Principles of Inheritance

Gregor Mendel observed the common pea plant and noticed that several characteristics were inherited faithfully from one generation to the next. For instance, flower color was either white or purple. Peas were either round or wrinkled and either yellow or green. He cultivated lots of pea plants over a number of generations in breeding experiments to see the characteristics of the offspring produced by particular parents.

Character means any observable feature, or trait, of an organism, whether acquired or inherited. An acquired character is a response to the environment; an inherited character is produced by genes transmitted from parent to offspring (their expressions are often modified by environmental conditions).

Trait is the inherited character like curly or straight hair.

Genes: Characteristics were determined by genes, or units of inheritance, which determined the characteristics displayed in an individual.

Alleles are the forms of the gene found in same locus.

Locus is a specific, fixed position on a chromosome where a particular gene or genetic marker is located.

Phenotype refers to the observable physical properties of an organism; these include the organism's appearance, development, and behavior.

Genotype is the genetic constitution of an organism. The genotype determines the hereditary potentials and limitations of an individual from embryonic formation through adulthood. Among organisms that reproduce sexually, an individual's genotype comprises the entire complex of genes inherited from both parents.

Dominant is the genetic trait if it is expressed in a person who has only one copy of that gene.

Recessive trait appears only in organisms who have received two copies of a mutant gene, one copy from each parent.

Wild type allele encodes the phenotype most common in a particular natural population is known as the wild type allele.

Mutant is the recessive allele which is less common and believed to be formed through mutation of wild type allele.

Homozygous means having identical alleles for a single trait only.

Heterozygous having the two alleles at corresponding loci on homologous chromosomes different for one or more loci.

Genome is the haploid set of chromosomes in a gamete or microorganism, or in each cell of a multicellular organism.

Gene pool refers to the total number of genes of every individual in a population.

Test cross is a genetic cross between a homozygous recessive individual and a corresponding suspected heterozygote to determine the genotype of the latter.

Back cross is a crossing of a hybrid with one of its parents or an individual genetically similar to its parent.

Reciprocal cross a pair of crosses between a male of one strain and a female of another, and vice versa.

Monohybrid cross is the cross between two organisms of a species which is made to study the inheritance of a single pair of alleles or factors of a character.

Dihybrid cross is a cross between two different lines/genes that differ in two observed traits.

Heredity is the passing of traits from parent to offspring.

Variation is the degree of differences in the offspring and between the progeny and the parents.

Chromosome theory of inheritance

The speculation that chromosomes might be the key to understanding heredity led several scientists to examine Mendel's publications and re-evaluate his model in terms of the behavior of chromosomes during mitosis and meiosis. In 1902, Theodor Boveri observed that proper embryonic development of sea urchins does not occur unless chromosomes are present. That same year, Walter Sutton observed the separation of chromosomes into daughter cells during meiosis. Together, these observations led to the development of the Chromosomal Theory of Inheritance, which identified chromosomes as the genetic material responsible for Mendelian inheritance.

The Chromosomal Theory of Inheritance was consistent with Mendel's laws and was supported by the following observations:

- Sperms and ova carry all hereditary trait and contribute equally in the heredity of offspring.
- During fertilization, sperm and egg nuclei are fused. Nucleus contains chromosome and carry the hereditary trait.
- Every chromosome pair has a definitive role in development. Loss of complete or part of chromosome leads to structural and functional deficiency in the organism.
- Both chromosomes as well as genes occur in pairs in the somatic or diploid cells.
- The gamete contains only one chromosome of a type and only one of the two alleles of a character.
- During meiosis, homologous chromosome pairs migrate as discrete structures that are independent of other chromosome pairs.
- The sorting of chromosomes from each homologous pair into pre-gametes appears to be random.
- Each parent synthesizes gametes that contain only half of their chromosomal complement.
- Even though male and female gametes (sperm and egg) differ in size and morphology, they have the same number of chromosomes, suggesting equal genetic contributions from each parent.
- The gametic chromosomes combine during fertilization to produce offspring with the same chromosome number as their parents.
- Genetic homogeneity and heterogeneity, dominance and recessiveness can be suggested by chromosomal type and behavior.
- In many organisms, sex of an individual is determined by specific chromosomes called sex chromosome.

