.
- These chromosomes also help in protein synthesis indirectly. The RNA present in the nucleolus serves as a means of transmission of genetic information to the cytoplasm, leading to the formation of specific protein.

(B) Lampbrush Chromosomes

These are the largest chromosomes which can be seen with naked eyes and are found in yolk rich oocytic nuclei of certain vertebrates such as fishes, amphibians, reptiles, andbirds. They are characterized by the fine lateral loops, arising from the chromomeres, during first prophase of meiosis. Because of these loops they appear like brush; that is why they are called lampbrush chromosomes first discovered by Flemming in 1882 and described in shark oocytes by Ruckert (1892).

Lampbrush chromosome consists of longitudinal axis formed by a single DNA molecule along which hundreds of beads like chromomeres are distributed. Two symmetrical lateral loops (one for each chromatid) emerge from each chromomere, which are able to expand or contract in response to various environmental conditions. About 5 to 10% of the DNA is in the lateral loops. The axis having compacted DNA and tightly associated proteins is transcriptionally inactive. The loops consist of uncompacted DNA and proteins but have a good amount of RNA and they are transcriptionally active. A chromomere and its associated loop correspond with one gene. In lampbrush chromosomes the DNA loops are the sites

of intensive RNA synthesis. rRNA and mRNA are synthesized in large amount and the transcription of rRNA causes the enlargement of nucleolus, or formation of numerous additional nucleoli. Due to the synthesis of large amounts of proteins, fats, carbohydrates, and other molecules in the cytoplasm neededfor further development of the embryo, the oocyte grows in size. Synthesis of proteins occurs near the loops.



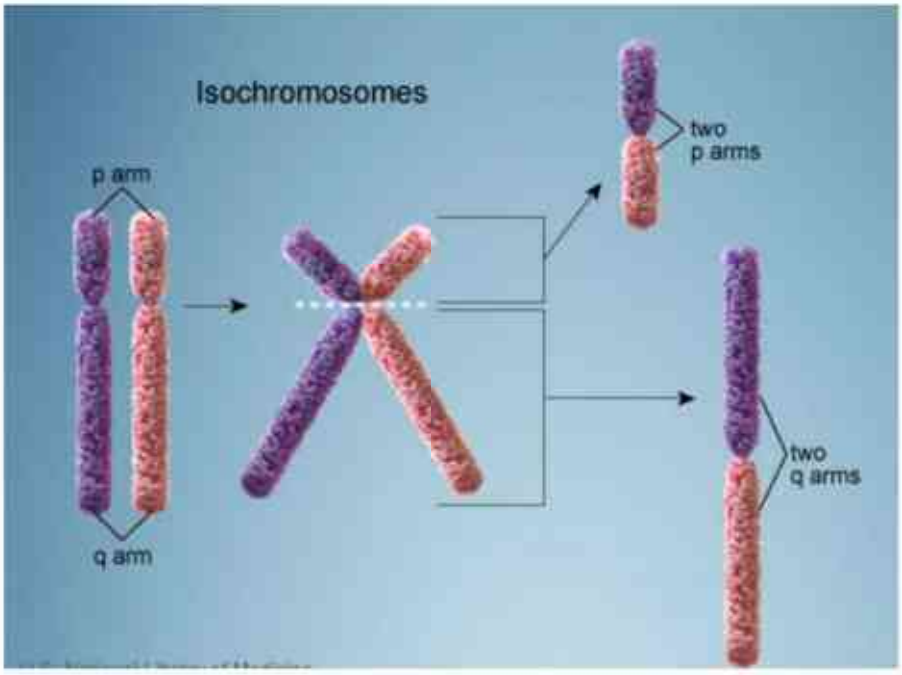
Detailed structure of lampbrush chromosome.

Functions of Lampbrush Chromosome:

- Involved in the synthesis of RNA and proteins by their loops.
- Probably help in the formation of certain amount of yolkmaterial for the egg.

(C) Iso-chromosomes:

A chromosome with two identical arms and identical genes is called as isochromosome. The arms are mirror images of each other. IT is thought to arise when a centromere divides in the wrong plane yielding two daughter chromosomes, each ofwhich carries the information of one arm only but present twice. At meiosis isochromosomes pair in three different ways. (i) Internal pairing (ii) Fraternal pairing (iii) Normal pairing



Structure of isochromosomes chromosome.

In internal pairing, the two arms of the isochromosomes pair with each other. In fraternal pairing, one or both of the arms of the isochromosomes pair with a homologous arm of another chromosome. In normal pairing, the isochromosome pairs with another one just like it.

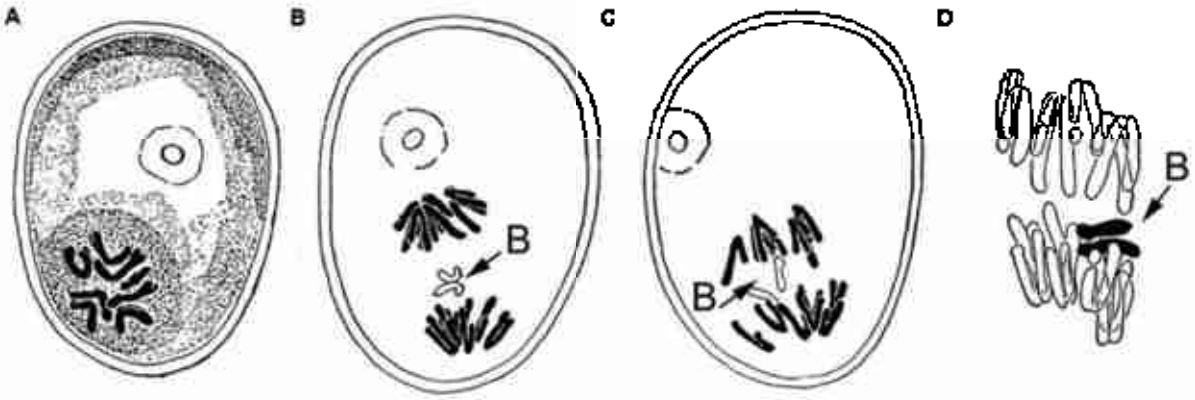
(D) 'B' chromosomes:

It is a particular kind of supernumerary chromosome that may or may not be found in organisms as extra chromosomes over and above the standard diploid or polyploidy chromosome complements. The standard complements are called 'A' chromosome. The 'B' chromosomes found in natural population are recognized on the basis of following characteristics.

- They are dispensable (not found is all the individuals of the species or all the cells of the organisms)
- They are not homologous with any of the basic 'A' chromosomes.

- Their inheritance is non Mendalian.
- They are usually smaller than the 'A' chromosomes.
- Generally, they are genetically inert.
- When it presents in higher number, they suppress the vigour and fertility.
- Their origin and functions are largely unknown.

The most significant effect of 'B' chromosome is on seed and pollen fertility. Flowering time is generally delayed by 'B' chromosomes and has negative on sequences for the organism as they have deleterious effect because of abnormal crossing over during meiosis.

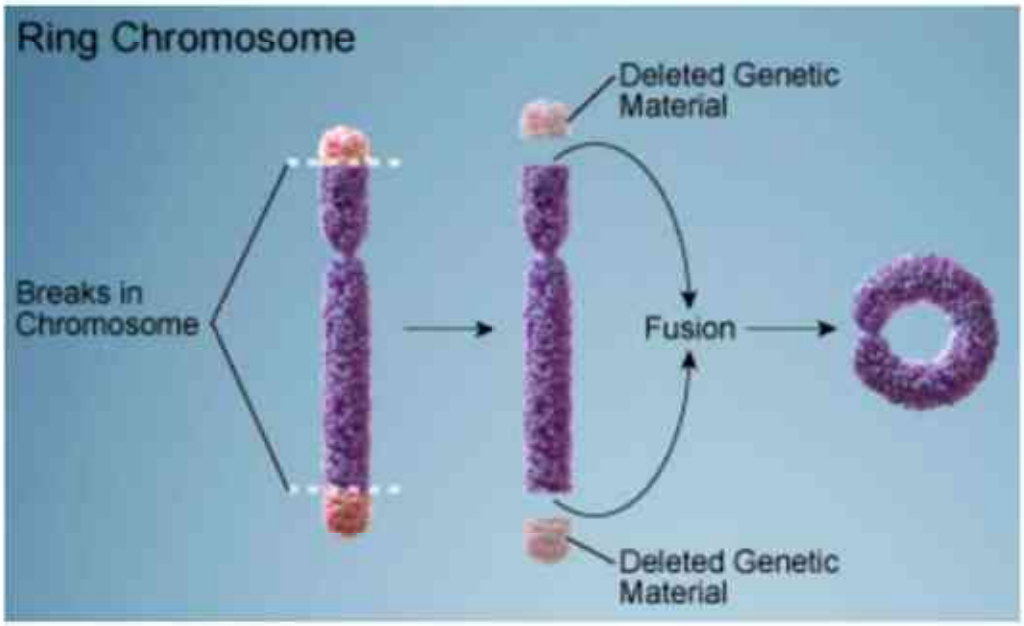


(A) metaphase, (B) lagging B chromosome due to non-disjunction. (C) Disjoined sister chromatids of the B chromosome going to different poles, (D) chromosome drive occurs, the future generative nucleus receives both sister chromatids of the B

(E) Ring chromosome:

The chromosomes of higher organisms usually have two ends and do not form a continuous ring. However, the chromosomes of lower organisms such as prokaryotes. (*E.,coli*) normally have ring shaped chromosomes. Often such chromosomes are referred to as gonophores. Which are more than 1 mm in length and consists of a single DNA molecule.

Chromosomes in higher organisms are not naturally ring shaped. However, ring chromosomes have been detected in humans, *Drosphila* and certain plant species. Ring chromosomes were most thoroughly studied in maize by Mc Clintock. Normal chromosomes do not form rings because they are believed to have telomeres on each end. Telomeres prevent the union of chromosome arms into ring formation. A chromosome can form a ring chromosome by fusion of the raw ends onlyif it has two terminal deletions producing centric segment with two raw ends and two acentric fragments. A ring chromosome lacks the genetic information that was carried by the terminally deleted fragments. Ring chromosomes are meiotically unstable, and they are associated with several syndromes.



Structure of ring chromosome.

HUMAN CHROMOSOMES

Of the 46 chromosomes in a normal human somatic cell, 44 are autosomes and 2 are sex chromosomes. The autosomes are designated as pairs 1–22. The numbers are assigned in descending order of the length, size, and centromere position of each chromosome pair. In a normal female the sex chromosomes are XX, and in a normal male, they are XY.

Until the advent of certain specialized staining techniques, arbitrary identification of individual chromosome pairs was based on the size and position of the centromere (4). Variability in the centromere position of different chromosomes allowed them to be classified into three basic categories. A chromosome with its centromere in the middle is metacentric, one with the centromere closer to one end is sub-metacentric, and one with the centromere almost at one end is acrocentric.

Based on decreasing relative size and centromere position, a karyotype comprised of seven groups labeled A through G was devised. The X chromosome belonged to the third or "C" group, whereas the Y was often placed separately. Although still used occasionally, these letter group names are now considered obsolete.

Chromosome Banding and Identification

Unequivocal identification of individual chromosomes and chromosome regions became possible with the technical developments of the late 1960s. When chromosome preparations are treated with dilute solutions of proteolytic enzymes (trypsin, pepsin, etc.) or salt solutions (2X SSC) and treated with a chromatin stain such as Giemsa, alternating dark and light stained demarcations called bands appear along the length of each chromosome. The banding patterns produced are specific for each chromosome pair, thus enabling the identification not only of individual chromosomes but also of regions within each chromosome. Methods commonly

used to produce these discriminative banding patterns include Giemsa or G-banding, quinacrine mustard or Q-banding, reverse or R-banding and constitutive heterochromatin or C-banding, each with its own uniqueness. In the United States and Canada, the most frequently used methods for routine cytogenetic analysis are G- and Q-bands, whereas in other countries (France, for example), R-banding is more common. Additional banding methods are occasionally employed to exemplify specific abnormalities or chromosome regions.

THE KARYOTYPE

A karyotype is the characteristic chromosome complement of a eukaryote species. Karyotype descriptions follow certain basic rules. When designating a karyotype, the first item specified is the total number of chromosomes, including the sex chromosomes present in that cell, followed by a comma and the sex chromosomes in that order. Thus, a normal female karyotype is written as 46, XX and a normal male karyotype as 46, XY. The characters are contiguous, without spaces between items. Chromosome abnormalities, when present, follow the sex chromosome designation using abbreviations or symbols denoting each abnormality. These are listed in a specific order: Sex chromosome abnormalities are described first, followed by autosomal changes in numerical order. For each chromosome described, numerical changes are listed before structural abnormalities. The chromosomes are depicted (by rearranging a microphotograph) in a standard format known as a karyogram or ideogram: in pairs, ordered by size and position of centromere for chromosomes of the same size. Karyotypes can be used for many purposes, such as, to study chromosomal aberrations, cellular function, taxonomic relationships, and to gather information about past evolutionary events.

Staining for the study of karyotypes:

The study of karyotypes is made possible by staining. Usually, a suitable dye is applied after cells have been arrested during cell division by a solution of colchicine. For humans, white blood cells are used most frequently because they are easily induced to divide and grow in tissue culture. Sometimes observations may be made on non-dividing (interphase) cells. The sex of an unborn fetus can be determined by observation of interphase cells (see amniotic centesis and Barr body).

Six different characteristics of karyotypes are usually observed and compared:

1- Differences in absolute sizes of chromosomes. Chromosomes can vary in absolute size by as much as twenty-fold between genera of the same family: Lotus tenuis and Vicia faba (legumes), both have six pairs of chromosomes (n=6) yet V. faba chromosomes are many times larger. This feature probably reflects different amounts of DNA duplication.

2- Differences in the position of centromeres. This is brought about by translocations.

3- Differences in relative size of chromosomes can only be caused by segmental interchange of unequal lengths.

4- Differences in basic number of chromosomes may occur due to successive unequal translocations which finally remove all the essential genetic material from a chromosome, permitting its loss without penalty to the organism (the dislocation hypothesis). Humans have one pair fewer chromosomes than the great apes, but the genes have been mostly translocated (added) to other chromosomes.

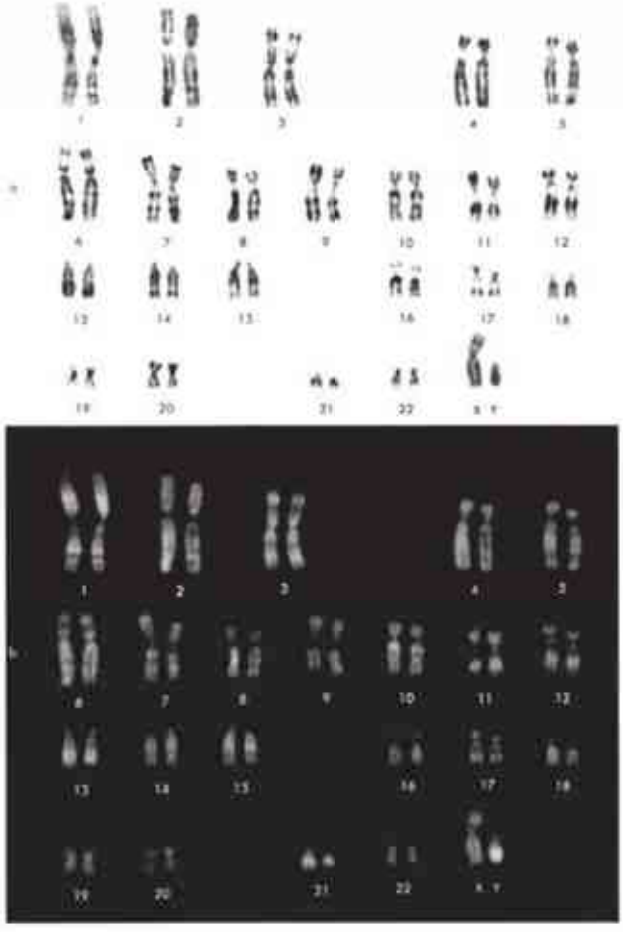
5- Differences in number and position of satellites, which (when they occur) are small bodies attached to a chromosome by a thin thread.

6- Differences in degree and distribution of heterochromatic regions.

Heterochromatin stains darker than euchromatin, indicating tighter packing, and mainly consists of genetically inactive repetitive DNA sequences.

A full account of a karyotype may therefore include the number, type, shape and banding of the chromosomes, as well as other cytogenetic information. Variation is often found:

- between the sexes
- between the germline and soma (between gametes and the rest of the body)
- between members of a population (chromosome polymorphism)
- geographical variation between races
- mosaics or otherwise abnormal individuals



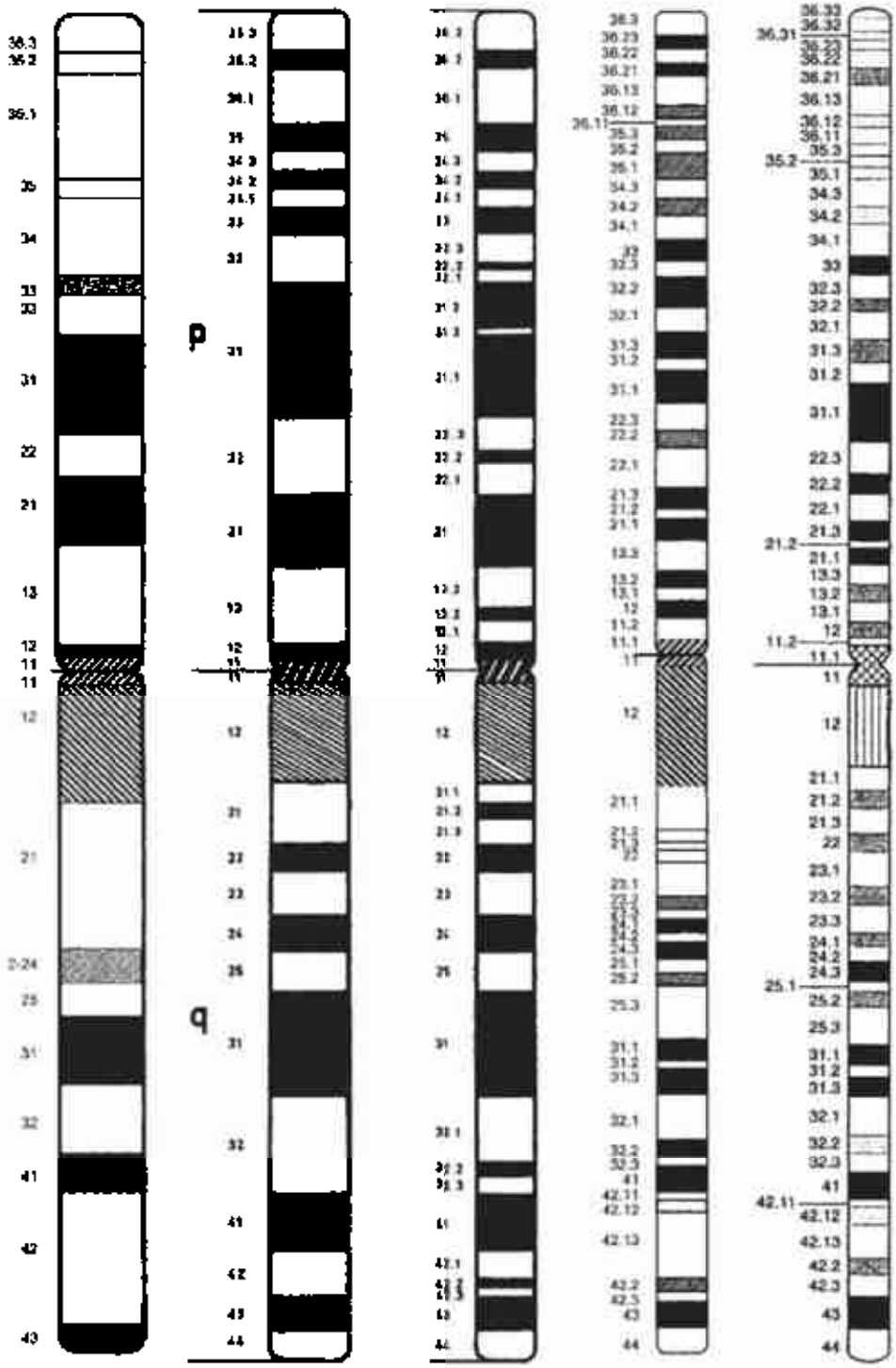
Normal 46, XY male karyotype. Characteristic G-band pattern (a) and fluorescent Q-banding.

