GENETICS

Definition : "Genetics is the study and understanding of the phenomena of heredity and variation."

The term 'genetics' was first coined by Bateson in 1906. In Latin, it means genesis or origination of organisms.

Heredity is the transmission of characters from one generation to the next, i.e., from parents to their offspring.

Variations are the visible differences between the parents and the offspring, or between two offsprings of the same parents.

- An offspring receives all the characters from its parents and yet, an offspring is never an exact copy of its parents. Similarly, no two offsprings of the same parents are identical (exception : identical twins).

Gregor Mendel

- Gregor Johann Mendel was born on July 22, 1822 in Moravia, Austria.
- He had his early education in a monastery in Brunn, Austria (now Brno in Czechoslovakia) and later studied science and mathematics at the University of Vienna. He graduated in 1840.
- Mendel returned to the monastery in Brno as a monk.
- Mendel carried out his legendary experiments on garden pea plants in the monastery garden from 1857 to 1865.
- He published his research paper containing his observations and conclusions in 1866 in the annual proceedings of the **Natural History Society of Brunn.** These conclusions are now known as **Mendel's Laws.** This work is a classic in biology for its elegance and simplicity and ranks amongst the most outstanding biological contributions of all times.
- But unfortunately, this work failed to attract the attention of the biologists of that time.
- One of the possible reasons for such neglect was the inability of the biologists of that time to understand and appreciate the statistical approach adapted by Mendel.
- Thus, Mendel was left bitterly disappointed, and died an unrecognized death in 1884.
- Sixteen years after Mendel's death, in 1900, Hugo de Vries (Holland), Karl Correns (Germany) and Von Tschermark (Austria) independently arrived at similar conclusions as those of Mendel.
- De Vries rediscovered the research paper of Mendel and it was published again in 1901.
- Hence, Mendel is called **The Father of Genetics.**

Terminology Used

1. **Factor :** A particle or unit in the organism which is responsible for the inheritance and expression of a particular character.
2. **Gene :** Mendel's factor is now known as gene. A gene is a particular segment of a DNA molecule which determines the inheritance and expression of a particular character.
3. **Alleles or Allelomorphs :** Two or more alternative forms of a gene are called alleles or allelomorphs. For example in pea, the gene for producing seed shape may occur in two alternative forms: round (R) and wrinkled (r). Round and wrinkled forms of the gene are alleles of each other. Alleles occupy same locus on homologous chromosomes.
4. **Dominant :** Of the two alternating forms (allomorphs) of a trait, the one which appears in the F1 hybrid is called the dominant trait (Dominant Allele).
5. **Recessive :** Of the two alternating allomorphs of a trait, one which is suppressed (does not appear) in the F1 hybrid is called the recessive trait (recessive allele).
6. **Genotype :** The genetic make-up or genetic constitution of an individual (which he/she inherits from the parents) is called the genotype, e.g., the genotype of pure round seeded parent will be RR.

7. **Phenotype :** The external (morphological) appearance of an individual for any trait or traits is called the phenotype, e.g. for seeds, round shape or wrinkled shape is the phenotype.

8. **Homozygous :** An individual possessing (receiving from parents) identical alleles for a trait is said to be homozygous or pure for that trait, e.g. plant with RR alleles is homozygous for the seed shape. A homozygous always breeds true for that trait.

9. **Heterozygous :** An individual receiving dissimilar alleles for a trait is said to be heterozygous or impure for that trait, e.g. a plant with Rr alleles is heterozygous for the seed shape. Heterozygous is also called a hybrid.

10. **Parent generations :** The parents used for the first cross represent the parent (or P1) generation.

11. **F_1 generation :** The progeny produced from a cross between two parents (P1) is called First Filial or F1 generation.

12. **Inbreeding :** When the individuals of a progeny (e.g. F1 generation) are allowed to cross with each other, it is called inbreeding.

13. **F_2 generation :** The progeny resulting from self hybridization or inbreeding of F1 individuals is called Second Filial or F2 generation.

14. **Monohybrid cross :** The cross between two parents differing in a single pair of contrasting characters is called monohybrid cross and the F1offspring as the hybrid(heterozygous for one trait only).

15. **Monohybrid ratio :** The phenotypic ratio of 3 dominants : 1 recessive obtained in the F2 generation from the monohybrid cross is called monohybrid ratio.