Despite compelling correlations between the behavior of chromosomes during meiosis and Mendel's abstract laws, the Chromosomal Theory of Inheritance was proposed long before there was any direct evidence that traits were carried on chromosomes. Critics pointed out that individuals had far more independently segregating traits than they had chromosomes. It was only after several years of carrying out crosses with the fruit fly, *Drosophila melanogaster*, that Thomas Hunt Morgan provided experimental evidence to support the Chromosomal Theory of Inheritance.

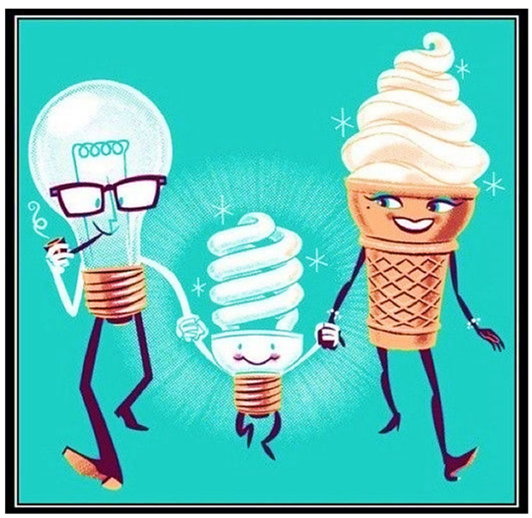
In 1910, Thomas Hunt Morgan started his work with *Drosophila melanogaster*, a fruit fly. He chose fruit flies because they can be cultured easily, are present in large numbers, have a short generation time, and have only four pair of chromosomes that can be easily identified under the microscope. They have three pair of autosomes and a pair of sex chromosomes. At that time, he already knew that X and Y have to do with gender. He used normal flies with red eyes and mutated flies with white eyes and cross bred them. In flies, the wild type eye color is red (XW) and is dominant to white eye color (Xw). He was able to conclude that the gene for eye color was on the X chromosome. This trait was thus determined to be X-linked and was the first X-linked trait to be identified. Males are said to be hemizygous, in that they have only one allele for any X-linked characteristic.

Incomplete dominance

Incomplete dominance is when a dominant allele, or form of a gene, does not completely mask the effects of a recessive allele, and resulting physical appearance shows an intermediate character or blending of both alleles. It is also called semi-dominance or partial dominance.

Incomplete dominance is a deviation from Mendel's law of segregation or monohybrid ratio.

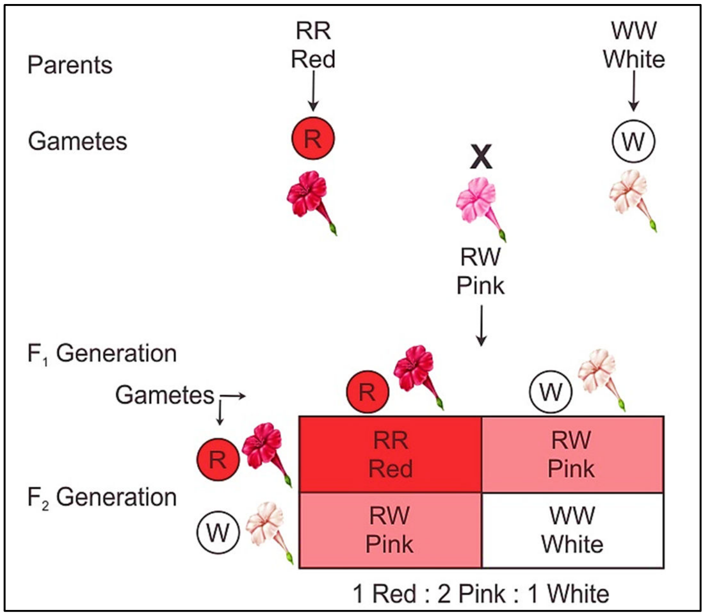
i. It is a form of intermediate inheritance in which one allele for a specific trait is not completely expressed over its paired allele.
ii. Neither allele is dominant.
iii. Organisms are Heterozygous.
iv. The intermediate phenotype is the blending of other two.