THE IDEOGRAMS

Ideograms are a schematic representation of chromosomes. They show the relative size of the chromosomes and their banding patterns. A banding pattern appears when a tightly coiled chromosome is stained with specific chemical solutions and then viewed under a microscope. Some parts of the chromosome are stained (G-bands) while others refuse to adopt the dye (R-bands). The resulting alternating stained parts form a characteristic banding pattern which can be used to identify a chromosome. The bands can also be used to describe the location of genes or interspersed elements on a chromosome.

Below is an ideogram of each human chromosome. Next to the known schematic representation a chromosome was added that was rendered from DNA data. The G-bands, areas with proportional more A-T base pairs, are normally colored black in schematic representations. To compare the schematic ideograms the rendered chromosomes, were colored the A-T bases black and the G-C bases white. Blue areas in the rendered chromosomes identify bases not known yet.

The results are interesting, when comparing the schematic ideograms with the rendered chromosomes from our project, a significant conformance can be seen. Most black areas on the left side show also black areas on the right side and white areas are also white on the "digital" chromosomes.



Ideogram showing the G-banding pattern for normal human chromosomes at different band resolutions. From left to right these are 300, 400, 550, 700, and 850 bands.

LINKAGE

Every individual organism bears several heritable characters which are represented by the innumerable genes present on the chromosomes. During meiosis, the chromosomes move into the gametes as units, all the genes presenton any given chromosome will segregate as a group and move together from generation to generation. This tendency of the genes located on the same chromosome, to stay together in hereditary transmission, is known as linkage. The genes located on the same chromosome are called linked genes.

The principle of linkage was discovered by Bateson and Punnet in 1906 in the sweat pea, plant, Lathyrus odoratus. However, linkage, as a concept was put forth by Thomas Hunt Morgan in 1910 based on his experiment on Drosophila melanogaster.

Chromosome Theory of Linkage

Morgan, along with Castle formulated the chromosome theory of linkage. It has the follwing postulates;

- Genes are found arranged in a linear manner in the chromosomes.
- Genes which exhibit linkage are located on the same chromosome.
- Genes generally tend to stay in parental combination, except in cases of crossing over.
- The distance between linked genes in a chromosome determines the strength of linkage.
- Genes located close to each other show stronger linkage than that are located far from each other, since the former are less likely to enter into crossing over.

Linkage Groups

All the genes located on a particular chromosome, form a linkage group. Since, the genes present on a particular chromosome have their alleles located on its homologous chromosome, genes on a pair of homologous chromosomes. Hence, the

number of linkage groups corresponds to the number of haploid chromosomes found in a species. *Drosophila melanogaster* has four linkage groups which can be distinguished into three large and one small linkage groups corresponding to the four pairs of chromosomes. Twenty-three linkage groups are present in humans correspondingto 23 pairs of chromosomes. Pea plant has seven linkage groups, corresponding to the seven pairs ofchromosomes.

Types of linkage: Linkage is classified on the basis of following three criteria.

- **Based on crossing over**

  a) Complete linkage

  Linkage in which crossing over does not occur is known as complete linkage or absolute linkage. In complete linkage test cross progenies possess only parental types.

  b) Incomplete linkage

  In some cases, frequency of crossing over occurs between linked genes, it is known as incomplete linkage. In incomplete linkage, the test cross yields some recombinants besides parental combinations.

- **Based on status of genes involved**

  a) Coupling linkage

  It refers to linkage either between dominant genes or between recessive genes.

  b) Repulsion linkage

  It refers to linkage of some dominant genes with some recessive genes.

- **Based on chromosomes involved**

  a) Autosomal linkage

  It refers to linkage of such genes, which located in other than sexchromosomes.

  b) X-chromosomal linkage

  It refers to the linkage of genes, which located in sex chromosomes.

CROSSING OVER

Crossing-over is a physical exchange between chromatids in a pair of homologous chromosomes. It results in a new association of genes in the same chromosome. The role of crossing-over is important for evolution to take place. In fact, crossing-over and independent assortment are mechanisms that produce new combinations of genes. Natural selection can then act to preserve those combinations that produce organisms with maximum fitness, that is, maximum probability of perpetuation of the genotype.

The Concept of Crossing-Over

Following are the important features of crossing-over:

i) A gene is located on chromosomes at a particular site called a locus (plural-loci). The loci of the genes on chromosomes are arranged in a linear sequence.

ii) In a heterozygote, the two alleles of a gene occupy corresponding positions in the homologous chromosomes, that is, allele A occupies the same position in homolog 1 that allele a occupies of a species is fixed or constant.

iii) Crossing-over involves the breakage and rejoining of two chromatids (of homologous chromosomes), resulting in reciprocal exchange of equal and corresponding segment between them.

iv) Chromosomes with recombined or new combinations of genes are formed by the occurrence of crossing-over.

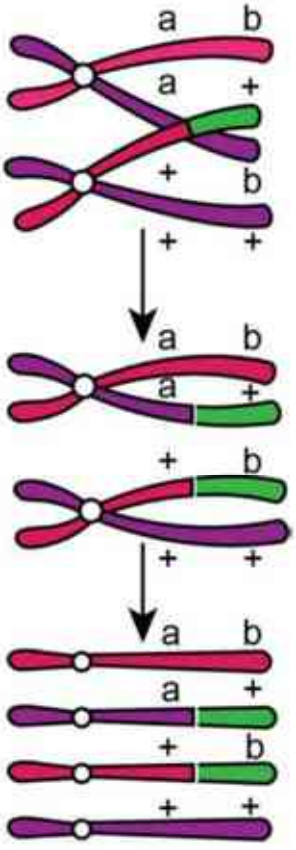
v) Crossing-over occurs more or less at random along the length of a chromosome pair. Thus, the probability of its occurrence between two genes increases with increasing physical separation of the genes along the chromosome.

When does Crossing-Over Occur?

Crossing-over begins at pachytene stage, after the synapsis of the homologous chromosomes has occurred in zygotene stage of prophase-I of meiosis. Since

chromosome replication occurs during interphase, meiotic crossing-over occurs in the post-replication four strand or tetrad stage. That is, after each chromosome has doubled such that four chromatids are present for each pair of homologous chromosomes.

Cytological basis of crossing over



Based on his results, Morgan suggested that recombination are formed as a result of pairing of homologous chromosomes during meiosis. A physical exchange of chromosome part takes place by a process called crossing-over. In the germs cells of many organisms at the time of meiosis, one can actually see certain cross-shaped structures in which two of the four chromatids of homologous chromosome pairs appear to exchange parts. These cross-shaped structures are called *Chiasmata* (singular *Chiasma).*

Molecular Mechanism of Crossing-Over

A cross-over involves a reciprocal, physical exchange between homologous chromosomes. This suggests that a reciprocal exchange essentially occurs between the double helices of the DNA molecules found in each non-sister chromatids. For this process to take place, two homologous chromosomes come close to one another. In eukaryotes, crossing-over has been associated with the formation of a structure (or set of structures) called the synaptonemal complex which forms during prophase of the first meiotic division. This structure is composed primarily of proteins and RNA and has been identified in a large number of eukaryotic species. Very little information is available about the functions of the various components of the synaptonemal complex. It is known that small amount of DNA synthesis occurs at the time when the synaptonemal

complex forms. This amount, however, is very small and is equivalent or even less than 1 per cent of the total DNA in the genome. It is believed that this DNA synthesis is involved in synapsis and/or crossing-over.

Kinds of crossing over

- According to its occurrence in the germinal or somatic cells following two types of crossing over have been recognized:

Germinal or meiotic crossing over

Commonly crossing over occurs in the germinal cells of reproductive organs during the process of gametogenesis which includes meiosis. This type of crossing over is called germinal or meiotic crossing over. It is universal in its occurrence and has great genetic significance.

Somatic or mitotic crossing over:

Sometimes crossing over may occur during mitosis or somatic cells. this type of crossing over in rare cases, has no genetic significance and is called somatic or mitotic crossing over. It has been observed in body cells of *Drosophila*.

- According to the number of chiasma, crossing over may be of the following types:

1. Single cross over: When only one chiasma occurs only at one point of the chromosome pair. It produces two non-crossover chromatids and two crossover chromatids.
2. Double cross over: when crossing over occurs at two points between any two given points in the same chromosome pair, it is called double crossing over. It produces four crossovers.
   (a) Reciprocal chiasma- same two chromatids
   (b) Complementary chiasma- both chromatids take part
3. Multiple crossing over- Crossing overs occurs at three or more points

Factors controlling crossing over

- High and low temperatures increase the frequency of crossing over.
- X-rays and other irradiations increase the crossing over frequency.
- The age of the individual also affects the crossing over frequency. It was found that crossing over frequency is higher in older ages.
- Gene mutations affected the frequency. Some mutations are known todecrease the frequency.
- Crossing over at one point of the chromosome tends to prevent othercrossing over in nearby places. This phenomenon is called interference.
- Crossing over does not take place in Drosophila male, and silk wormfemales. Thus, sex also affects the crossing over.
- Crossing over is less frequent near centromeres and the tips ofchromosomes.
- Inversions of chromosome segments suppress the crossing over.

Significance of Crossing Over

- Crossing over provides direct evidence for the linear arrangement of genes in the chromosome.
- Since crossing over results in recombination of genes variations are produced.
- Crossing over helps in the construction of chromosome maps.

SEX DETERMINATION

Nature contains a vast array of diverse mechanisms of sex determination. In lower organisms, the two sexes are phenotypically indistinguishable except for the reproductive organs and in some lower eukaryotes, the two genetically distinct type of gametes are sometime morphologically indistinguishable and called as isogamy (iso – means 'same' gametes) e.g. Green alga *Chlamydomonas reinhardtii.*

In higher form, there are many distinct morphological differences between male and female sexes. This phenomenon is called **sexual dimorphism**. Basically, the reproductive organs and sex cells are different between males and females. This forms primary sexual character. The male and female sexes differ from each other in many somatic characters. For example, mammary glands in females and beard in males are secondary sexual characters.

Two kinds of chromosomes

In dioecious organisms, chromosomes are two kinds:

- **Autosomes**

Chromosomes containing gene, which determine the various somatic characters.

- **Allosomes**

These are the chromosomes responsible for the determination of sex. Allosomes are of two types viz., X and Y. Modern geneticists have reported many different mechanisms of determination of sex in living organisms. Some important and common mechanisms of 'sex' determination are the following:

- **Homogametic and Heterogametic sexes**

The individuals carrying the same type of sex chromosomes namely XX are called homogametic. They give only one kind of gametes (X). The individuals having dissimilar sex chromosome namely XY are called heterogametic. They give two

kinds of gametes (X) and (Y). Among human being and *Drosophila*, the female is homogametic. In birds, moths and butterflies, the females are heterogametic, and males are homogametic.

1) XX-XY type of sex determination

In insect like *Drosophila* and in human beings, the male has dissimilar sex chromosomes XY chromosomes. In female, two similar sex chromosomes represent XX chromosomes. The female produces only one kind of egg (22 autosomes + one X chromosome) and hence homogametic. The male produces two kinds of sperms one with 22 autosome + one X chromosome and other with 22 autosome + one Y chromosome and hence heterogametic. The egg (X) fertilized by (X) sperm produces female offspring XX. The egg (X) fertilized by (Y) sperm produces male offspring XY.

In many species including most birds, moths, and some fish the sex determination is identical to that of XX-XY mechanism, but female is heterogametic (usually designed as ZW) and males being homogametic (usually designated as ZZ). This mechanism of sex determination is sometimes called ZZ – ZW. However, mechanically this system is identical to the XX – XY system but with the relationship between sex – chromosomesand sex phenotypes reversed. Stated differently in birds, the chromosomes compositionof the egg determines the sex of the offspring, whereas in humans and fruit flies, the chromosomes composition of the sperm determines the sex of the offspring.

2) The 'Y' chromosome and sex determination in mammals

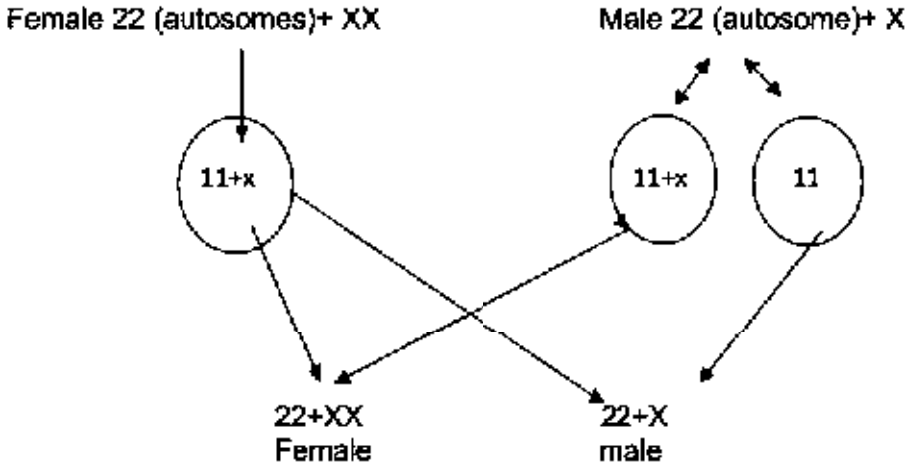
In both *Drosophila* and humans, normal females have XX sex chromosome composition and normal males have XY sex chromosome composition. Thus, it might be tempting to assume that in both species the gene for maleness is on Y chromosome. In mammals the presence of 'Y' chromosome is required for the

development of male sex phenotype.

In contrast recent evidence shows that Y chromosome plays no significant role in sex determination in *Drosophila*. In mammals surprisingly X chromosomes present in any number (e.g., XXX) in the absence of Y chromosome give rise to female sex phenotype. So, Y chromosome in human that is responsible for the development of testis is called TDF(for Testis Determining Factor). The TDF gene exhibits very dominant effect on the development of the sex phenotype.

3) XX-XO type of sex determination

In some of the insects like grasshoppers, all the eggs carry an X chromosome, but it was included in only half of the cells forming sperm. All the sperm however had the usual complement of other chromosomes (autosomes). Eggs fertilized by sperm containing the X chromosome produced zygote with two X chromosomes produced zygotes with one 'X' which become males. Males are referred as hemizygous for the X chromosomes or for genes located on the X chromosome.



Bridges genetic balance theory in *Drosophila*.

Soon after the identification of X chromosome, the sex determination in *Drosophila* was more complicated than the preliminary observation. C.B.Bridges showed that

female determining genes were located on the X chromosome and male determining genes were on the autosomes of *Drosophila*. The genetic balance theory of sex determination was devised to explain the mechanics of sex determination in D. *melanogaster*.

Bridges experimentally produced various combinations of X chromosomes and autosomes in *Drosophila*. A triploid female was crossed with a diploid male. The triploid female produces four types of eggs.

(i)X2n (A) (ii) XX2n(A) (iii)X n (A) (iv)XX n (A)

The diploid male produces two types of sperms.

(i)Xn (A) (ii) Yn(A)

When the four types of eggs are fertilized by the two types of sperm at random eightkinds of offspring are produced as the table:

Sex expression in *Drosophila* in relation to X/A rules

	Xn (A)	Yn(A)
X2n(A)	XX3n (A) = 2X/3 = 0.66 Inter sex	XY3n (A) = 1X/3 = 0.33 Super male
Xn (A)	XX2n (A) = 2X/2 = 1.00 Female	XY2n (A) = 1X/2 = 0.50 Male
XXn (A)	XXX3n (A) = 3X/3 = 1.00 Triploidfemale	XXY3n (A) = 2X/3= 0.66 Inter sex
XXn (A)	XXX2n (A) = 3X/2 1.50 Super female	XXY2n (A) = 2X/2 = 1.00 Female

Eight kinds of offspring are produced as follows:

1. Triploid female with three x chromosomes and three sets of autosomes.
2. Normal diploid female with two chromosomes and two sets of autosomes.
3. Diploid XXY female with two X chromosomes and one Y chromosome and two setsof autosomes.

4. Intersexes with two X chromosomes and three sets of autosomes.
5. Intersexes with two X chromosomes and one Y chromosome and three sets of autosomes.
6. Normal males with one x and one Y chromosome and two sets of autosomes.
7. Super females with three X chromosomes and two sets of autosomes.
8. Super males with one X and one Y chromosome and three sets of autosomes.

First, it was supposed that the XX individual is female and XY male. After finding of non-disjunction, this early formulation was altered slightly that the XX is female andX male.

The importance of Y chromosome in the sex determination was removed:

In Bridge's experiment, there is an individual with two X chromosomes. Yet it is not female. It is shifted out of the female class by the addition of one set of autosomes and it becomes an intersex. So, autosomes also play a positive role in the determinationof sex. The intersexes lead to the conclusion that in *Drosophila*, sex is determined by the X chromosomes as well as by the autosomes.

The intersex differs from female by the assumption of certain male characters. This occurs due to "the internal preponderance of male tendency genes" present in the autosomes, which are added as an additional set.

Every individual has both male and female potentialities, because X chromosomes have female tendency genes, and the autosomes have male tendency genes. The sex is decided by the balance that is, by preponderance of either male tendency genes or the female tendency genes. The deciding factor is the ratio between the number of X chromosome and number of the sets of autosomes in the zygote. This is called **'sexindex'** by Bridges.

$$\text{Sex index} = \frac{\text{Number of X chromosomes}}{\text{Number of sets of autosomes}}$$

If the ratio is 1.0, the individual will be female and if it is 0.5 male will result. The ratio between 0.5 and 1.0 result in intersex. The ratio 1.5 leads to super female and 0.33 leads to super males.

- **Haplo-diploidy sex determination**

In several species of Hymenoptera such as honeybees, ants, wasp and saw flies males develop parthenogenetically (from unfertilized eggs) and have a haploid chromosome number (16 in the drone / male honeybees). The queen honeybee and the workers, which arise from fertilized eggs carry the diploid chromosome number (32). So, in the honeybees, the sex is determined by the haploid and diploid chromosome numbers. It is sometimes said that a drone honeybee has no father but has a grandfather. This is possible by the haploid diploidy mechanism of sex determination.

Similarly in the parasitoid wasp *Bracon hebetor* (formerly Habrobracon), the females are diploid with 20 chromosomes and males are haploids with 10 chromosomes. Females originate from fertilized eggs and male from unfertilized eggs. This mechanismof sex determination is often referred to as haplo-diploidy.
Results of the experiments by Whiting showed that the sex determination depends upon the genetic composition of the certain region of the chromosome ie, homozygous, heterozygous, or hemizygous status of certain chromosome segments and not on diploidy versus haploidy per se. *If* Xa, Xb, Xc are different chromosomal segments, then female sex is produced by heterozygous of the certain chromosomal segments (Xa, xb / xa, Xc) and male phenotype is due to hemizygous or homozygous condition of chromosomal segments (Xa, xb, Xc/Xaxa, Xbxb, Xcxc).