16. **Dihybrid cross :** The cross between two parents in which two pairs of contrasting characters are studied simultaneously for the inheritance pattern. The F1 offspring is described as dihybrid or double heterozygous (i.e. with dissimilar alleles for two characters).

Mendel's Approach

1. He started with 34 varieties of garden peas that differed in a number of distinct traits, e.g. wrinkled peas vs. smooth peas or tall plants vs. short plants
2. Did two years worth of tests to determine the purity (true-breeders or not) of the varieties
3. He then performed reciprocal crosses, which test for differences due to sex, for all varieties

The parental generation (P) of a wrinkled-seeded female and a round-seeded male was crossed, and also a round-seeded female and a wrinkled-seeded male was crossed, produced, in both cases, **a first filial generation** (F_1) of all round offspring.Reciprocal crosses gave the same results regardless of the sex of the round parent.

1. Mendel referred to the offspring as hybrids.
2. This cross is called a monohybrid cross because they are hybrids for only one character
3. Because all of the offspring in the F_1 were round, he referred to round as the dominant trait and wrinkled as the recessive trait

Next, two individuals from the F_1 generation were crossed to yield the second filial F_2 generation of 5474 round and 1850 wrinkled.

Round seeds from the F_2

1. Some seeds only produce round progeny. They bred true.
2. Other plants when selfed, produce round and wrinkled in a 3 : 1 ratio

Wrinkled seeds from the F_2

1. bred true and only produced wrinkled seeds

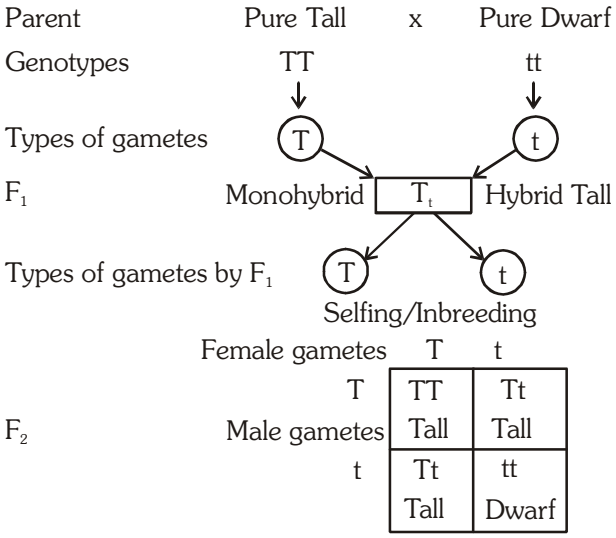


Fig. : MONOHYBRID CROSS

Genotype - genetic constitution, that is the suite of genes that an organism possesses

Phenotype - observable attributes of the organism, that is its appearance

Mendel found that of the round-seeded plants produced in the second generation, 1/3 produced only round seeds, and 2/3 produced round seeded- and wrinkled-seeded plants. Combining these observations with the wrinkled-seeded plants, he concluded that the second filial generation F2 is composed of 1/4 pure breeding round individuals, 1/2 segregating round individuals, and 1/4 pure breeding wrinkled individuals.

Mendel concluded that….

1. Each parent donated one hereditary unit (allele) to each offspring
2. As each parent donates one allele (via the gametes) all the offspring must possess 2 units (alleles)
3. In the F1 generation, all individuals possess one allele for round seeds and one allele for wrinkled seeds with round being dominant to wrinkled
4. At the gene (locus) for seed shape, there are two forms (alleles).

Mendel did seven such monohybrid crosses. All gave similar results and led to the same conclusions.

The explanation of the passage of these alleles is referred to as Mendel's first principle.

The Rule of Segregation - A gamete receives only one allele from the pair of alleles possessed by an organism; fertilization reestablishes the double number

OR

Two members of a gene pair (alleles) segregate from each other during the formation of gametes. As a result, half the gametes carry one allele and the other half carry the other allele.

Like any good scientist, Mendel wanted a different kind of cross to test his rule of segregation. The test cross gave him such a test. By crossing a homozygous recessive individual with a heterozygous individual, the rule of segregation would predict a 1:1 phenotypic ratio among the offspring. When Mendel did such a cross, he did observe a 1:1 ratio. This confirmed his prediction and supported the theory (rule of segregation) upon which the prediction was based.

Today, because the rule of segregation is so strongly supported, we use test crosses to determine the genotype of an individual with the dominant phenotype assuming. Of course, that the rule of segregation is still valid.