Examples

1. Flower color in four o'clock plant (*Mirabilis jalapa*) has two phenotypic expressions- red (dominant) and white (recessive). According to Mendel's law, only one of these is expressed-i.e., dominant phenotype in homozygous (AA) and heterozygous (Aa) conditions and recessive phenotype in only homozygous (aa) condition. However, in this case F1 (heterozygous) shows pink flowers which is intermediate between the dominant (red color of flower) and the recessive (white color of flower). This type of inheritance where heterozygote shows an intermediate

phenotype, is termed as incomplete dominance. Further, in F2 generation both phenotypic and genotypic ratios are also similar, i.e.,1 red (RR): 2 pink (Rr): 1 white (rr).



2. In snapdragon (*Antirrhinum* sp), when a true breeding (homozygous) red colored plant is crossed with true breeding (homozygous) white colored plant, all the F1 offspring (heterozygous) are pink. When pink F1 hybrid (heterozygous) were crossed, there were three types of offspring in F2, red: pink: white=1:2:1.

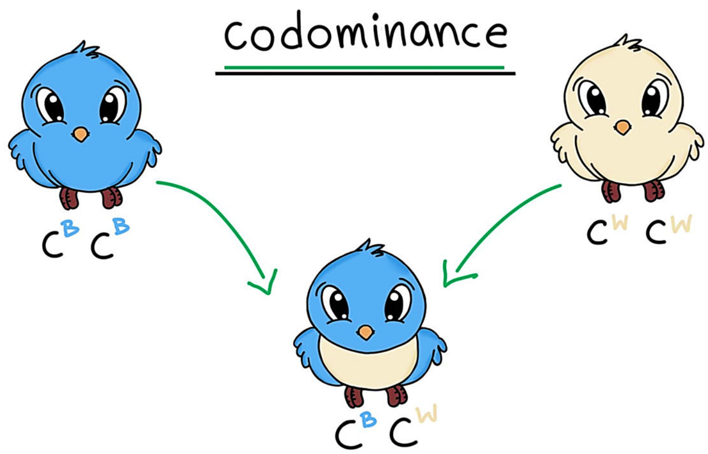
3. Andalusian fowls also show incomplete dominance. A cross between pure white splashed fowl and a pure black fowl resulted into a blue F1 hybrid. F2 generation produces the same phenotypic and genotypic ratios of white (WW): blue (Ww): black (ww)=1:2:1.

4. In Humans, a child born to a parent with straight hair and a parent with curly hair will usually have wavy hair, or hair that is a little curled, due to the expression of both curly and straight alleles. Incomplete dominance can be seen in many other physical characteristics such as skin color, height, hand size, and vocal pitch.

Codominance

The term codominance describes the relationship between two alleles at a locus when animals heterozygous for the two alleles display both of the phenotypes observed in animals homozygous for one allele or the other.

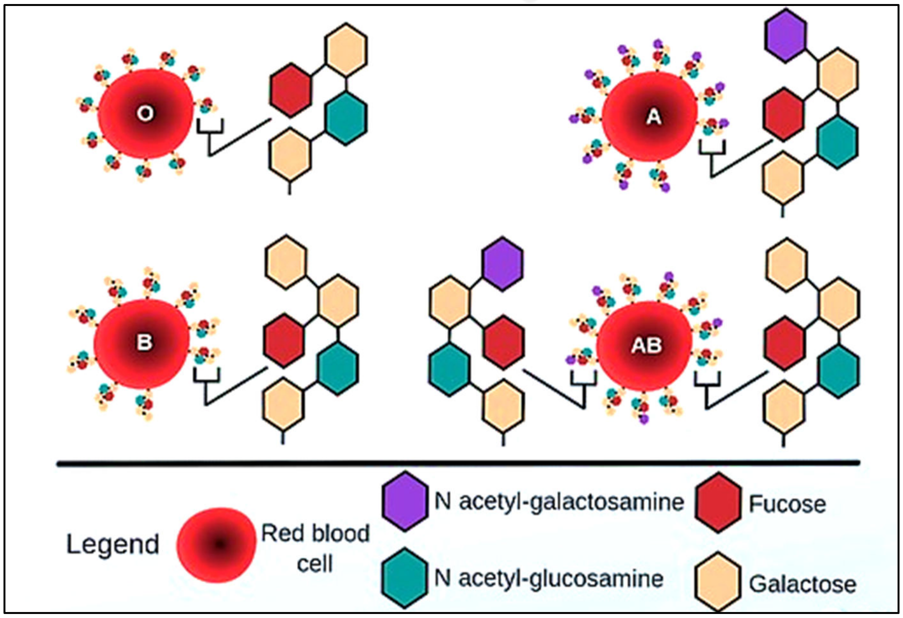
i. The alleles express themselves independently even when present together.
ii. In heterozygous condition both alleles would be present and each would express independent of the other.