- **Role of environment and sex determination:**

In some lower animals, sex determination is non-genetic and depends on factors in the external environments. Males and females have similar genotypes, but stimuli from environmental sources initiate development towards one sex or the other. In the case of Bonellia, for example, females are free living form with an ovoid body and long proboscis. The male are small, parasitic and lives in the reproductive tracts. of the larger female. Larvae of Bonellia are potentially capable of developing either into males or females. If the larvae are isolated, they will become females. If they are grown near the females, they will become males. Sex determination is non-genetic and depends on the external environment. The hormone like substances secreted by female has an effect to turn the larvae into males. So, presence or absence of this hormone like substance in the environment determines the sex in Bonellia.

- **Gynandromorphism:**

Gynandromorph is an individual in which one half is male and other half is female. The mosaic condition of sex chromosomes leads to phenotypic sex mosaic. The Gynandromorphism is best studied in *Drosophila*, where there are no dilutions of thecharacteristics i.e. the male side is fully male and the female side is fully female. Thereare three kinds of gynandromorphism.

(i)Bilateral gynandromorphs

It is found in *Drosophila*. One lateral side of the fly is male and other lateral side isfemale. This is due to abnormal mitosis during early cleavage of the zygote.

(ii)Anterior-Posterior gynandromorphs

Some gynanders posses' male characters on the anterior side and female character on the posterior side of the body or vice-versa. These are called anterior posterior gynanders.

(iii) Sex – piebald

In some ganders, the individual is predominantly a male or female with patches of opposite sex scattered on it. They are known as sex-piebald.

- **Sex – mosaics**

Mosaicism refers to a condition in which a person's cell consists of two or more populations, each with different chromosome complements. Murry Barr found a girl in whom both buccal and vaginal smears showed two Barr bodies, thus indicating the XXX chromosome complements. Blood cells showed no Barr body indicating a XO chromosome complement. These mosaics arise as results of errors in mitosis in early stages of embryonic development.

SEX LINKED INHERITANCE

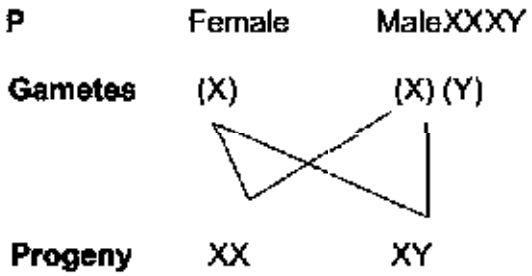
Inheritance through X chromosome is called sex linked inheritance. It was discovered by T.H. Morgan in 1910. Eye color and bar eye in *Drosophila*, color blindness and hemophilia in human and barred plumage in fowls are inherited through X chromosome.

Characteristic features of sex-linked genes.

1. Sex linked genes are located on 'X' chromosome only.
2. In diploid, homogametic sex contains two copies of sex-linked alleles whereas heterogametic sex contains only one sex linked allele.
3. A recessive gene, in a homogametic sex can express only when it is homozygous state, whereas in heterogametic sex a recessive allele expresses in hemizygous condition.
4. Sex linked genes follow the criss cross inheritance.
5. Sex linked gene exhibit several deviations from the normal segregation pattern.

Criss-cross inheritance of X-chromosome in *Drosophila*

Female is produced when an X egg is fertilized by X sperm. Male is produced when Y sperm fertilizes an X egg.



A male receives an X-chromosome only from the mother and never from father. The male receives Y chromosome only from his father, never front his mother. Thus, the inheritance of X chromosome in *Drosophila* follows specific pattern. The male

transmits his X chromosome to grandson only through his daughter. This is called criss- cross inheritance. The female transmits the X-chromosome both to her son and daughter. The criss – cross pattern of inheritance is characteristics of sex-linked genes. This distinctive criss-cross pattern, from father through daughter to grandson replacing the usual pattern for the F_1 and F_2 segregation is now interpreted as evidence of sex-linkage.

Criss-cross inheritance of eye colour in *Drosophila*

A cross was made between white-eyed male *Drosophila* and red-eyed female *Drosophila* by T.H. Morgan in 1910. The F_1 flies were red eyed. When F_1 files were intercrossed, three fourth of the F_2 flies possessed red eyes and one fourth white eyes. From this familiar 3:1 ratio, it is clear that this is a monohybrid inheritance where red is dominant over white. But, when the F_2 flies were classified for both eye color and sex. **It was found that:**

(i) All the F_2 females were red eyed.

(ii)Half of the F2 males were red eyed. (iii)Half of the F2 males were white eyed.

When reciprocal cross was made between white eyed female and red eyed male the F_1 was composed of two different phenotypes *ie*., red eyed females and white eyedmales. When these F_1 flies were intercrossed, the F_2 consisted of flies in the ratio-2red eyed: w white eyed. When these F_2 files were classified for both eye color and sex, it was found that:

(i) Of two red-eyed flies, one is male, and another is female.

(ii) Of two white-eyed flies, one is male, and another is female.

Direct crosses

P	X^wX^w	X	X^wY
	Red eyed female	↓	White eyed male
G	(X^w)		$(X^w)(y)$
		↓	
F_1	X^wX^w		X^wy
	Red eyed female		Red eyed maleG
	(X^w) X $(^w)$		X^wY

F_2	X^wX^w	X^wX^w	X^wy	X^wy
	Red eyed	Red eyed	Red eyed	White eyed
	Female	Female	Male	Male

Reciprocal cross

P	X^wX^w	X	X^wy
	White eyed female	↓	Red eyed MaleG
	(X^w)		(X^w) (y)
F_1	X^WX^w	↓	X^wy
	Red eyed female		White eyed MaleG
	(X^W) X $(^w)$		X^wY

F_2	X^WX^w	$X^w)X^w$	X^wy	X^wy
	Red eyed	White eyed	Red eyed	White eyed
	Female	fennale	male	male

In the normal Mendelian inheritance, the F_2 ratio does not differ from that of reciprocal cross. But in the inheritance of eye color in Drosophila, the F_2 ratio depends on the sex of the parent by which eye color is introduced.

In *Drosophila*, the white eye color follows a criss cross inheritance. The kind of inheritance from father to grandson only through daughter is called criss-cross inheritance. The male transmits his red eye color to his grandsons through his daughters, never to or through his sons. Thus, the transmissions of eye color and X chromosome are similar. Hence, it is assumed that the gene for eye color is located in the X chromosome and y chromosome carries no allele for eye color.

- **Holandric genes**

Most sex-linked genes in male heterogametic animals are on the Xchromosome. However, Y chromosome also contains few genes that produce visible effects on the phenotype of the organism. Such genes are called Y linked or holandric genes. Holandric genes would be transmitted directly from father to son and never appear in females.

- **Sex-influential dominance/Sex influenced character.**

The condition in which the same gene acts as dominant in one sex andrecessive in other sex is called as sex influenced dominance. That is, the sex influences the gene either to be dominant or recessive. The sex influenced genes are present in autosomes. This differential behavior of the gene is due to female andmale sex hormones.

For example, in human being baldness is due to sex influenced gene. This traitis dominant in men and recessive in women. A man is bald in homozygous recessive as well on heterozygous condition for baldness. Whereas women exhibit baldness only in homozygous recessive condition for baldness and heterozygous condition

for baldness in female sex produce normal phenotype.

H^NH^N -Normal female and normal male

H^NH^n -Normal female and bald male

H^BH^B -Bald female and male

- **Sex-limited gene expression/sex limited characters**

Sex – limited genes are those which produce characteristics that are expressed in only one fo the sexes. Sex limited genes may be located in any of the chromosomes. The sex hormone is found to be limiting factor in the expression of sex-limited gene. Sex limited genes are responsible for secondary sexual characteristics. For example beard in man and breast in women are produced by sex-limited genes. A woman does not have a beard, though she carries all the genes necessary for beard. Similarly, man does not have breasts though he carries all the genes necessary for breast. The expression of sex-limited characteristics depends upon the presence or absence of sex hormones.

CHROMOSOMAL ABERRATION

Two major kinds of chromosomal aberrations:

I- Structural aberrations

Chromosomes may undergo changes. This is called chromosomal mutation or chromosomal aberration. The change may occur either in structure of the chromosomes or in the number of chromosomes. Based on these, the chromosomal aberrations are grouped into two major kinds- variation in structure and variation in number.

Variation in chromosome structure

These are four kinds of variations in the structure of chromosomes.

1. Deletion
2. Duplication
3. Inversion
4. Translocation

(1) Deletion

Definition: It is an "intra-chromosomal aberration" in which, an interstitial or terminal chromosomal segment is lost. That is, some genes are deleted. Based on which it is called inter calary or terminal deficiency.

Cytological effect: In deletion heterozygotes, "deletion loop" occurs during pairing of homologous chromosomes. The portion of the normal chromosome homologous to the deficient segment bulges out.

Genetic effect: When a segment of a chromosome is absent, some genes are also absent. If these lost genes are physiologically important, deletion leads to death of the organism. Deficiencies produce unique phenotypic effects in *Drosophila*. The characters such as bended, delta, gull, minute, and notch are associated with some deletions in chromosomes.

In human beings, **Cri-du-chat' syndrome** is characterized by a mewing cat like cry during infancy, widely spaced eyes physical and mental retardations. This 'Cri- du-chat' syndrome is caused by a deletion in the short arm of 5th chromosome.

A terminal deletion involving the distal short arm of chromosome 5 [del(5)(p15.3)]. Patients with similar deletions are said to have cri du chat or cat cry syndrome because of the characteristic cat like cry present in many during infancy.

An interstitial deletion involving the long arm of chromosome 13 [del(13)(q21.3q33)].

(2) Duplication

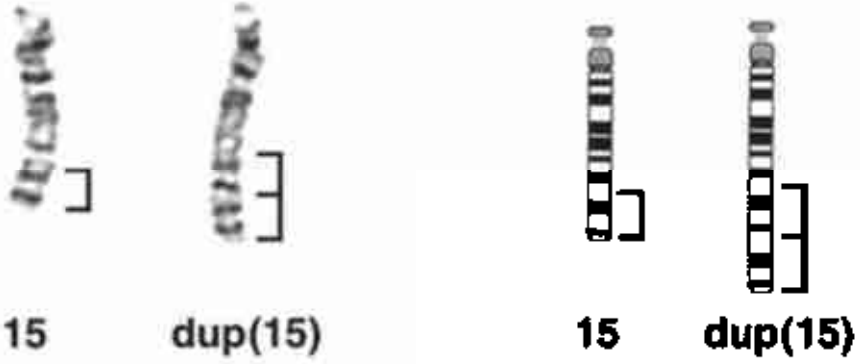
Definition: It is an 'intrachromosomal aberration' in which a segment isrepresented two or more times in a chromosome.

Cytological effect: During meiotic pairing of heterozygotes, the chromosome with duplicated segment forms a loop to maximize the juxtaposition of similar segments of homologous chromosomes.

Genetic effect: The duplications are not lethal. The unusual dosage of genes can be investigated. Duplications are useful in evolution of new characters without loss of original traits. Relocations of chromosomal materials, due to duplication,results in an altered phenotype. This is called position effect.

Position effect

The position effect is an altered phenotype due to relocation of chromosomal material. A fly homozygous for Bar eye has four 16 A segments, two in each chromosome. A fly heterozygous for ultra-Bar has also four 16 A segments – one in the normal chromosome and three in the duplicated number of 16A segments, they are expected to be similar in phenotype. But the flies homozygous for ultra-Bar (BB/+) produced smaller size eyes.



A duplication involving the distal long arm of chromosome 15 [dup (15)(q24q26.3)]. This duplication was initially observed in the bone marrow of a patient with mental retardation and leukemia. By obtaining a peripheral blood karyotype, we were able to demonstrate that the duplication was constitutional and apparently unrelated to his leukemia.

(3) Inversion

Definition: It is an intrachromosomal aberration. Inversions occur when a part of chromosome become detached, turn through 180° and reinserted in such a way that the genes are in reverse order.

Inversions are of two kinds:

(i) Pericentric inversion: The inverted segment includes centromere.

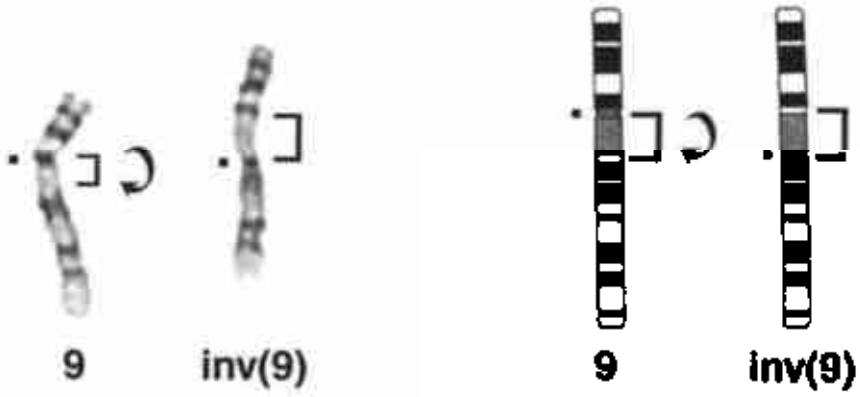
(ii) Paracentric inversion: The inverted segment does not include centromere.

Centromere lies outside the inverted portion.

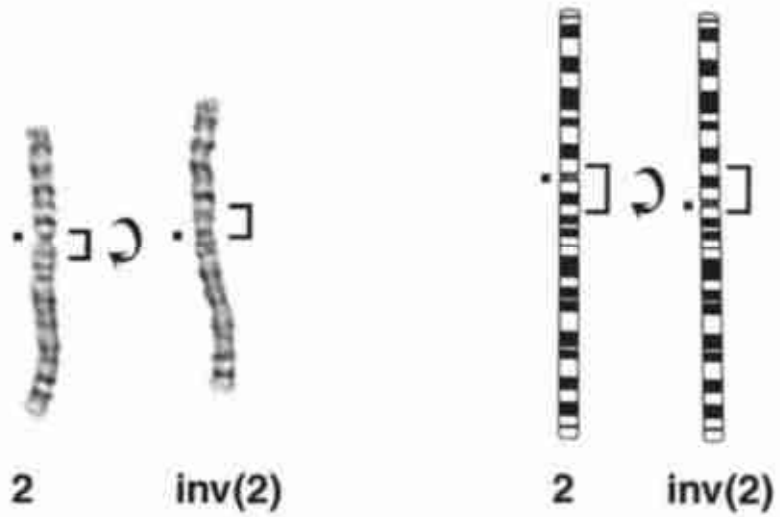
Origin of inversion: A chromosome may form a loop. Breakages occur at the pointof intersection. When the sticky ends unite with new partners, inversion results.

Cytological effect: In inversion heterozygote the part of the uninverted chromosome corresponding to the inversion forms a loop. A similar loop is formed by the inverted section of the homologous chromosome but in reverse direction.

Genetic effects: Paracentric inversion produce dicentric and acentric chromosomes. Pericentric inversion produce duplications and deficiencies. Inversion acts as cross over suppressor and inversion maintains heterozygosity from generation to generation.



This benign inversion of chromosome 9 [inv(9)(p11q13)] represents a pericentric inversion with breakpoints in both chromosome arms.



Although this recurring pericentric inversion [inv(2) (p11q13)] is considered to be benign, individuals who carry this inversion might have a slightly increased risk for miscarriages.

(4) Translocation

Definition: It is an inter-chromosomal aberration where in exchange of chromosomal a segment occurs between non-homologous chromosomes.

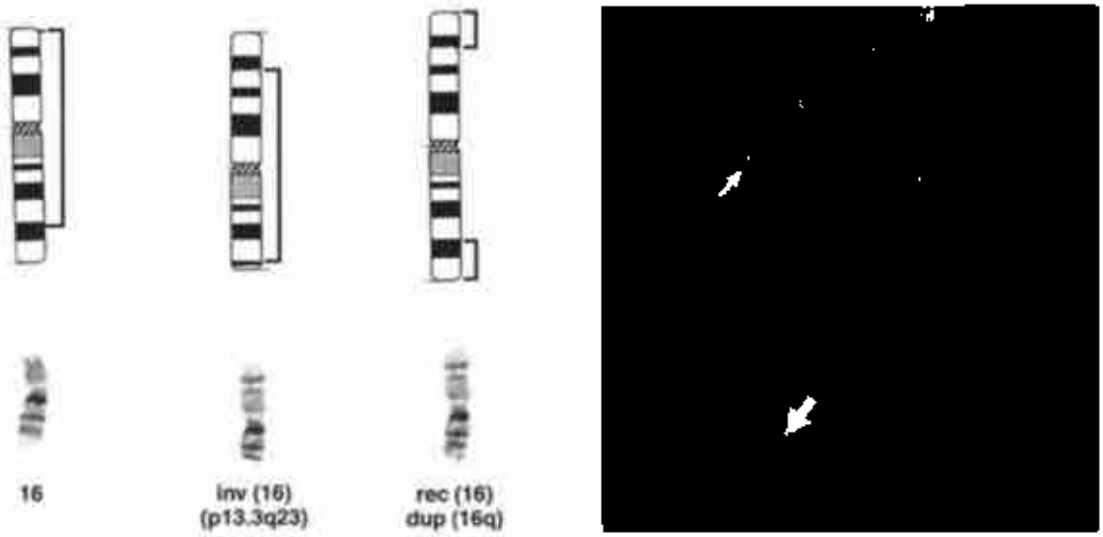
Cytological effect: In the translocation heterzygote, pairing of homologous chromosomal segments is affected by a cross-shaped configuration. This cross opens out into a ring as chiasma terminalizes. The meiotic products are of three kinds (i) normal, (ii) balanced and (iii) unbalanced.

Genetic effect: Translocation gives three kinds of genetic effects.

i. Translocations alter the linkage relationships of genes.

ii. Heterozygotic translocation causes semi sterility because most of the gametes fail to receive full, balanced complement of genes required for viable development.

iii. The phenotypic expression of a gene may be modified when it is translocatedto a new position.



A normal 16, an inverted chromosome 16, and a recombinant chromosome 16 [rec(16) dup(16q) inv(16)(p13.3q23)] resulting from recombination within the inversion loop of the parental inversion carrier. The recombinant chromosome 16 is missing the material distal to the short arm breakpoint and contains a duplication of the material distal to the breakpoint within the long arm.

II- Numerical aberrations(Variation in Chromosome number):

Variation in number of chromosomes is called **ploidy**. A set of chromosomes present in an organism is called **genome.** In a genome, each type of chromosome is represented only once. Most of the sexually reproducing plant species are diploids i.e.,have two set of chromosomes. Any change in the chromosome number from the diploid condition is referred to as heteroploidy. The heteroploidy is of two types namely, aneuploidy and euploidy. The variation in number may involve any chromosome or in entire sets.

- **Aneuploidy**

Loss or gain of one or more particular chromosomes occur within a set is called aneuploidy. The aneuploidy organism bears irregular number of chromosomes. Aneuploidy arises due to non-disjunction. Aneuploidies are of three types.

Types of Aneuploids:

Types	Genomic constitution
Monosomic	2n-1
Double monosomic	2n-1-1
Nullisomic	2n-2
Trisomic	2n+1
Double trisomic	2n+1+1
Tetrasomic	2n+2
Pentasomic	2n+3

1. Monosomic

A monosomic is an individual that lacks one chromosome of the normalcomplement of somatic cells (2n-1). If the lost chromosome is one that is not absolutely essential for the organism, it may survive but if the lost chromosome isvery important, the organism may not survive.

2. Nullisomic

A nullisomic is an individual that lacks both members of one specific pair of chromosomes (2n-2). A nullisomic diploid does not survive. However, a nullisomic polyploidy (hexaploidy wheat 6x-2) may survive but exhibit reduced vigour and fertility. Nullisomic analysis helps to identify genes with specific chromosomes in a polyploidy species.