Examples

1. AB blood group in Human

Type AB blood of the ABO blood type system is an example of codominance in humans. The red blood cells have antigens on their surface. One of these antigens is the H antigen that is controlled by three alleles: I^A, I^B, and *i*. Both I^A and I^B are dominant alleles that when expressed produce enzymes that modify the H antigen. I^A particularly adds N-acetylgalactosamine whereas I^B adds galactose to the H antigen. With *ii* alleles, thus lacking the dominant alleles, there would be no such modifications on the H antigen on the red blood cells. A genotype of I^AI^A or I^Ai would result in H antigens with N-acetylgalactosamine on the red blood cells – a trait indicating type A blood. A genotype of I^BI^B or I^Bi would result in H antigens with galactose – a trait indicating type B blood. A genotype of I^AI^B would result in H antigens with both N-acetylgalactosamine and galactose. This indicates a type AB blood. Conversely, a genotype of *ii* means lacking such modifications on the H antigen and an indication of a type O blood. In codominance, blood type AB implies that both dominant alleles are present and expressed together.



	Codominance	Incomplete Dominance
DEFINITION	The phenomenon where the offspring receives both the parent genes as a combination of both the genes.	The phenomenon where neither one of the parent genes is expressed but a combination of the parent genes is expressed.
EFFECT OF THE HYBRID	Independent effect	Intermediate of the two alleles
EFFECT OF THE ALLELE	Both alleles are equally conspicuous	One allele is more conspicuous over the other
EXPRESSED PHENOTYPE	Both parental characteristics express in unequal proportions.	None of the parental characteristics is The phenotype is a novel one.
QUANTITATIVE EFFECT	Absent	Present

Multiple alleles

More than two alternative or allelic forms of a gene known as multiple allele.

i. Multiple alleles always occupy the same locus on the chromosome.
ii. Multiple alleles always influence the same character.
iii. There is no crossing over between the members of multiple alleles.
iv. Multiple alleles never show complementation with each other.
v. The wild type (normal) allele is nearly always dominant while the other mutant alleles in the series may show dominance or there may be an intermediate phenotypic effect.

Examples

1. ABO blood group

An example of multiple alleles is the ABO blood-type system in humans. In this case, there are three alleles in the population. The I^A allele codes for A antigen on the red blood cells, the I^B allele codes for B antigen on the surface of red blood cells, and the *i* allele codes for no antigen on the red blood cells. Although there are three alleles present in a population, each individual only gets two of the alleles from their parents. Instead of three genotypes, there are six different genotypes are found when there are three alleles. The number of possible phenotypes depends on the dominance relationships between the three alleles.

Inheritance of the ABO Blood System in Humans

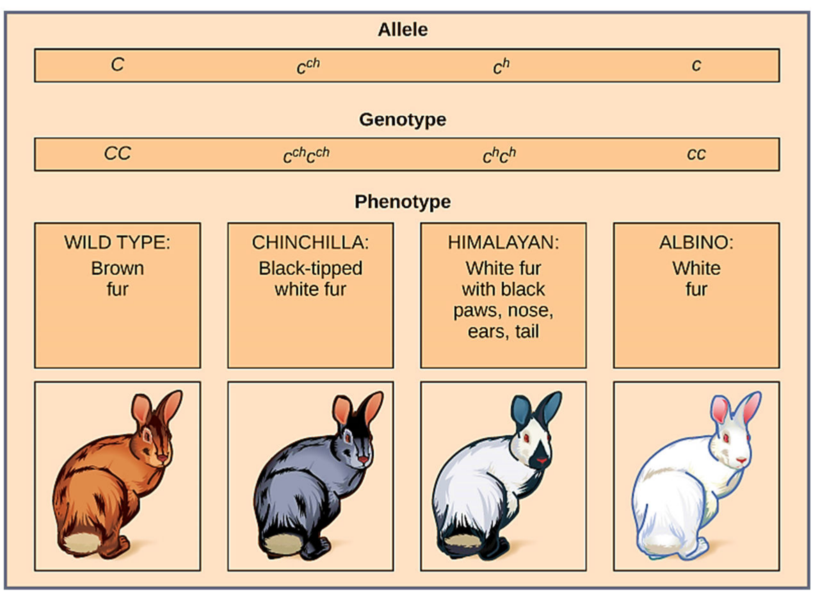
	I^A	I^B	i
I^A	I^AI^A A	I^AI^B AB	I^Ai A
I^B	I^BI^A AB	I^BI^B B	I^Bi B
i	$i\,I^A$ A	$i\,I^B$ B	$i\,i$ O