3. Polysomic

An individual having either single or one pair of extra chromosome in the diploid complement is known as polysomics. Polysomics are called as hyperploids. Polysomics are of two types (i) trisomics and (ii) tetrasomics.

(i) Trisomics

A trisomic is an individual with one chromosome more than the normal

complement of the somatic cells (2n+1). In general the extra chromosome does not produced so striking effect as a missing one. In wheat, trisomics (2n=43) are nearly indistinguishable from normal plants. Trisomics give rise to two kinds of gamets *i.e.*, one kind with 'n' chromosomes and other with 'n+1' chromosomes. Trisomics are more stable genetically than monosomics.

(ii) Tetrasomics

Addition of two chromosomes of one pair or two different pairs is known as tetras my and such individuals are called as tetrasomics.

Use of aneuploidy

i. Aneploids are extremely useful in several genetic studies.
ii. They are useful to determine the phenotypic effects of loss or gain of different chromosomes.
iii. Aneuploids have been used to produce chromosome substitution lineswhich give information on the effects of different chromosomes of avariety.
iv. They are used to produce alien addition and alien substitution lines which are useful in gene transfers from one species into another.
v. Aneuploid analysis permits the location of a gene as well as of a linkage group of a specific chromosome.

Aneuploids in Human beings

I-Down's syndrome

It is due to trisomic condition of 21st chromosome. It is also called Mongolian idiocy. Affected individuals are mentally deficit and physically retarded, broad face and flat stubby nose.

II- Kline felters syndrome (44+XXY)

It is due to trisomic condition of sex chromosome. The individual is male withXXY

Chromosome. The individuals with this syndrome have defective dev elopement of testis, famine character like Enlarged breast, under- developed body hair, presence of one barr body in the body cells.

III- Turners' syndrome

It is due to monosomic condition of sex chromosome. The individual isfemale with 44 autosomes and one'X' chromosome. The female individual is without menstrual cycle. No barr body is present in body cells.

The origin of aneuploids

i. Spontaneous
ii. Meiotic irregularities
iii. Triploid individuals
iv. Translocation heterozygote

Use of aneuploids in crop improvement

a. Aneuploids are useful tools for locating the genes on a specific chromosome. Monosomics and nullisomics are used for this prupose.
b. Monosomics are also used in interspecific gene transfer *ie* monosomics are used in transferring chromosomes with a desirable genes from one species to another.
c. Aneuploids are used for developing alien addition and alien substitution lines in various crops.
d. Primary trisomics are useful in identification of chromosomes involved in translocations.

- **Polyploidy**

These are variation that involves entire set of chromosomes. In Euploids the chromosome number is an exact multiple of the basic or genomic number. Euploids are differ in multiple of n or x.

Types	Genomic formula
Monoploids	n
Diploid	2n
Triploid	3n
Tetraploid	4n
Pentaploid	5n
Hexaploid	6n

1. Monoploid

The monoploid organisms have one set of chromosomes or one genome (n) in the nuclei of their body cells. The monoploids are often weak and sterile. Monploids differ from haloids which carry half or gametic chromosome number (n). In true diploid species, both monoploid and haploid chromosome number is the same (n =x) thus a monoploid can be a haploid but all haploids cannot be monoploids.

2. Diploids

Normal diploids are known as disomic. They have regular bivalent pairingduring meiosis. Diploids also have disomic genetics with two alleles at each locus.

3. Polyploids

Polyploids refer to any organism in which the number of chromosomes sets exceeds two *i.e.*, an organism with more than two set of chromosomes or genome. They have larger cells than diploids. These larger cell sizes contribute to largerplant size and

higher yield. Polyploids have generally larger, thicker and darker green leaves bigger flower, fruits than the diploids. In each genus, there is an optimum level of polyploidy beyond which growth may be depressed with increasing number of chromosomes. (eg) triploid (3n).

There are two types of Polyploids.

I.Autopolyploid

In autoployploids the multiple sets of chromosomes are identical (eg). Genome is identical with each other. Autopolyploids arise by abnormal mitosis and meiosis and induced artificiallyby colchicines.

Auto triploid - 3x

Auto tetraploid- 4x

Auto hexaploid- 6x

(eg). Banana 2n=3 x=33, Groundnut 2n=4x=40; Sweet potato 2n=6x=90 andPotato 2n=4x=48

II.Autotriploid

The triploid organisms have three sets of chromosomes. A triploid may originate by the union of a monoploid gamete (n) with a diploid gamete (2n). Since anautotriploid remains sterile and cannot produce seeds, it has great commercial value inproducing seedless varieties of economic plantgs. Eg. Seedless water melon.

III.Autotetraploid:

The organisms with four genomes (4n) in the nuclei of their somatic cells are called tetraploids. They arise due to somatic doubling of chromosome number. Doubling is accomplished by either spontaneously or it can be induced by chemicals such as colchicines.

Morphological and Cytological features of polyploids are

i. Larger in size than diploids
ii. Generally more vigorous than diploids
iii. Slower in growth and late in flowering
iv. Polyploids may have reduced fertility than diploids

Role of polyploids and their evoluation

- About 1/3 of angiosperms are polyploids. These suggest that polyploids have significant role in the evolution of crop species.
- Allopolyploids have contributed great extent in the evolution of plants than auto polyploids.
- The identification of diploid parental species is primarily based on paising between the chromosome of diploid and the allotetraploid species.
- Allopolyploids combine the genome of different species, hence the resulting individuals differ from progenitor.
- Evolution is a slow process; but due to allopolyploids new species originatevery quickly.
- Polyploids have wider adaptation to different environmental condition than diploids.

GENETIC DISORDERS

Disease	Gene/Defect	Inheritance	Clinical Features
Achondroplasia	Fibroblast growth factor receptor 3 (FGR3) – constitutively active (gain of function)	Autosomal dominant (normal parents can have an affected child due to new mutation, and risk of recurrence in subsequent children is low)	Short limbs relative to trunk, prominent forehead, low nasal root, redundant skin folds on arms and legs
Cystic Fibrosis	Cystic fibrosis trans-membrane regulator (CFTR) – impaired chloride ion channel function	Autosomal Recessive (most common genetic disorder among Caucasians in North America)	Pancreatic insufficiency due to fibroticlesions, obstruction of lungs due to thick mucus, lung infections (Staph. aureus, Pseud. aeruginosa)
Duchenne Muscular Dystrophy	Dystrophin (DMD) -deletions	X-linked recessive	Gradual degeneration of skeletal muscle, impaired heart and respiratorymusculature
Hypercholesterolemia	LDL receptor (commonly)	Autosomaldominant (haploinsufficiency)	Impaired uptake of LDL, elevated levels of LDL cholesterol, cardiovescular disease and stroke. Symptoms more severe in homozygous individuals
Fragile X Syndrome	(FMR1) – CGG trinucleotide repeat expansion in 5' untranslated region of the gene (expansion occurs exclusively in the mother)	X-linked dominant (females less severely affected) Inheritance characterized by anticipation	Disorder shows anticipation (female transmitters in succeeding generations produce increasing numbers of affected males) Boys have long faces, prominent jaws, large ears, and mentally retarded.
Gaucher's Disease	B-Glucosidase	Autosomal recessive	Lysosomal storage disease characterized by splenomegaly, hepatomegaly, & bone marrow infiltration. Neurological symptoms are not common
Glucose 6-phosphate dehydrogenase deficiency	Glucose 6-phosphate dehydrogenase	X-linked recessive (Prominent among individuals of Mediterranean and African descent)	Anemia (due to increased hemolysis) induced by oxidizing drugs, sulfonamide antibiotics, sulfones (e.g.dapsone), & certain foods (e.g. fava beans)

Hemochromatosis	Unknown gene on the short arm of chromosome 6	Autosomal recessive (Incidence ~0.3% in Caucasoid population. Women less affected due to increased iron loss through menstruation)	Enhanced absorption of dietary iron with accumulation of abnormal, pigmented, iron-protein aggregates (hemosiderin) in visceral organs. Cirrhosis, cardiomyopathy, diabetes, skin pigmentation, and arthritis.
Holoproencephaly	Sonic Hedgehog (SHH)	Autosomal dominant (haploinsufficiency?)	Malformation of the brain (no or reduced evidence of an interhemispheric fissure), dysmorphic facial features, mental retardation
Huntington Disease (Huntington Chorea)	Huntingtin (HD) – CAG repeat expansion within exon 1 (expansion occurs in father)	Autosomal dominant (gain-of-function mutation)Shows anticipation	Disorder is characterized by progressive motor, cognitive & psychiatric abnormalities. Chorea – nonrepetitive involuntary jerks is in 90% of patients
Klinefelter Syndrome	47,XXY males	50% of cases due to errors in paternal meiosis I	Sterile males with long limbs, small genitalia, breast development, and feminine body contours, and learning disabilities
Marfan Syndrome	Fibrillin-1 gene (FBN1) encodes a microfibril forming connective tissue protein	Autosomal dominant (dominant negative effect)	Abnormalities of the skeleton (disproportionate tall stature, scoliosis), heart (mitral valve prolapse, aortic dilatation, dissection of the ascending aorta), pulmonary system, skin (excessive elasticity), and joints (hypermobility). A frequent cause of death is congestive heart failure.
Myoclonic Epilepsywith Ragged Red Fibers (MERRF)	Mitochondrial DNA mutation in the tRNAlys gene	Maternal transmission, heteroplasty	Age of onset varies depending on fraction of mutant mitochondrial DNA inherited. Symptoms include myopathy. (disease takes its name from abnormal histological appearance of skeletal muscle biopsies), dementia, myoclonic seizures, ataxia, and deafness

Myotonic Dystrophy	A protein kinase gene (DMPK) – CTG repeat expansion in 3' untranslated region of the gene	Autosomal dominant Shows anticipation	Disorder shows anticipation. Muscle weakness, cardiac arrhythmias, cataracts and testicular atrophy in males. Children born with congenital form have a characteristic open triangle-shaped mouth
Neurofibromatosis I	Microdeletion at 17q11.2 involving the NF1 gene	Autosomal dominant	The disorder is characterized by numerous benign tumors (neurofibromas) of the peripheral nervous system, but a minority of patients also show increased incidence of malignancy(neurofibrosarcoma, astrocytoma, Schwann cell cancers and childhood CML – chronic myelogenous leukemia)
Osteogenesis Imperfecta	Either of the genes encoding the α1 or α2 chains of type I collagen	Usually autosomal dominant (null mutations result in haploinsufficiency, missense mutations often produce a dominant negative effect	Null mutations produce a milder form of the disease. Missense mutations that act in a dominant negative manner are often perinatal lethal. The disorders are associated with deformed, under mineralized bones that are subject to frequent fracture.
Phenylketonuria	Usually due to a mutation in Phenylananine hydroxylase (PAH)	Autosomal recessive	Mental retardation, if untreated, possibly due to inhibition of myelination and disruption of neurotransmitter synthesis. Detectable by newborn screening and treatable
Polycystic Kidney Disease	Mutations in either polycystin-1 (PKD1) or polycystin-2 (PKD2) gene	Autosomal dominant (disease appears to follow a "two- hit model", requiring the loss of both alleles of PDK1 or PDK2 for the disease to be evident.	Heterozygous individuals are predisposed to polycystic kidney disease because they are likely to loose the second good copy of the gene during their lifetime. Multiple renal cysts, blood in urine, end-stage renal disease and kidney failure.

Prader Willi/Angelman (PWS/AS)	Deletion of the PWS region and AS gene located at 15q11- q13. Can also be caused by uniparental disomy involving chromosome 15	Complex Parent of origin effects due to genomic imprinting.	Inheriting the deletion through the mother gives rise to Angelman syndrome, which is characterized by short stature, severe mental retardation, spasticity, seizures, and a characteristic stance. Inheriting the deletion from the father produces the more common Pader-Willi syndrome, which is characterized by obesity, excessive and indiscriminate gorging, small hands, feet, hypogonadism and mental retardation. In rare cases, uniparental disomy involving chromosome 15 produces PWS when both copies are inherited from the mother and AS when both copies are inherited from the father.
Sex Reversal	Variety of causes	Various	See Thompson & Thompson, Medical Genetics, 6th ed.
Tay-Sachs Disease	B-Hexosaminidase (A isoenzyme (HEXA)	Autosomal recessive (common among Jew of Eastern European ancestry and French Canadians).	Hypotonia, spasticity, seizures, blindness, death by age 2. An early indication is a cherry red spot on the retina. (Incidence greatly reduced by screening)
Thalasemias		Autosomal Recessive	Severe anemia
Turner Syndrome	45,X females	Usually due to a paternal error in sex chromosome transmission	Although usually lethal in utero, the defect poses little risk to survival in infants that do come to term. Short stature, webbed necks, broad chest with widely spaced nipples, and sterility. Infants show evidence of lymphedema in fetal life. Intelligence is normal.

DNA AND RNA AS A GENETIC MATERIAL

Deoxyribonucleic acid (DNA) and Ribonucleic acid (RNA) the principal genetic materials of living organisms are chemically called nucleic acids. Nucleic acid especially the DNA, a universal genetic material of most of the organisms, is having all the features required to be a good genetic material. DNA is a macromolecule and is a helically twisted double chain of poly deoxyribonucleotides.

In prokaryotes it occurs in nucleoid and as plasmids, both are double stranded circular DNA. In Eukaryotes most of the DNA is found in chromatin of nucleus. It is linear. Some small quantitative of DNA are found in mitochondria and plastids which is generally double stranded and circular RNA also acts as genetic material in majority of plant viruses.

Features of DNA to act as genetic material:

- Genetic material can store information used to control both the development andmetabolic activities of cell.
- It should be chemically stable so that it can be replicated accurately during cell division.
- It should be transmitted for generations.
- It should be able to undergo mutations providing genetic variability required for theevolution.

(A) Structure of DNA

Nucleic acid (DNA or RNA) first called nuclein by a Swiss chemist Friedreich Miescher (1869) as he removed nuclei from pus cells and isolated DNA i.e., "nuclein" from it. Nucleic acid (DNA or RNA) are macromolecules composed of repeating subunit called nucleotides.

Constitution of a nucleotide:

- A phosphate groups.
- A five-carbon sugar (ribose in RNA and deoxyribose in DNA).
- A cyclic nitrogen containing compound called a base (purines and pyrimidines).

Most commonly DNA occurs as a double helix. The two spiral strands of DNA are collectively called DNA duplex. Two separate and anti-parallel chains of DNA are wound around each otherin a right-handed helical manner. The DNA double helix comes to have two types of alternate grooves major and minor with the sugar phosphate backbone on the outer sides. The bases paired by hydrogen bonding are stocked on each other.

Chemical Composition of DNA

Deoxyribonucleotides (monomer) of *DNA* are composed by three different types of chemicals.

(1)**Phosphoric acid (H_3PO_4)** has three reactive (-OH) groups of which two are involved informing sugar phosphate back bone of DNA.

(2)**Pentose sugar ($C_5H_{10}O_4$)** - DNA contains 2'-deoxy-D-ribose, hence the name deoxyribose.

(3)**Nitrogen bases**- DNA contained four different nitrogen bases **(A, G, C & T).** These four bases are grouped in to two classes on the basis their chemical structure.

(a) Purine bases - DNA has two types of purines (adenine and guanine). Each purine is a type of nitrogen base having a double ring structure (i.e., 9 member double rings with nitrogen at 1, 3, 7 and 9 positions).

Some of the common names of these bases reflect the circumstances of their discovery. Guanine, for example, was first isolated from guano (bird manure),

and thymine was firstisolated from thymus tissue.

(b) Pyrimidine bases: DNA has two types of pyrimidine bases (cytosine and thymine). Each pyrimidine is a type of nitrogen containing base having a single ring structure (i.e.6 member rings with nitrogen at 1 and 3 positions).

Nucleosides: A nitrogenous base with a molecule of deoxyribose sugar (without phosphate group) is known as nucleosides. In nucleic acids, the nitrogen bases are covalently attached to the 1'-position of a pentose sugar ring with the help of glycosidic bond.

Nitrogen base + sugar = nucleoside.

- Adenine + deoxyribose = deoxyadenosine
- Guanine + deoxyribose = deoxyguanosine
- Cytosine + deoxyribose = deoxycytidine
- Thymine + deoxyribose = deoxythymidine

Nucleotides- A nucleotide is formed of one molecule of deoxyribose sugar, one molecule of phosphoric acid and anyone of the nitrogen base. Phosphoric molecule is attached to the 5^{th} – carbon atom of deoxyribose ring with the help of phosphoester bond.

Nucleosides + phosphoric acid = nucleotides

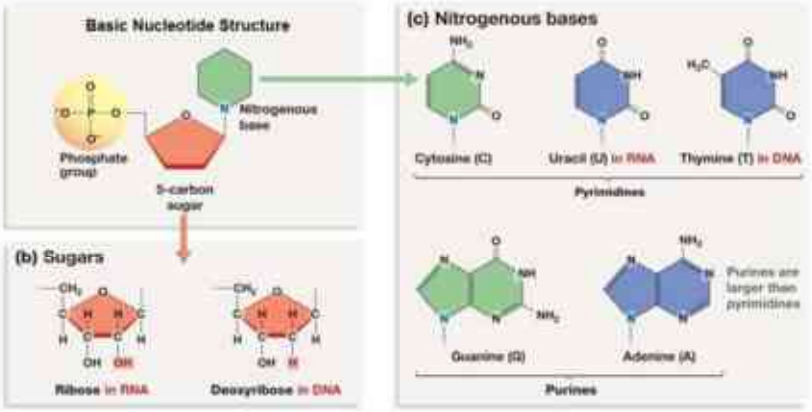
Different nucleotides of DNA are as follows:

(1) Adenine + deoxyribose + phosphoric acid = deoxyadenylic acid or deoxyadenylate / dAMP

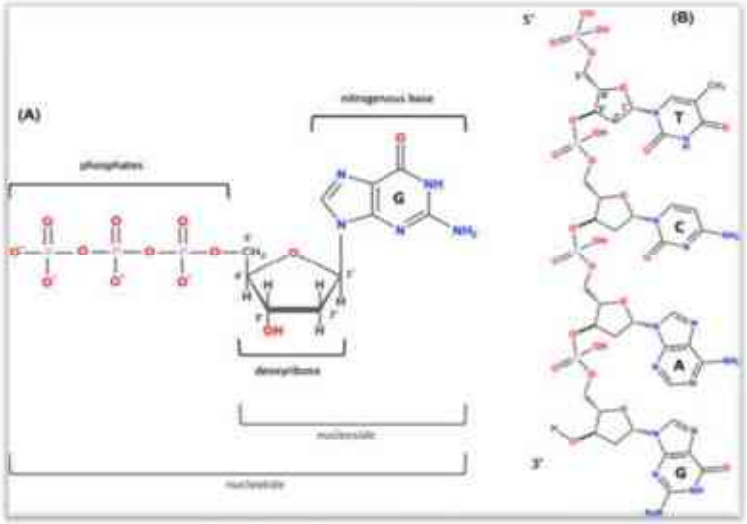
(2) Guanine + deoxyribose + phosphoric acid = deoxyguanylic acid or deoxyguanylate / dGMP

(3)Cytosine + deoxyribose + phosphoric acid = deoxycytidylic acid or deoxycytidylate /dCMP

(4)Thymine+deoxyribose+phosphoric acid = deoxythymidylic acid or deoxythymidylate / dTMP



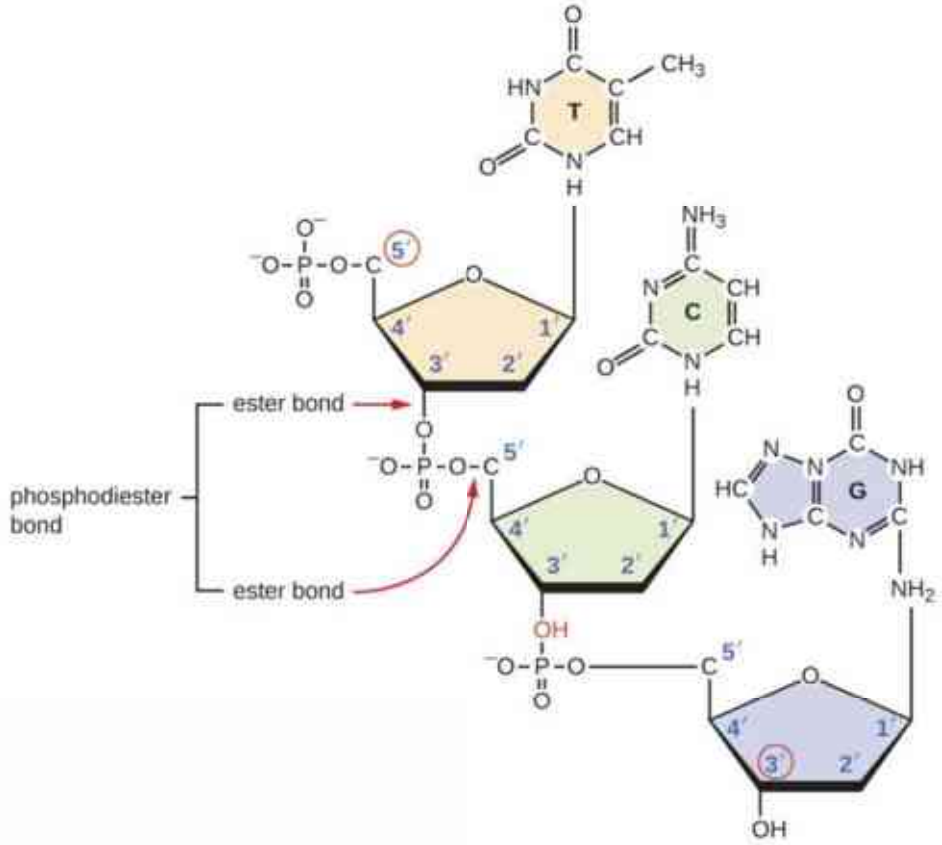
Chemical structure of nucleic acids structure.

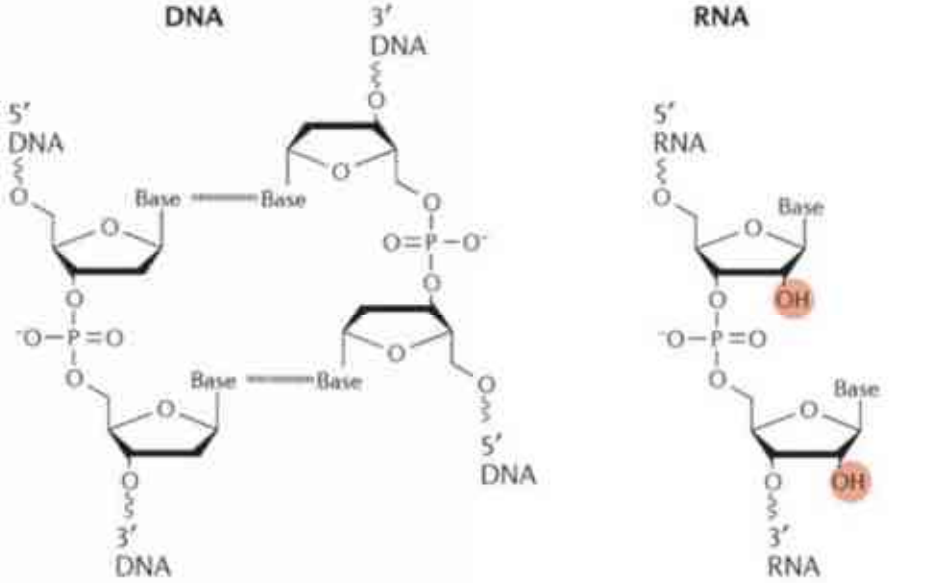


(a) Progressive formation of nucleoside to nucleotide (from lower to higher energy compounds, (b) Backbone of DNA. (The backbones are formed by 3 -to-5 phosphodiester linkages).

Nitrogen base	Nucleoside (Nitrogen base + sugar)	Nucleotide (nucleocide +phosphate gp.)
Adenine (A)	A+S⁻ Adenosine	Adenylic acid adenosine monophosphate (AMP)
Guanine (G)	G+S= Guanosine	Guanylic acid Guanosine monophusphate (GMP)
Thyamine (T)	T+S = Thyamidine	Thyamidylic acid Thyadine monophosphate (TMP)
Cytosine (C)	C+S = Cytidine	Cytidylic acid Cytidine monophosphate (CMP)

Nitrogen bases, their respective nucleosides, and nucleotides of DNA.





Chemical constituents of a nucleotide and DNA & RNA chain formation.

Watson and Crick Double Helix Model of DNA:

The structure of DNA was deduced by American J. D. Watson and F.H.C. Crick in 1953 for which they received the Nobel Prize in 1962. Their double- helix model of DNA structure model is widely accepted. Their double helix model of DNA was based on the data and informationgiven by so many workers like E. Chargaff, M.H.F. Wilkins, R. Franklin and their coworkers. Main contributions in deducing this model were of: Chargaff's rule, Franklin's X-ray diffraction patterns and Kornberg's results.

Chargaff's rule- In 1940's Erwin Chargaff analyzed base content of DNA using new chemical techniques and their observations and generalizations were called as Chargaff 's rule. Chargaff's rule strongly suggested that thymine and adenine as well as cytosine and guanine were present in DNA, always bonded to each other by H-bonds and shows some fixed inter relationship.

- The proportion of A always equals that of T, and the proportion of G always equals thatof C or A – T and G – C.
- The amount of A, T, G, and C in DNA vary from species to species but A+T/G+C =constant for a particular species.

Franklin's X-ray diffraction patterns- Watson and Crick made use of the data of x-ray crystallographic of DNA structure from the studies of M.H.F. Wilkins, R. Franklin, and their coworkers. According to their data, DNA was a highly ordered, multiple stranded structure with repeating sub structure spaced every 3.4A° along the axis of the molecule.

Korenberg's results: Korenberg and his associates tried to synthesize DNA in a medium free of DNA but in the presence of enzyme **DNA polymerase** and nucleotides-the building blocks of DNA. They found that in a DNA free medium

with all necessary compounds DNA synthesis does not occur but the same happens i.e., DNA synthesis starts only when some DNA was added as a primer to the same medium.

The important features of their model of DNA are:

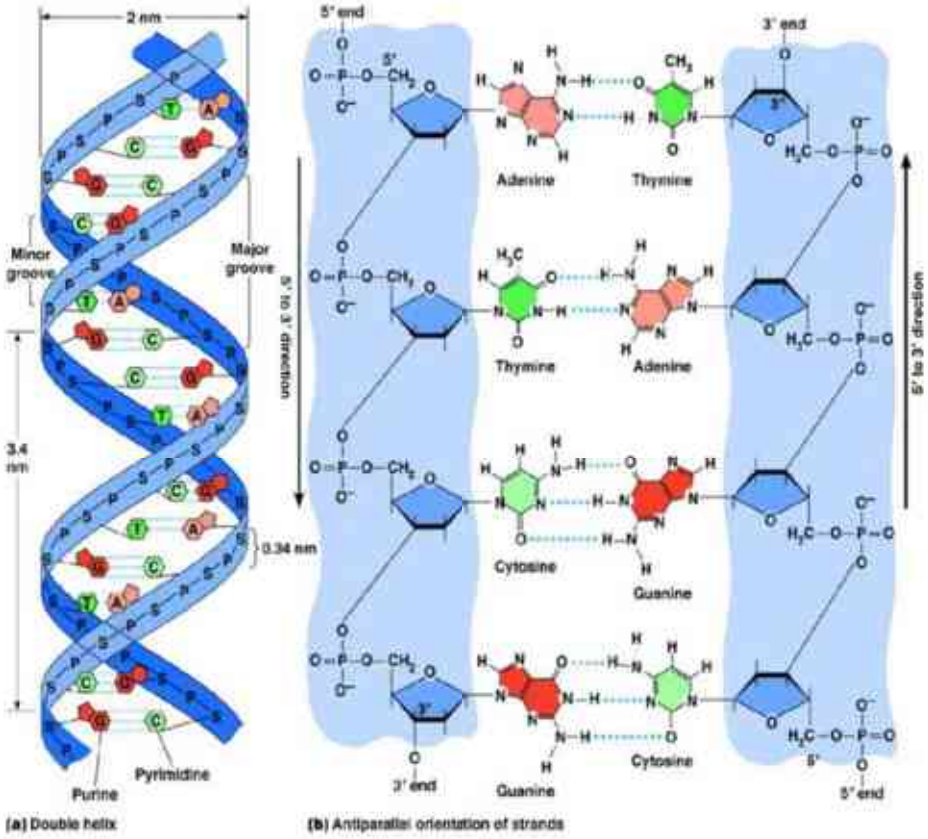
a. Two helical polynucleotide chains are coiled around common axis, where the backbone isconstituted by sugar phosphate and the bases project inside.
b. The polynucleotide chains run in opposite directions. It means, if one chain has the polarity 5'P→ 3'OH, the other has 3'OH→ 5'P.
c. The two chains are held together by hydrogen bonds between their bases. Three hydrogen bonds occur between cytosine and guanine (C≡G) and two hydrogen bonds between adenine and thymine (A=T).
d. The diameter of the helix is $20A^0$ and bases are separated by 3.4 A^0 along the helix axisand related by a rotation of 36^0.
e. The helical structure repeated after 10 residues on each chain, and intervals of 34 A^0

Functions of DNA:

1- DNA is genetic material which able to store information used to control both thedevelopment and metabolic activities of cells.
2- DNA can be replicated accurately during cell division and transmitted for generations.
3- Crossing over during meiosis produces natural recombination of DNA which is passed onto next generation to produce variants in all sexually reproducing organisms.
4- DNA ahle to undergo mutations providing genetic variability required for evolution

5- Differentiation of various body parts is due to differential functioning of specific parts ofDNA.

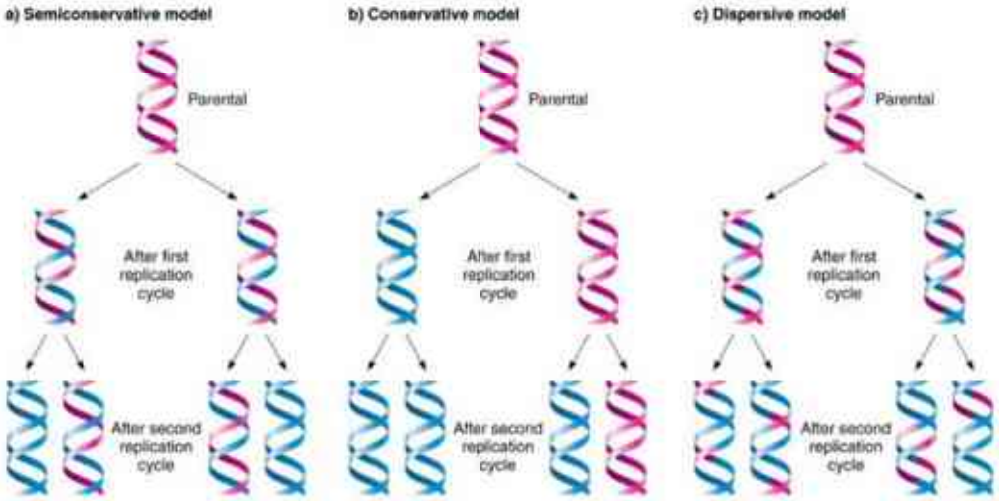
6- Developmental stages occur in the life cycle of an organism by an internal clock of DNA functioning.



Watson and Crick Double Helix Model of DNA.

Replication of DNA:

Replication is the process of formation of carbon copies on DNA. DNA functions as its own template. DNA replication is an autocatalytic function of DNA. During DNA replication the weak hydrogen bonds between nitrogen bases of the nucleotides separate so that the two polynucleotide chains of DNA separate and uncoil. The chains thus separated are complementary to one another. Each stand acts as a template and makes its own complimentary copy over it so that the new formed DNA duplex has one parental stand and one newly formed strand. This method of formation of new daughter DNA molecules is called semi-conservative method of replication.



DNA replication.

Mechanism of DNA Replication:

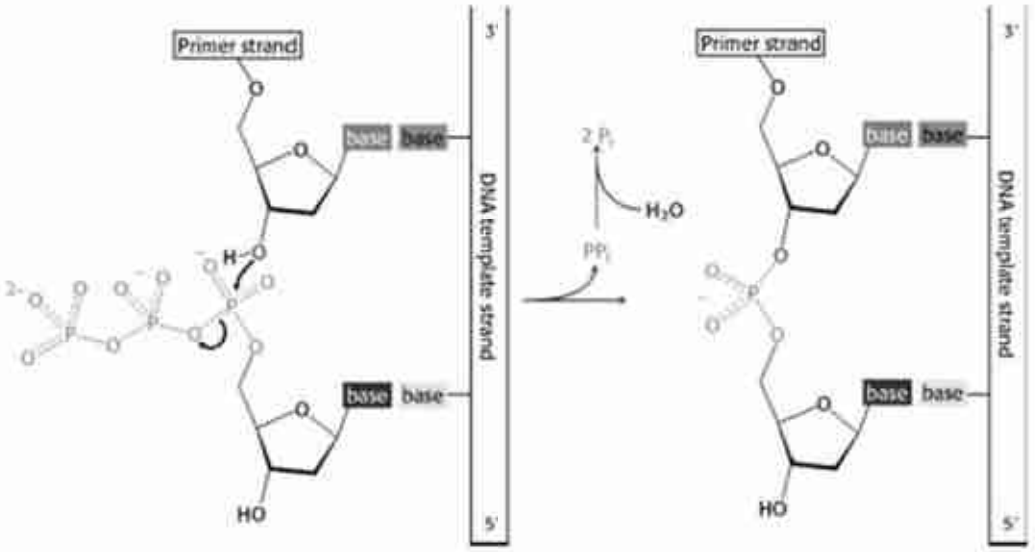
DNA replication is the process of copying a DNA molecule and involves following four major steps:

1. Initiation of DNA replication.
2. Unwinding of helix.
3. Formation of primer strand.
4. Elongation of new strand.

1. **Initiation of DNA replication-** Replication is regulated by the rate of initiation. Replication of DNA in E. coli always begins at a definite site called **origin of replication**. The ***E. coli,*** origin of replication lies within the genetic locus **'ori'** and is bond to the cell membrane. 'Ori' contains four 9bp binding sites for the initiator protein (DnaA-ATP). The helicase DnaB (or mobilepromoter) binds and extends the single-stranded region for copying.

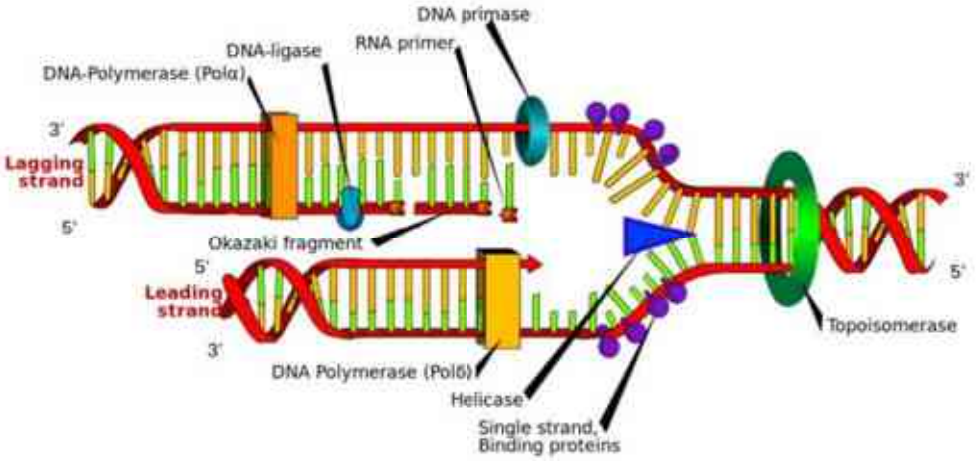
2. **Unwinding of helix-** Unwinding of DNA molecule into two strands results in the formationof Y shaped structure called **replication fork.** Due to unwinding positive super coiling has to be relieved by the **enzyme topoisomerase or DNA Gyrase**.

3. **Formation of Primer strand:** As the newly formed replication fork displaces the parental lagging strand, a mobile complex called a **primosome**, which includes the DnaB, Helicase and DNA primase help in the synthesizes **of RNA primers.** Both leading and lagging strand primers are elongated by **DNA polymerase III.** Need of primer is there to facilitate the action of DNA polymerase III as this enzyme cannot initiate the process but can add activated deoxyribonucleotides to the 3' OH end of primer.



DNA Replication (Phosphodiester Bridge is catalyzed by DNA polymerases).

4. **Elongation of new strand:** after the formation of primer strand, DNA replication occurs in 5' → 3'direction and complementary deoxyribonucleotides are added only to the free 3'OH end of the primer. A dimer of DNA polymerase III elongates both leading (3' → 5') and lagging strands. The leading strand shows continuous replication while the lagging strand shows discontinuous replication. These short pieces of DNA replicated against lagging strand are known as **Okazaki fragments.** Okazaki fragments are 1000-2000 nucleotides long in prokaryotes. A separate RNA primer is used for the synthesis of each Okazaki fragments which, after replacing the RNA primers from deoxyribonucleotides, are later joined together with the help of **DNA ligase** or **DNA synthetase** forming a continuous lagging strand. Hence DNA replication is semi- discontinuous as the leadingstrand is synthesized continuously and lagging strand is formed discontinuously in short pieces join later.



DNA Replication. During DNA replication, a number of different enzymes work together to pull apart the two strands so each strand can be used as a template to synthesize new complementary strands. The two new daughter DNA molecules each contain one pre-existing strand and one newly synthesized strand.

Recombinant DNA:

The tools and technologies of molecular biology for breaking and rejoining DNA sequences from two or more different organisms are known as DNA recombinant technologies. These modified DNA fragments are called recombinant DNA. A recombinant DNA molecule is a vector in which the desired DNA fragment has been inserted to enable its cloning in an appropriate host. This is achieved by using specific enzymes (restriction enzymes) for cutting the DNA into suitable fragments and then for joining together the appropriate fragments by ligation.

(B) Structure of RNA:

RNA is generally involved in protein synthesis but in majority of plant and some animal virusesit also acts as genetic material. There are two major types of RNA:

1. **Genetic RNA**- H. Fraenkel-Conrat showed that RNA present in **Tobacco Mosaic Virus** isits genetic material and this RNA is responsible for the infection in tobacco plant.

2. **Non- genetic RNA-** Prokaryotes and Eukaryotes where genetic information is contained in the DNA molecule, functions of such cells are performed by a different kind of nucleic acids called non- genetic ribonucleic acid. Non-genetic RNA is synthesized on DNA template. Suchnon genetic RNAs can be of many types like mRNA, r RNA, & t RNA.

Chemical structure of RNA:

RNA is single stranded polyribonucleotide. Each ribonucleotide is made of:

- Phosphoric acid- H3PO4
- Ribose sugar- C5H10O5
- Nitrogen base- Adenine (A), Guanine (G), Cytocine (C) and Uracil (U)

Many ribonucleotides join with each other by phosphor-ester bonds to make a linear chain of polyribonucleotide's. The chain will remain straight under all conditions in mRNA, may fold randomly in r-RNA or specifically to form t-RNA

Types of RNA:

The RNA is of following three major types: t RNA, mRNA, and r RNA.