2. Coat color in rabbit

In rabbits, four kinds of skin colour are known. Rabbits are accordingly classified as coloured (agouti), chinchilla, himalayan albino, and albino**.** If homozygous coloured *(CC)* is crossed with albino *(c^ac^a), F_1* heterozygous *(Cc^a)* individual is coloured showing that coloured is dominant over albino. F_1 heterozygous coloured *(Cc^a)* gives a 3: 1 ratio in F_2.

Still another type is known in rabbits and is called chinchilla. This colour is lighter than the wild (agouti). Coloured character is completely dominant over chinchilla. However, F_1 hybrids between chinchilla and himalayan albino *($c^{ch}c^h$)* or between chinchilla and albino *($c^{ch}c^a$)* show light gray skin color. A summary of different genotypes involved in this series, along with their phenotypes, is given in Table.

Genotypes	Phenotypes
CC, Cc^{ch}, Cc^a	coloured (wild)
$c^{ch}c^{ch}$	chinchilla
$c^{ch}c^h$, $c^{ch}c^a$	light grey
c^hc^h, c^hc^a	himalayan albino
c^ac^a	albino



Lethal alleles

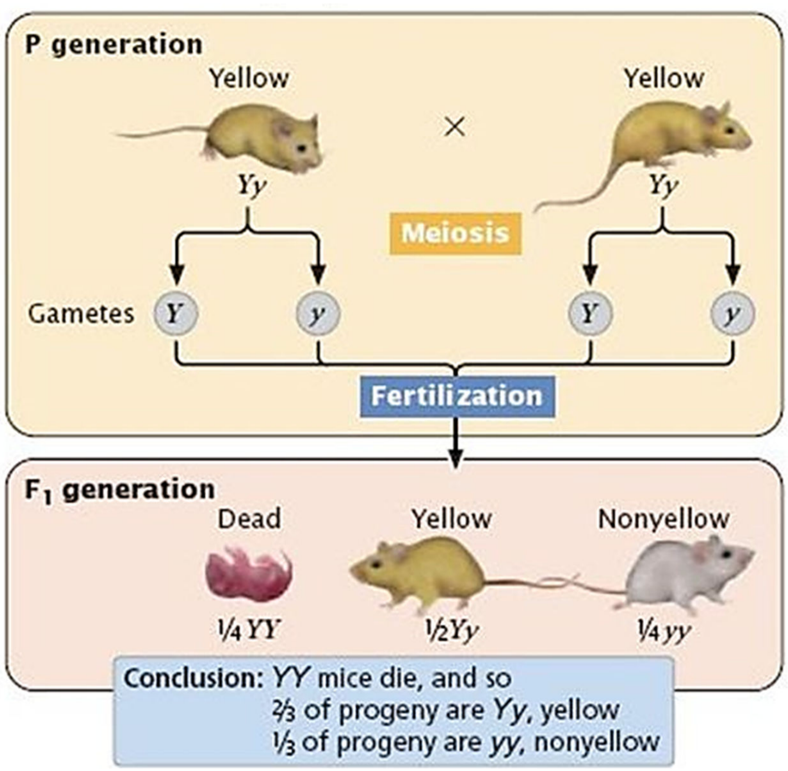
A gene that under certain conditions (such as homozygous recessive) causes the viability reduction of organism or death of an organism known as lethal gene.