(1) Transfer RNA or t-RNA:

It is also called **soluble or s-RNA**. There are over 100 types of t-RNA. t-RNA is the smallestRNA with 70-85 nucleotides and sedimentation co-efficient of 4S. It is about 10-15% of the total weight of tRNA of the cell. Each tRNA has a corresponding **anticodon** that can recognize the codon on mRNA and exhibit high affinity for specific activated amino acids combine with them and carry them to the site of protein synthesis.

Robert Holley (1965) and his colleagues reported the complete nucleotide sequence of alanine tRNA of yeast. R. Holley (1965) first of all proposed a **clover leaf model for yeast tRNA^{ala}. Cloverleaf structure**-. Five parts or arms of cloverleaf structure:

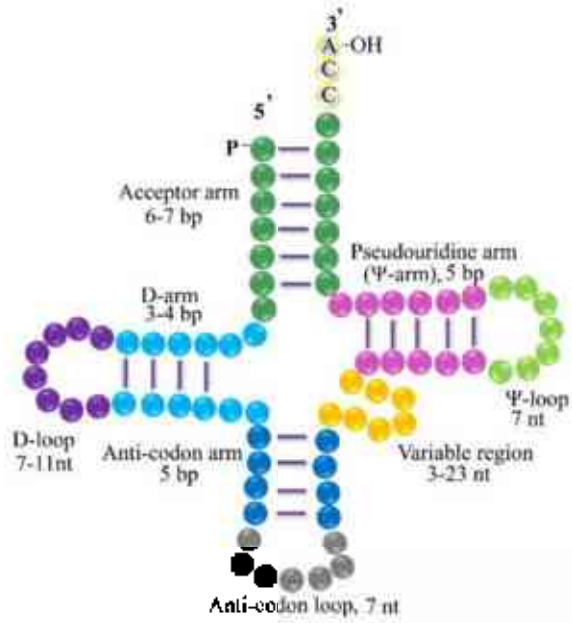
(1) Acceptor stem or arm - this is a region of the tRNA which acts as a site of attachment for the appropriate amino acid. It is also called **amino acid carrier arm**. It is formed by seven regular Watson & Crick base pairs between the 5' and 3' end of the tRNA. **The 3' terminal end** of all tRNA is **always CCA-OH**. It is not base- paired and is the site of attachment of the amino acid. The amino acid is covalently bound through an ester linkage between the carboxyl group of the amino acid and the 3' hydroxyl group of the ribose of the tRNA.

(2) Anti-codon loop or arm - The anti-codon loop contains the three-nucleotide sequence that is complementary to the codon of mRNA to which it corresponds. It consists of a total of 7 unpaired bases, three of which constitute the anti-codon. With this site tRNA attaches to mRNA and helps in the transport of amino acids to the site of protein synthesis

(3) **DHU loop or D loop or arm** - The DHU loop is composed of three or four base pairs. It is depending on the species of tRNA. It is also variable in size containing 8 to 12 unpaired bases. The D-loop helps in binding of amino-acyl synthetase. It bas modified bases called dihydrouridine hence named so.

(4) **T φC loop or arm-** is named so because of the presence of triplet sequence of pseudouridine (φ). It acts as ribosome recognize arm, help in determining the site of ribosome (A, P or E site) where the tRNA must come and attach during translation.

(5) **The extra arm-** is variable in nucleotides composition and is lacking entirely in some tRNA



t-RNA structure.

Functions of t-RNA:

The tRNA plays important role in protein synthesis. T-RNA picks up a specific amino acid from the cytoplasm carries it to the site of protein synthesis and attaches itself to ribosome in accord with the sequence specified by mRNA. It transmits its amino acid to the polypeptide chain. In protein synthesis tRNA acts an adaptor molecule which is meant for transferring amino acids to ribosomes for synthesis of polypeptides. There are different tRNAs for different amino acids. Codons are recognized by anticodons of tRNA. They hold peptidyl chains over the mRNAs.

(2) Messenger RNA or (mRNA):

The structure of mRNA:

m-RNA is **always single stranded** having normal bases like A, G, U and C along with only afew unusual, substituted bases. There is never base pairing in mRNA. It functions as a templatefor protein synthesis it carries genetic information from DNA to a ribosome and helps to assemble amino acids in their correct order. Each amino acid in a protein is specified by a set of three nucleotides in the mRNA called **codons.** Both prokaryotic and eukaryotic mRNA contains three primary regions:

a) **5' untranslated region (5'UTR) -** the 5' untranslated region is a sequence of nucleotides atthe 5' end of the mRNA that does not code for the amino acid sequence of a protein. In **prokaryotic** (bacterial cell) mRNA contains a consensus sequence called the **Shine-Dalgarno sequence** (5'AGGAGGU3'), which serves as **the ribosome binding site during translation**, itis formed of approximately 7 nucleotides upstream of the first or start codon. Eukaryotic mRNA has no such equivalent sequences in its 5' untranslated region. This is the sequence of the mRNA extending from the 5' end of the mRNA to the initiation codon. It is not translated into polypeptide sequence. It has a **function**

analogous to the function of a promoter on a gene. Itwill direct the binding of the ribosome to the initiation codon.

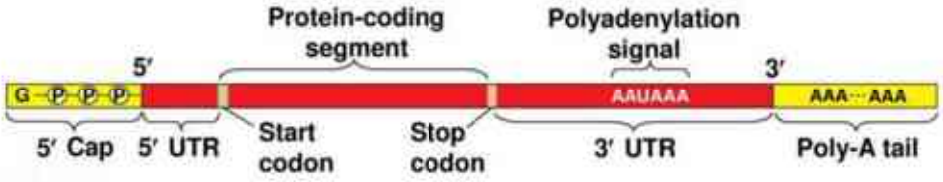
b) **Protein coding region**- this region comprises the codon that specify the amino acid sequence of the protein. This region begins with a start codon and ends with a stop codon. This region has 3 regions namely initiation codon, coding region, stop codon.

- **Initiation codon-** it is always **AUG** and codes for a **methionine.** This is the triplet codon at which polypeptide synthesis begins. All polypeptides are synthesized with an amino terminal methionine.
- **Coding region-**this is the sequence of mRNA that contains **the consecutive triplet codons** that direct polypeptide synthesis. This region starts from the start codon and continue up to the stop codon. The coding region is often referred to as the open reading frame or ORF.
- **Stop codon**-this is the triplet codon that signals the **termination of translation**. There are three possible stop codon sequences **UAA, UAG, UGA**. Stop codons have no corresponding tRNA or amino acid.

c) **3' Untranslated region (3'UTR)**-This region of mRNA is the 3' un-translated region, a sequence of nucleotides at the 3'end of mRNA that is not translated into protein. This is the nucleotide sequence downstream from the stop codon. It extends from the stop codon to the 3' end of the mRNA. It does not code for amino acid sequence. It may function in stabilizing the mRNA. In eukaryotes it is transcribes as hnRNA which is converted into functional mRNA in the cytoplasm by removing introns (intervening sequences) and joining together exons (expressible sequences)

For the convenience the mRNA structure can be summarized as:

1. **Cap-** at 5' end, has methylated structure, does not translate.
2. **Noncoding region-**1- has 10-100 nucleotides, rich in U and A bases, does not translate.
3. **The initiation codon-** AUG, codes for methionine amino acid
4. **The coding region**-about 1500 nucleotides on an average, translate proteins.
5. **Termination codon-** either of UAA, UAG or UGA i.e., present, helps in termination of tnkin
6. **Noncoding region-2-** made of 50-150 nucleotides, does not translate, has sequence likeAAUAAA.
7. **Poly(A) sequence-** 200-250 A nucleotides, does not translate, makes tail of mRNA.



mRNA showing different regions.

Functions of m-RNA:

m-RNA carries coded information to be translation into polypeptide. It directly takes part in protein synthesis in a cell. In some viruses having RNA as genetic material, it may undergo reverse transcription to from compact genes which are used in genetic engineering. The phenomenon also occurs in nature and has added certain genes in the genomes.

(3) Ribosomal rRNA (r-RNA):

Ribosomal, stable, or insoluble RNA constitutes the largest part (up to 80%) of the total cellular RNA. It was reported by **Kuntz.** It is found primarily in the cytoplasm as well as organelle. In prokaryotes it is transcribed from ribosomal DNA which is

a part of nuclear DNA but in eukaryotes ribosome is formed on nucleolar DNA. The genetic instruction contained in mRNA is translated into the amino acid sequences of polypeptides only with the help of ribosomes. Thus, ribosomes play an integral part in the transfer of genetic information from genotype to phenotype. R-RNA is most stable type of RNA.

Structure and processing of ribosome RNA:

It forms about 80% of the total cellular RNA. r- RNA consists of a single stranded RNA which gets twisted over itself in certain regions due to complementary base pairing. R-RNA strand unfold on heating and refold on coiling. It is one the most stable RNA among all types of RNAs. R-RNA and ribo-proteins constitute ribosomes.

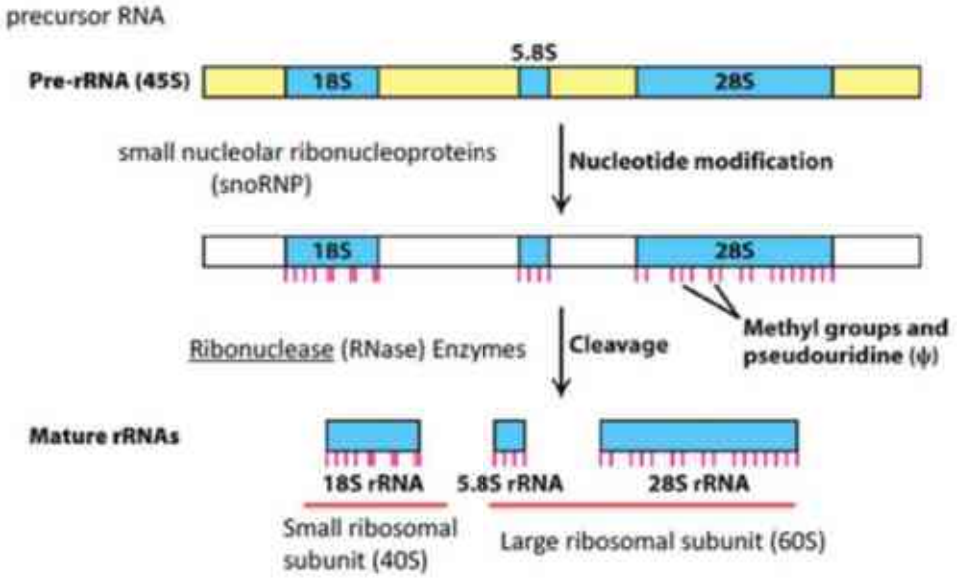
In **eukaryotes** 4 types of rRNAs found are **28s, 18s, 5.85s, and 5s.** In the nucleolus of eukaryotes, RNA polymerase-I transcribes the rRNA genes, which usually exit in tandem repeats to yield a long, single pre-rRNA which contains one copy each of the 18s, 5.8s and 28s sequences. Various spacer sequences are removed from the long pre-rRNA molecule by a seriesof specific cleavages. Many specific ribose methylations take place directed by small ribonucleoprotein particles (snRNPs) and the mature rRNA molecule fold and complex with ribosomal proteins. RNA pol. III synthesizes the 5srRNA from unlinked genes (Figure 90).

Functions of r-RNA:

r-RNA binds to protein molecules and give rise to ribosomes. 3'end of 18s rRNA (16s in prokaryotes) has unpaired nucleotides complementary to those of region or m-RNA, it is the site where ribosomes bind to mRNA during translation. 5s rRNA and surrounding protein complex provide binding site for tRNA.

Important features of RNA:

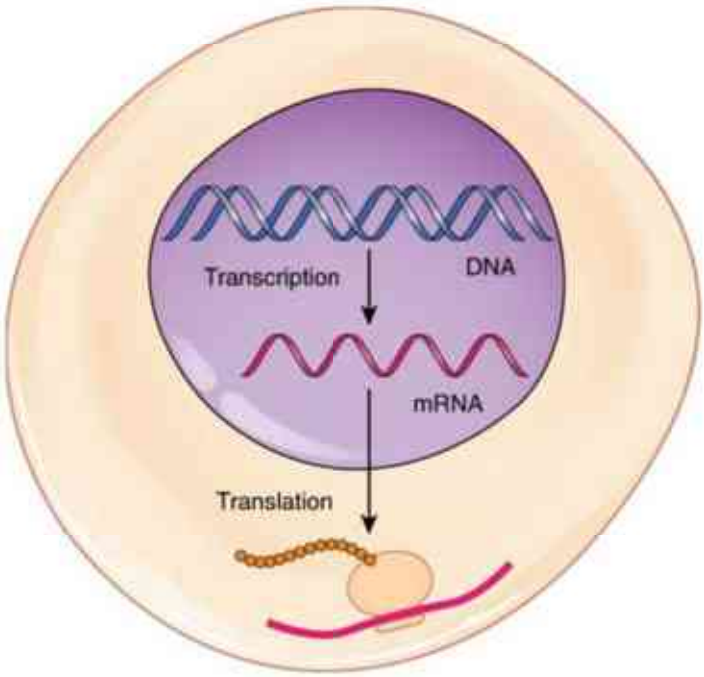
- RNA is copied from one strand of the double helix called the template strand.
- RNA differs from DNA in that it is single stranded, has uracil inserted of thymine and has ribose sugar instead of deoxyribose ribose.
- Messenger RNA (mRNA) carries the genetic information that specifies a particular amino acid sequence of protein synthesized.
- mRNA bases constitute codons, each codon is made of three consecutive bases in a row.
- rRNA joins certain proteins to form ribosomes. Ribosomes physically support the other structures involved in protein synthesis, and some rRNA catalyses' formation of peptide bonds.
- tRNA is clover leaf-shaped and connects mRNA codon to an amino.
- In prokaryotes, RNA is translated as soon as it is transcribed while in eukaryotes, RNA is often altered (or modified) before it is actively translated.
- mRNA gains a modified nucleotide cap and a poly A tail.
- Many genes have intervening sequences called introns, which are not transcribed and cutout from the mRNA. The protein encoding sequences in mRNA, exons, are then reattached. *Ribozymes* are small RNAs with catalytic activity that can splice introns. They join proteins to form snurps, which associate to form spliceosomes.
- After being processed the RNA must be exported from the nucleus before it is translated.



Processing of rRNA in a eukaryotic cell.

PROTEIN SYNTHESIS

The replication of DNA serves to carry genetic information from cell to cell and from generation to generation. This information is translated into protein that determines the phenotype of cell by controlling its biochemical reactions. Protein synthesis is the vital function of the cell where in the genetic information stored in DNA is passed on to RNA, especially mRNA by the process of **transcription.** All the three types of RNA i.e., mRNA, tRNA and rRNA together help in translating the coded information in the form of a polypeptide **(translation)**. The linear chain of amino acids translated is the primary protein which undergoes configurationally changes to form secondary, tertiary or quaternary proteins.



From DNA to Protein (central dogma): Transcription through Translation. Transcription within the cell nucleus produces an mRNA molecule, which is modified and then sent into the cytoplasm for translation.

Protein Synthesis and its Mechanism:

A gene expresses itself by protein synthesis. Protein synthesis is under direct controlof DNA in most cases or else under the control of genetic RNA where DNA is absent. Information for structure of a polypeptide is stored in a polynucleotide chain of DNA orRNA.

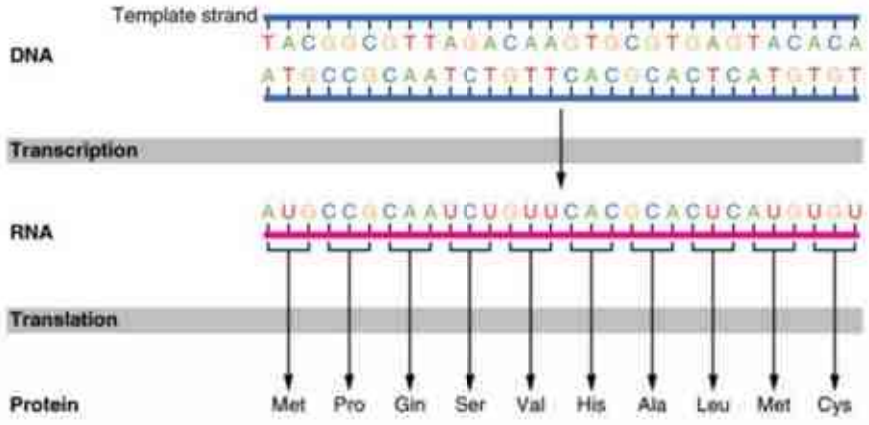
In 1958 **F. Crick** proposed that the concept of central dogma, which states that when a particular gene is expressed (control a function or a reactions) its information is copied into another nucleic acid (mRNA) which in turn directs the synthesis of specific proteins. So the central dogma was proposed as unidirectional flow of molecular information from DNA to mRNA and finally to polypeptide. Later a reverse of central dogma was also found in retroviruses. **H. Temin and D. Baltimore** (1970) reported that retro viruses operate a central dogma in reverse manner (inverse flow of information) or teminism inside host cells. This discovery was important in understanding cancer and hence, these two scientists were awadd Nobel Prize.

Genetic RNA of these viruses first synthesizes DNA through reverse transcription. This process is catalyzed by the enzyme reverse transcriptase. DNA then transfers information to messenger RNA which takes part in translation of the coded information to from polypeptide.

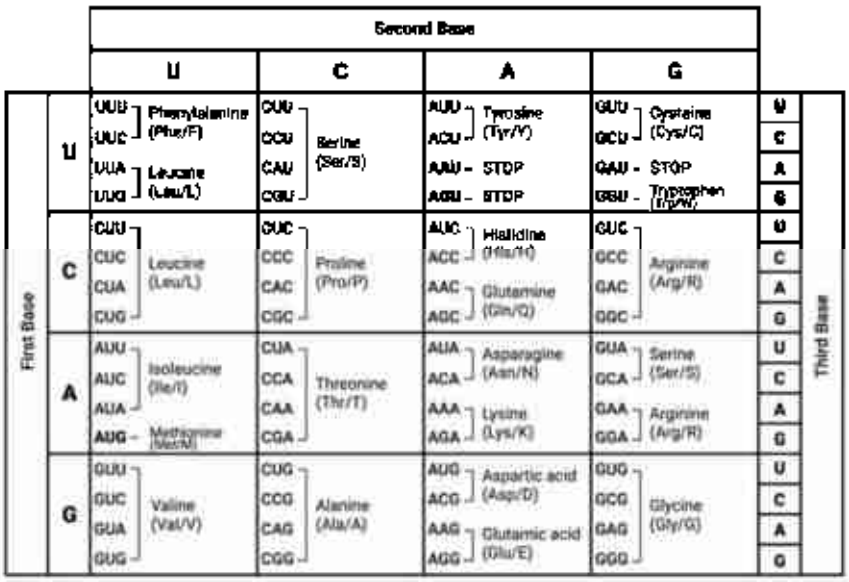
Necessary Materials:

(1) **Amino acids**- there are some 20 amino acids and amides which constitute building blocks or monomers of proteins. They are found in the cellular pool or cytoplasm.

The genetic code: it is a set of rules defining how the four-letter code of DNA is translated into the 20-letter code of amino acids, which are the building blocks of proteins. The genetic code is a set of three-letter combinations of nucleotides called codons **(triplet)**, each of which corresponds to a specific amino acid or stop signal. The concept of codons was first described by Francis Crick and his colleagues in 1961. There are 64 possible permutations, or combinations, of three-letter nucleotide sequences that can be made from the four nucleotides. Of these 64 codons, 61 represent amino acids, and three are stop signals. Although each codon is specific for only one amino acid (or one stop signal), the genetic code is described as degenerate, or redundant, because a single amino acid may be coded for by more than one codon. It is also important to note that the genetic code does not overlap, meaning that each nucleotide is part of only one codon-a single nucleotide cannot be part of two adjacent codons. Furthermore, the genetic code is nearly universal, with only rare variations reported.



The Genetic Code. DNA holds all the genetic information necessary to build a cell's proteins.



The 20 amino acids formation from 4 nucleotides.

(2) **Ribosome**- ribosome comprises two subunits which exists as separate subunits prior to the translation of mRNA and contain following sites (Figure 94):

- **P site (peptidyl site or D site- donor site)** - P site is jointly contributed by thetwo ribosomal subunits, most frequently occupied by peptidyl-tRNA or the tRNA carrying growing peptide chain. . The P-site is also referred to as the puromycin sensitive site. Puromycin is an antibiotic which shows similarities with a part of amino acyl-tRNA
- **A site (amino acyl site)** - A site is situated on the larger subunit of ribosome. It faces the tunnel between the two subunits, frequently occupied by amino acyl-tRNA, functions as acceptor for growing protein during peptide bond formation.
- **E-site** – the exit site, the ribosomal site harboring decylated tRNA on transit out from the ribosome.

The different parts of ribosomes, connected with protein synthesis are:

a- **A tunnel**- It lies between the two subunits, acts as a place for mRNA.

b- **The longitudinal groove**-is part of the longer subunits which acts as a passage of newly synthesized polypeptide.

c- **Reactive sites**- P, A and E-site

d- **P-site**- acts as a donor of peptide chain to the newly coming tRNA

e- **A-site**- acts as abinding site for new tRNA with its amino acid for the elongation of **mRNA**- carrying genetic information of DNA into cytoplasm for its translation.

(3) tRNA- to transport the respective amino acids as per their anticodons against thecodons of mRNA.

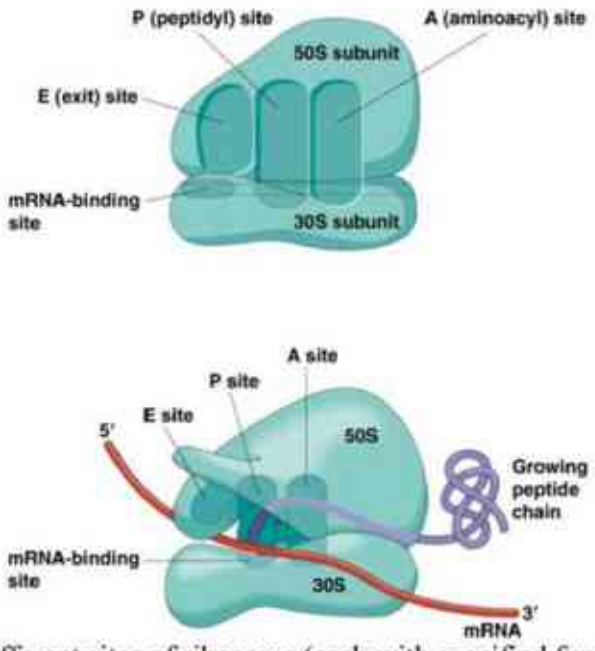
(4) Enzymes- amino acid activating system **(aminoacyl- tRNA synthetase),** Peptidepolymerase system.

(5) ATP- as energy source.

(6) GTP- for synthesis of peptide bonds.

(7) Soluble protein initiation and transfer factors

(8) Various inorganic cations (K^+, NH_4^+, Mg^{++} or Mn^{++})



Different sites of ribosome (each with specified function).

Mechanism of protein Synthesis:

Two major steps are involved in protein synthesis are: -

I- **Transcription**: involving transfer of genetic information from DNA to mRNA.

II- **Translation:** involving translation of the language of nucleic acid into that of apolypeptide.

I- Transcription process:

The transfer of genetic information from DNA to mRNA in general is known as transcription. The segment of DNA that takes part in transcription is called transcription unit. It has three components:

a) A promoter
b) The structural gene
c) A terminator

a) A promoter- promoter sequences are present upstream (5'end) of the structural genes of a transcription unit. The binding sites for RNA polymerase lies within the promoter sequence. In prokaryotes 10bp upstream from the start point lies a conserved sequence described as 10 nucleotide sequences **TATAAT or "pribnow box"** and 35 nucleotide sequences **TTGACA as "recognition sequence".**

b) The structural gene- structure gene is part of that DNA strand which has 3'-5' polarity as transcription occur in 5'- 3' direction. The strand of DNA that directs the synthesis of mRNA is called **template or non-coding strand**. The complementary strand is called **non-template or coding strand,** it is identical in base sequence to RNA transcribed from gene, only with U in place of T.

c) A terminator- terminator is present at 3' end of coding strand and defines the end of the process of transcription. The base sequence of the mRNA molecule is complementary to that ofthe antisense strand which served as it template. Like DNA synthesis RNA synthesis also proceeds from 5' to 3' direction (5'-3').

Transcription of mRNA in Eukaryotes:

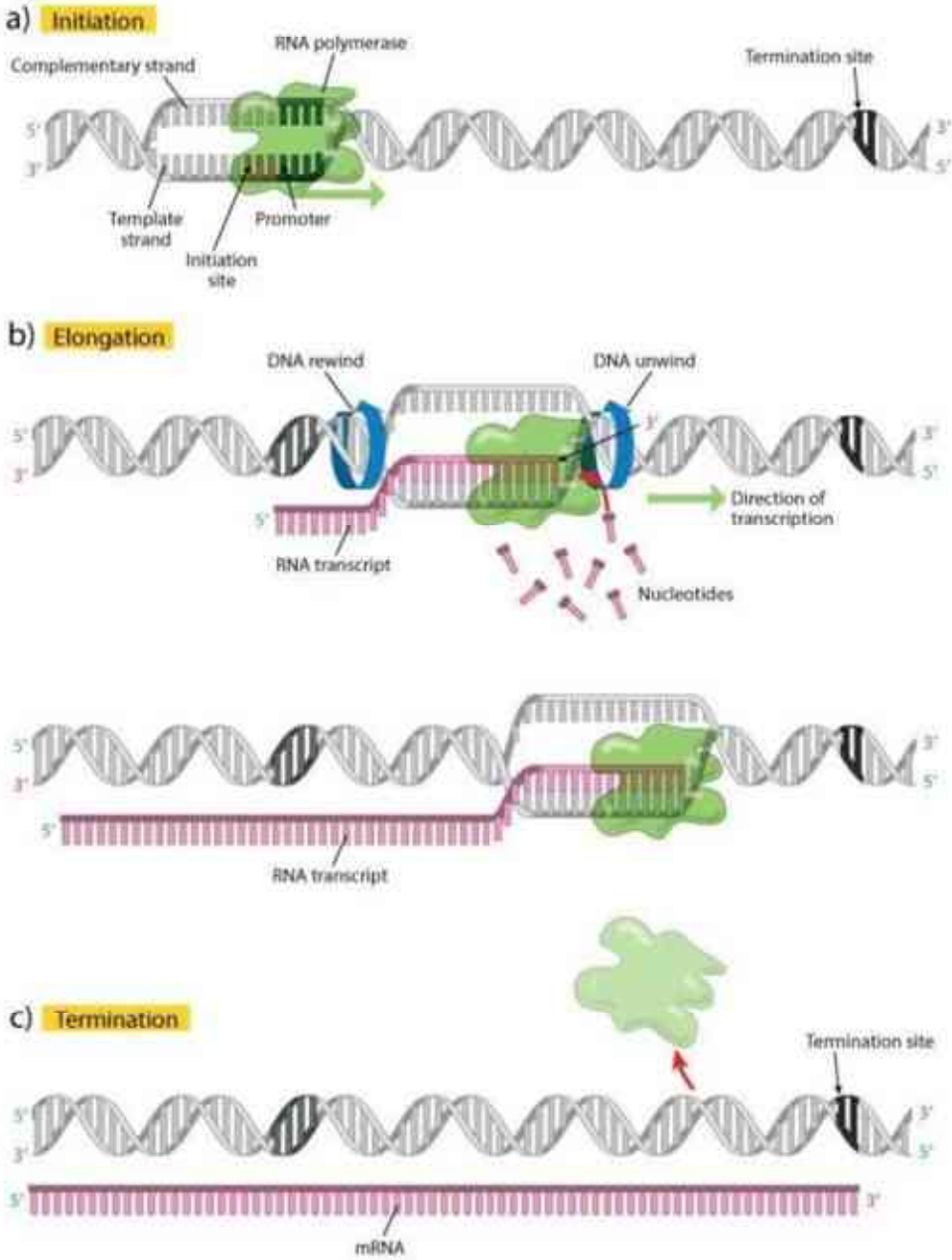
Eukaryotes-total 4 types of RNA polymerase, 3 types of RNA polymerase in nucleus, one inorganelles,

- **RNA-Polymerase** I: transcribes **rRNA (28S, 18S & 5.8S)**
- **RNA polymerase II:** transcribes **precursor of mRNA (hnRNA**- heterogeneous nuclear RNA)
- **RNA polymerase III:** transcribes **tRNA, 5SrRNA & snRNAs** (smallnuclear RNAs)

1. **Initiation**: binding of **RNA polymerase** to the **promoter region** with the help of an **Initiation Factor- Sigma factor** (binding of σ-factor alter the property of enzyme; make to function as an initiation enzyme).
2. **Elongation**- RNA polymerase will keep on making a complementary strand against template strand with the help of ribonucleotides. The newly transcribed strand keeps separating and the DNA duplex keep on folding back instantaneously. During elongation, same RNA polymerase acts as elongation enzyme due to separation of σ- factor from it. **The direction of transcription is also from 5' 3'like replication**. So the template against which it is transcribed has polarity of 3'—5'.
3. **Termination**- after reaching the terminator region newly formed or nascent RNA falls off along with RNA polymerase. Termination is assisted by Rho-factor(ρ-factor)

   In eukaryotes the promoter site is recognized by presence of specific nucleotide sequence called **TATA box or Hogness box or Pribnow Box** (7 base pair long-TATAAA or TATAATs) located 19-27bp upstream to the start point. Another sequence is CAAT box present between -70 and -80bp. The nucleotide sequence at the two ends of all mRNA molecules is the same. Normally mRNA carries the

codons of signal complete protein molecule (monocistronic mRNA) in eukaryotes, but in prokaryotes, it carries codons from several adjacent DNA cistron and becomes much longer in size (polycistronic mRNA).

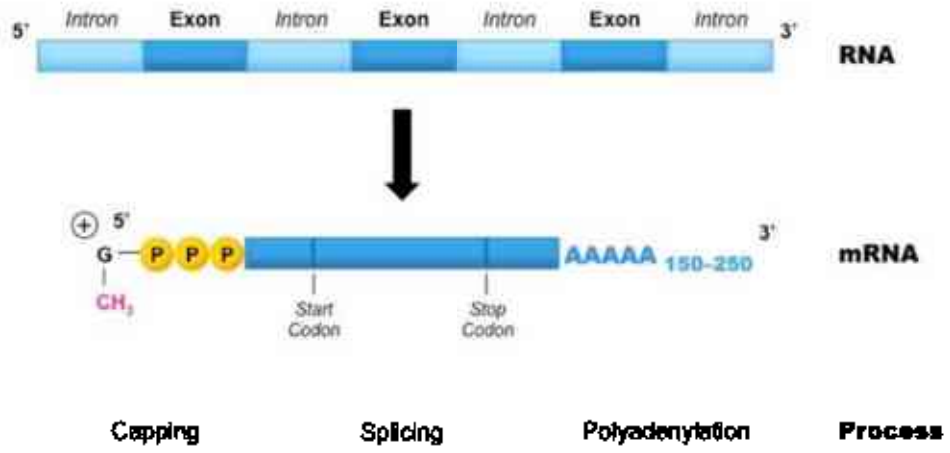


Eukaryotic cells transcription process.

Processing of Eukaryotic Transcript:

- **Splicing-** removal of **non-functional introns** and joining of all **functional exons** to make it a functional transcript. Splicing is important to remove the non-functional partof genetic information the DNA has kept but RNA does not need it. During copying from DNA, RNA does receive this non informative part in the form of introns but remove it with the help of some enzymes to make it functional.
- **Capping-** addition of methyl-guanosine triphosphate at 5' end of hnRNA
- **Tailing-** addition of 200-300 adenylated nucleotides at 3'end of hnRNA, addition of these nucleotides has no relation with the template.

The fully processed hnRNA is called mRNA, transported to the cytoplasm for translation.



Processing of Eukaryotic Transcript

II- Translation process:

Components of Translation:

- **mRNA**– the mRNA serves at the template that will determine the sequence of aminoacids in the new polypeptide. It has following components:
  - 5' untranslated region or 5'UTR.
  - Initiation codon.
  - Coding region.
  - Stop codon.
  - 3' untranslated region or 3'UTR.
- **t-RNA-** tRNA, a clover leaf shaped molecule, delivers the correct amino acid to the ribosome as directed by the codon on the mRNA for incorporation into the polypeptide. It has following arms, each with specified function:
  - 3'amino acid carrier arm or acceptor arm with –CCA sequence.
  - Ribosome recognizing arm-to recognize A or P or E-site.
  - Anticodon arm- with 3 nucleotides to bind to complementary codon.
  - Enzyme recognizing arm- to recognize specific aminoacyl synthetase.
  - 5énd with G.
- **Ribosome-** protein synthesizing machinery, help in holding mRNA and tRNA forspecific codon translation, has following components:
  - Smaller subunit (30S or 40S).
  - Larger subunit (50S or 60S).
  - Groove or tunnel between two subunits to hold mRNA.
  - Three sites- P, A and E-site.
  - Enzyme, peptidyl transferase, helps in peptide bond formation.

General steps of eukaryote translation:

1- **Activation of amino acids or charging of amino acids:** the amino acids attachment to the tRNA molecules is an active process and requires a lot of energy. In the presence of ATP, an amino acid combines with its specific amino acyl-tRNA synthetase; Mg2+ is also required in this reaction.

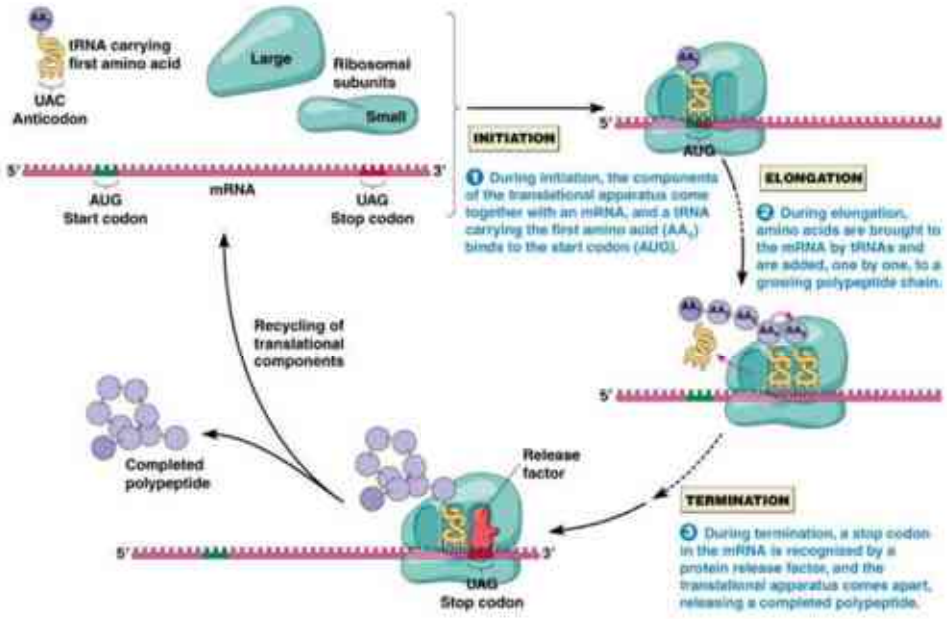
2- **Aminoacylation of tRNA or charging of tRNA:** It is the loading of tRNA with the activated amino acid.

3- **Initiation of translation**: In the first step there is binding of mRNA with smaller subunit of ribosome. Translation of Initiation codon (AUG) by a charged tRNA with Methionine (n-formyl methionine, f-Met, in prokaryote) amino acids takes place. It is followed by the translation of second codon by 2nd charged tRNA. After the translation of first two codons, the association of bigger subunit of ribosome takes place to form a complete translational complex. When two such charged tRNA comes close, the peptide bond between two amino acids, they carry, will take place with the help of a ribozyme called- Peptidyl transferase (23SrRNA molecule) enzyme. Formation of peptide bond between 1st& 2nd amino acid takes place. UTR- (Un- Translated-Regions) is the flanks of mRNA before Initiation and after the stop codon, which are not to be translated, but they play role in efficient translation.

4- **Elongation:** The translated part of mRNA translocate from one to next codon. Regular addition of new amino acids takes place at A Polypeptide chain (PPC) keeps elongating at the expense of energy provided by GTP. PPC hangs in the groove of bigger subunit of ribosome on the P-site.

5- **Termination-** Binding of releasing factors to the stop codon helps in the release of polypeptide and terminates translation. Synthesis of polypeptide terminates

when a nonsense codon of mRNA reaches the A-site. There are three nonsense codons- UAA, UAG & UGA. These codons are not recognized by any of the tRNAs. There is no tRNA having anticodon complementary to stop codon i.e., none of the tRNA has AUU, AUC or ACU anticodon. Finally, the ribosome encounters a stop codon. The polypeptide, tRNA and mRNA are released. The small and large subunits dissociate from one another.



Eukaryote translation process.

The operon:

According to the operon model, several gene codes for an enzyme in some metabolic pathways are located in sequence on chromosome. The expressions of structural genes are controlled by some regulatory genes. The **Operon means a unit of gene expression** and regulation which typically includes:

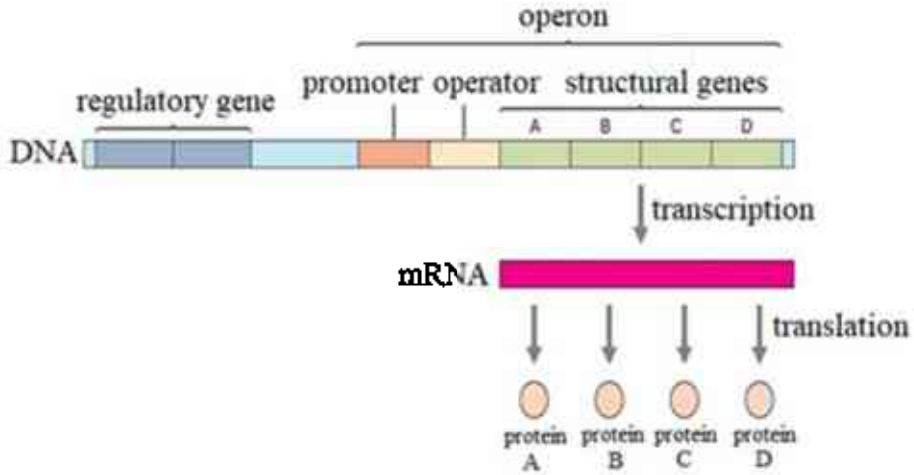
1- **The structural genes:** also called cistron are any gene/s other than the regulatory genes, whose products or enzymes are involved in a specific biosynthetic pathway and whose expression is coordinately controlled.

2- **Operator sequence**: control elements such as an operator sequence, which is a DNA sequence that regulates transcription of the structural genes.

3- **Regulator gene (s):** the genes, whose products recognize the control elements e.g., a repressor which binds told regulates the operator sequence of the same operon.