There are some genetic factors or genes, when present in any organism cause its death during early stage of development.

Examples

A French Geneticist L. Cuenot (1905) reported on the inheritance of mouse body color. He found that "yellow" body colour was dominant over normal "brown" color and was governed by single gene "Y". It was observed that yellow mice could never be obtained in homozygous condition.

When yellow coated mice was crossed with another yellow coated mice, segregation for yellow and brown body color was obtained in 2: 1 ratio. The brown individuals were pure and homozygous whereas yellow individuals were heterozygous. These results may be explained on the assumption that the dominant allele for yellow body color is lethal in homozygous condition.



Lethal genes may be classified in to the following groups:

1. Recessive lethal

It is expressed only when they are in homozygous condition. The survival of heterozygotes is not affected e.g., coat color in mice.

According to Cuenot, Castle and Little, the dominant allele Y is a recessive lethal and it causes death of homozygous YY embryos at an early stage of development.

2. Dominant lethal

Alleles that need only be present in one copy in an organism to be fatal are referred to as dominant lethal alleles. These alleles are not commonly found in populations because they usually result in the death of an organism before it can transmit its lethal allele on to its offspring. Dominant lethal genes are expressed in both homozygotes and heterozygotes.

An example of this in humans is Huntington's disease in which the nervous system gradually wastes away. People who are heterozygous for the dominant Huntington allele (Hh) will inevitably develop the fatal disease. However, the onset of Huntington's disease may not occur until age 40, at which point the afflicted persons may have already passed the allele to 50 percent of their offspring.

3. Conditional lethal

Conditional lethal mutations are changes in the sequence of genetic material, which kill the organism, but only when it faces certain environmental conditions; under other conditions, the organism can survive and grow.

Many mutants of barley, maize, *Neurospora*, *Drosophila* and many other organisms are termed as temperature sensitive mutations. Each of them needs a definite, generally high temperature to express their lethal action.

A chlorophyll mutant of barley allows normal chlorophyll development at a temperature of 19°C or above, but it develops albina or abnormal white seedlings at temperature below 8°C.

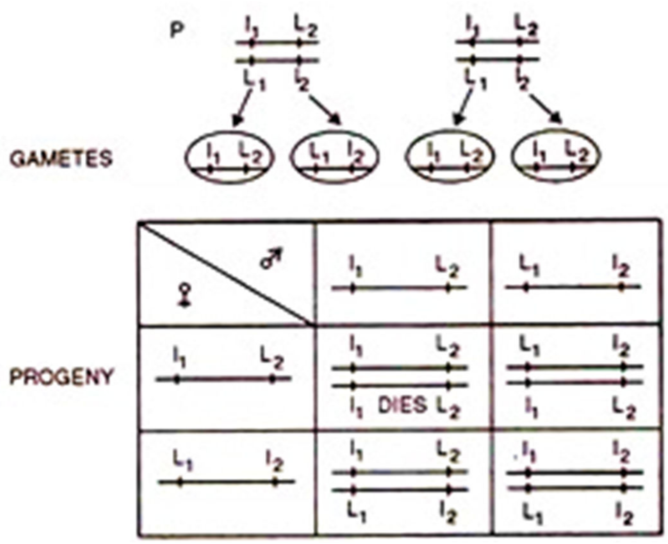
Temperature is not only responsible to bring out conditional lethals. Some conditional lethals require light, nutrition etc.

4. Balanced lethal

The balancing effect between two different lethals in self permanent stock is called balanced lethal system- Muller (1918). Lethal genes linked in repulsion phase of linkage are said as balanced lethals. They are maintained in repulsion phase due to tight linkage. Crossing over is very low. In repulsion phase, the recessive allele of one gene and the dominant allele of the other gene are present in the same chromosome.

Mating between individuals heterozygous for these balanced lethals will produce 4 types of zygotes. 1/4 will be homozygous for the recessive lethal and will not survive. Another 1/4 of the zygotes shall be homozygous for the other recessive lethal and will die.

The only progeny which will survive, will be the heterozygotes for the 2 recessive lethals. Therefore, a balanced lethal system maintains the genes closely linked to the lethal genes in a permanent heterozygous state. Balanced lethals are seen in mice, Oenothra, *Drosophila* etc.