Operon has structural and regulatory genes that function as a single unit, it includes the following:

- A regulator gene is located outside the operon codes for a repressor or Apo-repressor protein molecule.
- A promoter is a sequence of DNA where RNA polymerase attaches when a gene is to be transcribed.
- An operator is a short sequence of DNA where repressor binds, preventing RNA polymerase from attaching to the promoter.
- Structural genes code for enzymes of a metabolic pathway and are transcribed as a unit.



The operon structure.

REGULATION OG GENE EXPRESION

The gene expression is regulated at many different levels. They are

i. Transcriptional level
ii. mRNA processing
iii. mRNA turn over
iv. translation level
v. enzyme function

Most of the data indicate that regulation of transcription is the most important mode of control of gene expression.

Synthesis of enzyme depends mainly on two factors. In degradative process (catabolic pathway) the synthesis of enzyme depends on the availability of the molecule to be degraded. In biosynthetic pathway the synthesis of an enzyme governed by end product. There are two types of gene regulation *viz*., (1) negative regulation and (2) positive regulation.

The operon model

E.Jacob and J.Monad (1961) proposed the operon model to explain the regulation of genes coding the enzymes required for lactose utilization in *E.coli*. The operon is a co-ordinated unit of the gene expression. The operon consists of structural genes, the operator and promoter.

Structural genes

The lac operon of *E.coli* consists of three structural genes namely z,y and a . These structural genes transcribe a single polycistronic mRNA molecule. This mRNA molecule controls the synthesis of three different enzymes *viz*., β-galactosidase, galactosidase permease and galactosidase transacetylase. All the above three enzymes are involved in breakdown of lactose. The function of all the structural

genesis regulated by two controlling elements namely regulator and operator. Thus, the main function of structural genes is to control synthesis of protein through mRNA.

Operator gene

The operator is usually located between the promoter and the structural genes. In lac oeron of *E.coli*, operator is located contiguous to the structural genes. It is the binding site for the protein called repressor. When the repressor is bound to the operator, transcription of the structural genes cannot occur. Because the binding of therepressor to the operator strictly prevents RNA polymerase from binding at the promoter site.

The promoter gene is always located contiguous with or even overlapping with operator sequence or operator. The promoter segment is a place where mRNA polymerase enzyme binds with DNA. The main function of promoter gene is toinitiate mRNA transcription. The promoter starts mRNA transcription only when operator is free or when repressor is not bound to the operator. The binding of repressor with operator inactivates the promoter gene and prevents transcription.

Regulator gene

The regulator gene is located either on one end of the operon or away from the operon. The function of the regulator gene is to synthesis a protein called repressor. The repressor may be either active or inactive.

In the case of an inducible operon, the free repressor binds to the operator and turning off the transcription. When the effectors molecule (the inducer) is present, it binds to the repressor and becomes repressor-inducer complex, which cannot bind the operator. There by the regulator gene turn on the transcription of structural genes in the operon. In the case of reversible operon, the repressor is inactive and cannot bind

to the operon there by transcription of structural genes in the operon is turned on. The only repressor effectors molecule (co-repressor) is active in binding to the operator and turn off the transcription of structural genes in the operon.

Mechanism of gene regulation in lac operon

In the absence of lactose in the medium, the regulator gene produces the active repressor molecule. These repressor molecules will bound to the operator and it strictly prevents the RNA polymerase from binding to the adjoining promoter. Thereby synthesis of enzymes by structural genes involved in lactose metabolism *viz.*,β galactosidase, galactosidase permease and galactosidase transcetylase were switched off. When the lactose (effectors molecule) is added to the medium, which act as inducer, will bind to the repressor and become repressor-inducer complex. This complex is inactive in nature, which cannot bind to the operator. The operator is now free from repressor and RNA polymerase will bind with promoter region and start the transcription of structural genes involved in lactose metabolism.

Traditionally, the gene has been defined as the unit of genetic material controlling the inheritance of one phenotypic characteristic or one trait and alsobelieved that gene was not to be sub divisible by mutation or recombination. To day the gene is precisely defined as the unit of genetic material coding for one polypeptide.

The functional allelism of the gene is operationally defined by the cis-trans or complementation test. Alleles may be arranged in two ways viz when two wild alleles are located in one homolog and their corresponding mutant allele in another member of the homologous chromosomes (++ / m_1 m_2), it known as cis-arrangement and the organism is called as cis-heterozygotes. On the other hand when one wild and one mutant type alleles are located in each member of a given homologous chromosome(+ m2 / m1 +), it is known as transposition and the organism is called

as trans heterozygote. Complementation test is used to determine whether two mutant alleles (mutations) belong to the same gene or two different genes.

The two mutations are considered to be in the same gene if their cis- heterozygotes produce wild type phenotype and trans heterozygote produce mutant phenotype (because no functional gene product will be synthesized). If both the cis-heterozygotes and trans heterozygote lead to the development of wild type phenotype, then the two mutations are in two different genes (both gene products will be synthesized in the common protoplasm).

Modern concept of gene

Now the gene can be defined as the unit of genetic material coding for one polypeptide. So the gene can also be called as cistern.

Cistron: The portion of DNA specifying a single polypeptide chain.

Muton: Muton is defined as the smallest unit of genetic material which when changed to produce different phenotypes.

Recon: It is smallest unit of DNA capable of recombination.

The cistron contains so many mutons and recons, the smallest unit of mutation or recombination. It's a single nucleiotide pair. So the unit of genetic material not sub divisible by mutation or recombination is known to be single nucleotide – pair.

Split Genes: In prokaryotes, polypeptide chains are encoded by continuous array of tripletin DNA. In eukaryotes, the genes are discontinuous. For example, the gene for β chain of hemoglobin interrupted by a long noncoding sequence of 550 base pairs and a short one of 120 base pairs. Thus, the β-globin chain is split into three coding sequences. The coding sequences are called exons (regions which are expressed) and the intervening sequences are called introns. All avian and mammalian genes mapped so far are split genes, except the histone gene..

PROBLEMS

(1) Gene A is dominant over gene a. What will be the phenotypic ratio in the offspring obtained from the following mating?

a) Aa X aa b) AA X aa c) Aa X Aa d) Aa X AA

(2) In a cross between pure breeding, round yellow seeded plant with wrinkled, green seeded plant, he observed that all the F1s were round yellow seeded and on selfing the F2 progenies segregated as 304 round yellow, 102 round green, 95 wrinkled yellow and 35 wrinkled green. Depict the cross diagrammatically and give proof for your inference.

(3) In the garden pea, Mendel found that yellow seed colour was dominant to green and roundseed shape was dominant to shrunken.

a) What phenotypic ratio would be expected in the F_2 from a cross of a pure yellow roundx green shrunken?

b) What is the F_2 ratio of yellow: green and of round: shrunken

c) Give the test cross ratio.

(4) In Drosophila, ebony body colour is produced by a recessive gene e and wild type (gray) body colour by its dominant allele e+. Vestigial wings are governed by a recessive gene vg and normal wing size (wild type) by its dominant allele Vg+. If wild type dihybrid flies are crossed and produce 256 progeny, how many of these progeny flies are expected in each phenotypic class?

(5) The normal clovern-footed condition in swine is produced by homozygous recessive genotype mm. Amule footed condition is produced by the dominant genotype M-. white coat colour is governed by adominant allele of another locus B and black by its recessive allele b. a white mule footed boar is crossed to a sow of the same phenotype. Among the F_1 offspring, all black mule footed types were to be crossed. What phenotypic ratio would be expected among the test cross progeny? If the sow was to be test crossed what phenotypic ratio is to be expected?

(6) A genetic condition on chromosome 2 in the fruit fly is lethal when homozygous (pm/pm), but when heterozygous (pm/pm+) produces a purplish eye colour called plum. The other homozygous condition (pm+/pm+) produces wild type colour. On chromosome 3, a gene called stubble produces short, thick bristles when heterozygous (sb/sb+), but is lethal when homozygous (sb/sb). The homozygous condition of its alternative allele (sb+/sb+) produces bristles of normal size (wild type).

a) What phenotypic ratio would be expected among progeny from crossed between plum, stubble parents?

b) If the F_1 progeny are allowed to mate at random to produce an F_2, what is the phenotypic ratio that is expected?

(7) Tall tomato plants are produced by the action of a dominant allele D and dwarf plants by its recessive allele d. hairy stem are produced by dominant gene H and hairless stem by recessive allele h. A dihybrid tall, hairy plant is test crossed. The progeny were observed tobe 118 tall hairy, 121 dwarf hairless, 112 tall hairless, 109 dwarf hairy.

a) Represent the cross diagrammatically?

b) What is the ratio of tall: dwarf or hairy: hairless?

c) Are these loci assorting independently? Give proof.

(8) In man, assume that brown eyes (B) are dominant over blue eyes (b) and right-handedness (L) is dominant over left-handedness (l). A brown eyed, right-handed man marries a blue-eyed right-handed woman and their first child is blue eyed and left handed. What are the genotypes of the two parents?

(9) In soybean, broad leaf is incompletely dominant over narrow. The heterozygote is intermediate. Purple is dominant over white.

a) What will be the phenotypic ratio of F_2 of a broad-leaved plant with a homozygous purple flower crossed with a narrow leaf white flowered plant?

b) What will be the offspring of the cross between F_1 and narrow leaf white flowered plant?

(10) An inhibition of pigment production in onion bulbs (I-) exhibits dominant epistasis over another locus, the genotype iiR-producing red bulbs and iirr producing yellow bulbs. (a) A pure white strain crossed to a pure red strain and produce all white F1s and F2 white 12/16 white: 3/16 red and 1/16 yellow. What are the genotypes of the parents? (b) In F2, 32 were found to be of genotype iirr. Workout the proportion of others.

(11) The dominant condition at one locus (A) expresses a phenotype whose expression is intensified by another dominant gene in another locus (B). The recessive genotype of locus A suppresses the expression of the dominant allele at B locus which is similar to the doublerecessive.

(12) In Shepherd's purse, triangular capsule is dominant over round, and it is due to duplicate genes C and D. What are the genotypes of the parents that would produce the following results.

a) 15 Triangular and one round

b) 3 Triangular and one round

(13) Matings between black rats of identical genotype produced offspring as 14 cream coloured, 47 black and 19 albinos.

a) What epistatic ratio is approximated by these offspring?

b) What type of epistasis is operative?

c) What are the genotypes of parents and offsprings?

(14) The black leghorn breed of chickens had feathered shanks. When Langshans are crossed to the Buff Rock breed with unfeathered shanks, all F1 have feathered shanks. Out of the 360 F2 progenies, 24 were found to have non-feathered shanks and 336 had feathered shanks.

a) What is the mode of interaction of this trait?

b) Give proof using chi-square test.

(15) An inhibitor of pigment production in onion bulbs (I-) exhibits dominant epistasis over another locus. The genotype ii R- producing red bulbs and iirr producing yellow bulbs. A pure white strain is crossed to a pure red strain and produces all white F1 and F2 with 12/16 white, 3/16 red and 1/16 yellow. What were the genotypes of the parents? Prove with statistical analysis.

(16) When pure breeding two white flowered sweet pea plants were crossed, the F1 was purple. In F2, the progenies segregated into 94 purple and 75 white. (Statistically would this be considered as 1: 1 ratio. If not, how do you interpret i.e., and) what would be the genotype of the parents?

(17) In paddy, purple sheath is dominant over green. In a cross with purple sheath with green sheath, the F1 is found to be green. In F2 the progenies segregated as 1291 green and 307 purple. Interpret the segregation and give proof.

(18) Three fruit shape are recognized in summer squash (Cucurbita pepo.): Disk, elongated and sphere shape. Pure disk was crossed with elongated and 45 disks were observed.

a) interpret the interaction.

b) Give proof.

(19) A dominant gene S in Drosophila produces a peculiar eye condition called star. Its recessive allele S+ produces normal eye of wild type. The expression of S can be suppressed by the dominant allele of another locus su-s. The recessive allele of the locus su-s+ has no effect on s+. What is the type of interaction involved?

(20) Two white flowered strains of sweet pea (Lathyrus odoratus) were produced an F1 with purple flowers. Random crossing among F1 produced 96 progeny

plants, 53 exhibiting purple flowers and 43 with white flowers.

a) What phenotypic ratio is approximated by the F_2?

b) What is the type of interaction involved?

c) What are the probable genotypes of parents and offspring?

(21) Three fruit types are recognized in summer squash (*Curcurbita pepo*): disc shaped, elongated and spear shaped. A pure disc shaped variety was crossed to a pure elongated variety. The F1 were all disc shaped. Among 80 F2, there were 30 spear shaped, 5 elongated and 45 disc shaped. Reduce the F2 numbers to their lowest ratio and comment on their inheritance.

(22) A homozygous yellow rat when mated with a homozygous black rat produces F1 all grey in colour. Brother-sister mating of F1 produced F2 progeny in the phenotypic ratio of 27 grey: 9 yellow: 8 black:3cream coloured.

a) Explain the type of inheritance.

b) Give the genotypes of F_2 progeny.

c) What proportion of F_2 rats are expected to be homozygous among the black coloured progeny?

(23) In a study on the inheritance of skin colour in man, the following results were observed comment on the inheritance.

Negros x White

Mullatoes (F_1)

The intermating among F_1 progenies produces the following F_2 children.

1/16 Negroes -4/16 Dark - 6/16 Intermediate - 4/16 Light - 1/16 White

(24) In tomato, genotype aab bcc. produces 100 g tomatoes and AABBCC produces 160 g tomatoes, each gene (capital letters) causing an increase of 10g. Give the weight of tomatoes in the parents and progenies in the following crosses:

a) AAbbcc x aaBBcc

b) AAbbcc x AaBbCc

c) aaBbCc x aaBbCc

d) AaBbCc x aaBBCc

(25) Height in man is caused by polygenes.

a) Can matings between individuals with intermediate height produce children taller thaneither of the parent?

b) Can mating between two short parents produce children taller than either of the parents.

(26) If the wheat kernel colour is determined by three pairs of polygenes, in a cross AABBCC x aabbcc. What fraction of F2 would be expected to be like other parent? How may F2 phenotypic classes result?

(27) A yellow mouse crossed with another yellow mouse gave 8 yellow, 2 black and tan offspring. Two of these black and tan offspring gave at least one black progeny of their own. What is the probability of obtaining yellow, black and tan and black offspring from:

a) a cross of F_1 black and tan to F_1 black and tan

b) a cross of F_2 black to F_2 black

c) a cross of F_1 yellow to F_1 yellow

The coat colour in mouse is controlled by a series of alleles consisting of :

AY = yellow AL = Yellow with black belly;

A = Agouti at = black and tan a = black

(28) Plumage colour in mallard ducks is dependent upon a set of three alleles; MR Restricted mallard pattern: M mallard and 'm' dusky mallard. The dominance hierarchy is MR M m. Determine the genotypic and phenotypic ratios expected in the F2 from the following crosses.

a) M^RM^R x M^RM

b) M^RM x Mm

c) M^Rm x mm

(29) Write the phenotype and genotype segregation in the following multiple allelic series crosses where the dominance relationship is:

$C > C^{ch} > c^h > c$

C: Coloured, C^{ch} ; Chinchilla, c^h: Himalayan ;c: colourless

1) $C\ c^h$ x $c^{ch}c^h$ 2) $C\ c$ x $c^{ch}\ c^h$ 3) $c^{ch}\ c$ x c^hc

4) C c x C c 5) cc x C c^{ch}

(30) A couple believed that they have brought the wrong baby home from the hospital. The wife is group O, her husband is group B and the child is group O. Could the baby be theirs?

(31) A couple preparing for marriage have their blood typed along with other required blood tests. Both are AB. They ask you what type of blood group their children may have? What would you tell them and how would you explain your conclusions?

(32) A man has type A blood, and his wife has type B blood. A physician types the blood of their four children and is amazed to find one each of the four blood types among them. He is not familiar with genetics and calls upon you to explain how such a thing could happen. What would you tell?

(33) A wealthy, elderly couple dried together in an accident soon, a man shows up to claim their fortune, contending that he is their only son who ran away from home when a boy. Other relatives dispute this claim. Hospital records show that the deceased couple were blood type AB and O. The claimant to the fortune fortunately has the type O. Do you think that the claimant was an impostor? Explain.

(34) Two sets of parents. Mr. X and Mrs. X and Mr. Y and Mrs. Y are claiming the same baby. Blood tests give the information that Mr. X and Mrs. X belongs to A group of blood and Mr.Y. belong to O group and Mrs. Y is of AB groups. The child belongs to O. Explain with reasons to which parents' child could be given.

(35) Two (Pisum sativum) plants were crossed, and the following progenies were obtained. What will be the most likely genotypes of the parents and offspring?

a) Tall x Tall gene 86 Tall, 29 dwarf

b) Tall x Tall gene 124 tall

c) Tall x dwarf gene 14 tall, 6 dwarf

d) Tall x dwarf gene 5 tall, 4 dwarf

(36) John and Sue are planning to start a family. They visit a genetic counselor seeking advice about a genetic disease that both John's and Sue's families have suffered from in the past. There is no genetic test for this recessive trait. Its onset, which can be gradual, occurs after age 40. Both John and Sue are in their early 30's. They would like to determine the chances of their children inheriting the disease.

A review of John's family history of the disease shows that John's paternal grandfather (on his father's side) had the disease, but John's paternal grandmother and John's father do not. One of the brothers of John's father has the disease. John's mother has the disease. Sue's family can only trace the occurrence of the disease back to her maternal grandparents (on her mother's side), neither of whom had the disease. Sue's mother, father, sister, and brothers have the disease. Construct a pedigree diagram and use Punnett squares to answer questions 1-3.

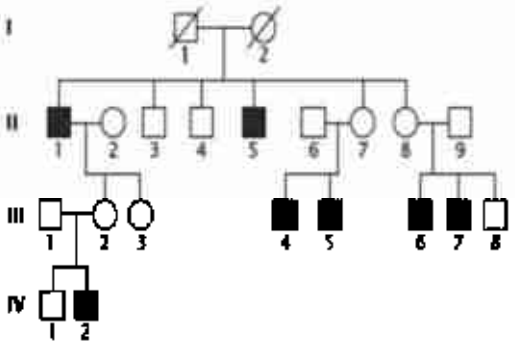
1. What are the genotypes of John's and Sue's parents and grandparents?
2. What are the possible genotypes of John and Sue?
3. If you are John and Sue's genetic counselor and, given their family histories, how would you explain the chances of their children inheriting the disease?

(37) Joe is color blind. Both his mother and father have normal vision, but his mother's father (Joe's maternal grandfather) is color blind. All Joe's other grandparents have normal color vision. Joe has three sisters—Patty, Betsy, and Lora—all with normal color vision. Joe's oldest sister, Patty, is married to a man with normal color vision; they have two children, a 9-year-old color-blind boy and a 4-year-old girl with normal color vision.

a) Using standard symbols and labels, draw a pedigree of Joe's family.

b) What is the most likely mode of inheritance for color blindness in Joe's family?

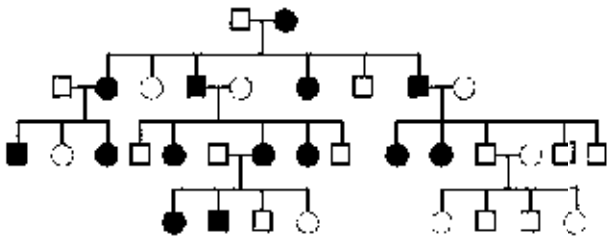
(38) Dent disease is a rare disorder of the kidney, in which reabsorption of filtered solutes is impaired and there is progressive renal failure. R. R. Hoopes and colleagues studied mutations associated with Dent disease in the following family.



On the basis of this pedigree, what is the most likely mode of inheritance for the disease? Explain your reasoning.

(39) For each of the following pedigrees, give the most likely mode of inheritance, assuming that the trait is rare. Carefully explain your reasoning.

(A)



(B)