[A balanced lethal system having 2 recessive lethal genes (l1 and l2). Only 2 of the 4 heterozygotes survive (l1L2/L1l2)]

5. Gametic Lethal

Some genes make the gametes incapable of fertilization. Such genes are said as gametic lethals. Sometimes the term 'Meiotic drive' is used to describe gametic lethals. Meiotic drive may be called a mechanism that leads to the production of unequal numbers of functional gametes by a heterozygote.

It has been found in certain males of *Drosophila pseudoobscura,* produce only half amount of sperm as compared to a normal male. When these males are mated to normal females, most of the progeny are females. It demonstrates that the sperm cells produced by these males contain the 'X' chromosome only and their sperms having 'Y' chromosome are non-functional.

Sex linked inheritance

Genes that are carried by either sex chromosome are said to be sex linked. Men normally have an X and a Y combination of sex chromosomes, while women have two X's. Since only men inherit Y chromosomes, they are the only ones to inherit Y-linked traits.

Characteristics of Sex Linked Inheritance:

(a) It is a criss-cross inheritance as the father passes its sex-linked character to his daughter who in turn passes it to the grandson.

(b) Daughter does not express the recessive trait but act as carrier in the heterozygous condition.

(c) Female homozygous for recessive trait expresses the trait.

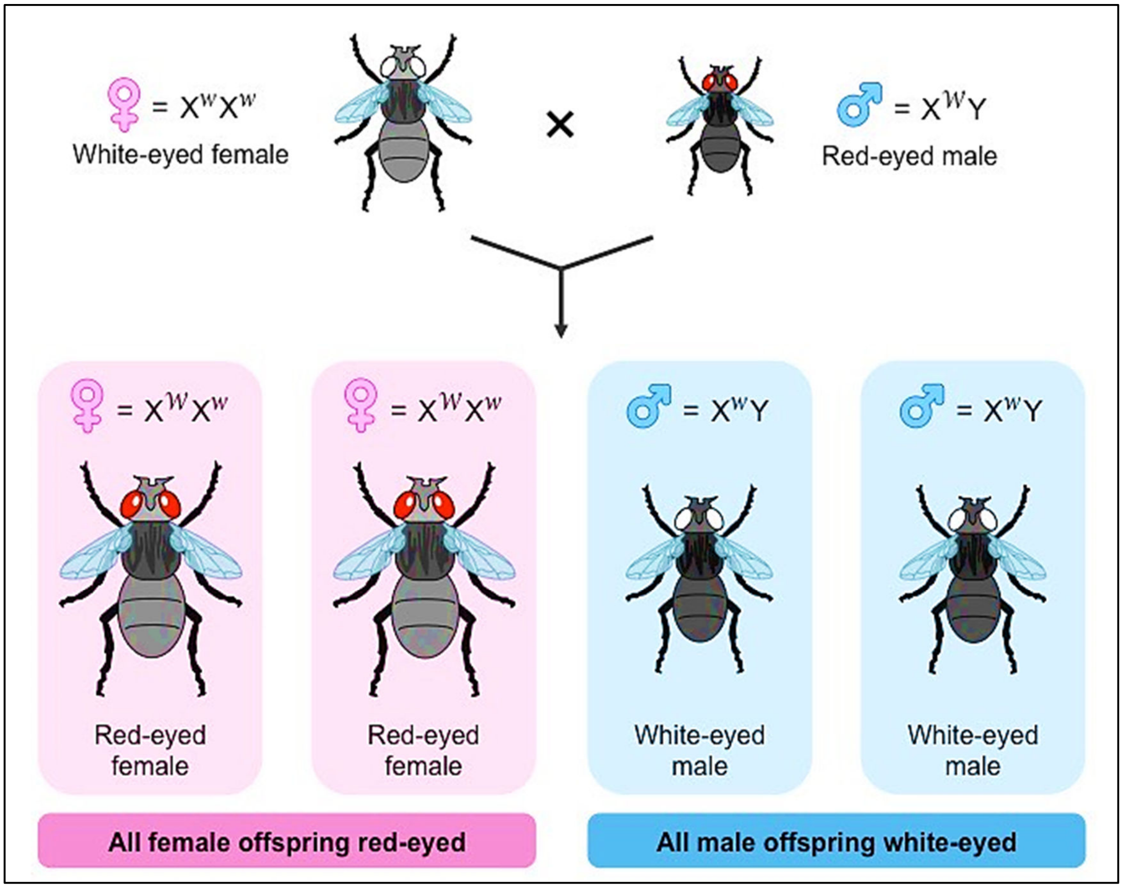
(d) Any recessive gene borne by the X chromosome of male is immediately expressed as Y chromosome has no allele to counteract.

Drosophila (White eye locus)

T.H. Morgan (1910) for the first time discovered sex-linkage in Drosophila melanogaster. Morgan when experimenting noted the sudden appearance of one white-eyed male (mutant form) in the culture of normal red-eyed Drosophila. This white-eyed male was crossed with red eyed female. The F1 flies (both male and female) were all red-eyed indicating that white eye color is recessive to the normal red eye color.

When these F1 flies were inter-crossed freely, the red-and white-eyed flies appeared in the ratio 3: 1 in the F2 generation. White- eyed flies were male. Among the red eyed flies two-third were female and one-third were male. The females were all red eyed whereas 50% males were white eyed and the remaining 50% males were red eyed.

If a reciprocal cross is performed between white eyed female and red eyed male individual, all female individuals in F_2 generation are red eyed and all male individuals, are white eyed. When these two types of individuals from F1 generation are inter crossed, female population in F_2 generation will consist of 50% red eyed and 50% white eyed individuals.



The inheritance of white-eye color in Drosophila can be explained on the basis of the following assumptions:

(i) Gene for white eye colour in male Drosophila is located in X-chromosome and Y chromosome is carrying no normal allele for eye color.

(ii) In white eyed female Drosophila there are two X chromosomes, each one bearing a gene for white eye color (w). It transmits one gene for white eye color (w) to each offspring.

(iii) As we can see in the above reciprocal crosses, the gene for recessive white eye color (w) passes by father on to daughter (F_1 generation). The daughter in turn passes this gene to her sons (F_2 generation). The character thus seems to alter or cross from one sex to the other in its passage from generation to generation. In other words, character is transferred from mother to son and never from father to the son.

Autosomal recessive inheritance

Autosomal recessive inheritance refers to genetic conditions that occur only when mutations are present in both copies of a given gene.

i. Recessive traits and disorders are manifest or express only when the mutant allele is present in a double dose (i.e., homozygosity).
ii. Individuals heterozygous for such mutant alleles show no features of the disorder and are perfectly healthy; they are described as carriers.
iii. Autosomal recessive phenotypes are often associated with deficient activity of enzymes and are thus termed inborn errors of metabolism. Such disorders include phenylketonuria, Tay-Sachs disease, and the various glycogen storage diseases.
iv. Autosomal recessive phenotypes tend to be more severe, less variable, and less age dependent than dominant conditions.
v. When an autosomal recessive condition is quite rare, the chance that the parents of affected offspring are consanguineous for the phenotype is increased. As a result, the prevalence of rare recessive conditions is high among inbred groups.

Thalassemia

Thalassemia is actually a group of inherited diseases of the blood that affect a person's ability to produce hemoglobin, resulting in anemia. Hemoglobin is a protein in red blood cells that carries oxygen and nutrients to cells in the body. About 100,000 babies worldwide are born with severe forms of thalassemia each year. Thalassemia occurs most frequently in people of Italian, Greek, Middle Eastern, Southern Asian and African Ancestry.

The two main types of thalassemia are called "alpha" and "beta," depending on which part of an oxygen-carrying protein in the red blood cells is lacking. Both types of thalassemia are inherited in the same manner. The disease is passed to children by parents who carry the mutated thalassemia gene. A child who inherits one mutated gene is a carrier, which is sometimes called "thalassemia trait." Most carriers lead completely normal, healthy lives.

Thalassemia major and thalassemia intermedia are inherited in an **autosomal recessive pattern,** which means both copies of the HBB gene in each cell have mutations.

The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. A child who inherits two thalassemia trait genes - one from each parent - will have the disease. A child of two carriers has a 25 percent chance of receiving two trait genes and developing the disease, and a 50 percent chance of being a thalassemia trait carrier.