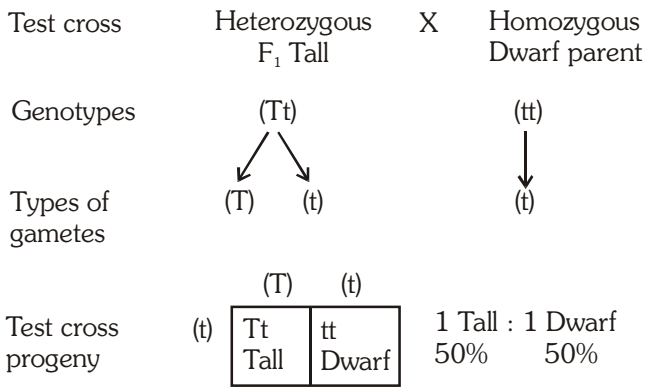


Fig. : Test Cross

Multiple alleles - a gene can have 2 or more alleles segregating in a population. However, a single individual cannot have more than 2 alleles.

Example: The ABO blood group in humans is an example of such a locus. If 3 alleles are segregating at a locus, then there are 3 + 2 + 1 = 6 possible genotypes among the individuals in the population.

Rule of Independent Assortment : Mendel extended his experiments to dihybrid crosses. From these data, he postulated the Rule of Independent Assortment. The parental generation consisted of a round yellow pea (RRYY) and a wrinkled green pea (rryy). The F_1 generation was round and yellow (RrYy). The F_1 generation was selfed to yield the F2generation.

Yellow Round × Green Wrinkled

↓

F1 Yellow Round

Similarly, a cross between yellow wrinkled and green round also produced only yellow round seeds in F1

Yellow Wrinkled × Green Round

↓

F1 Yellow Round

The F2 generation consisted of

9 round, yellow

3 round, green

3 wrinkled, yellow

1 wrinkled, green

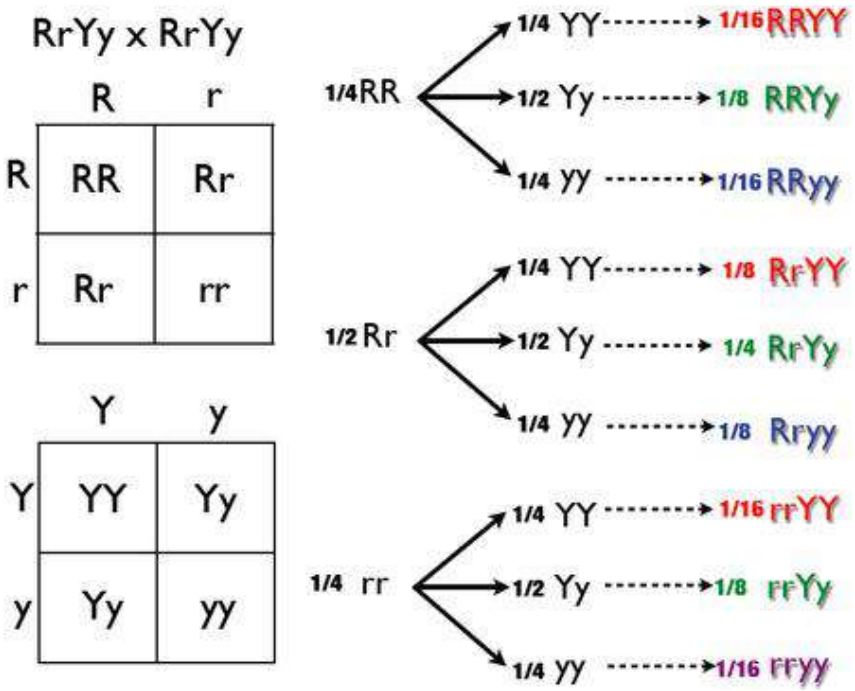
Mendel's second principle states that, during gamete formation, the alleles at one locus segregate into the gametes independently of the pair of alleles found at a different locus.

The genotypes of the two F1s are given below.

RrYy x RrYy

Given independent assortment of the alleles in an F1 plant, we would expect 4 types of gametes to be produced by each of the F1s.

RY, rY, Ry, ry



Each gamete receives one allele for seed color and one allele for seed shape.

	Genotypic ratio		Phenotypic ratio
RRYY	1		
RrYY	2	round, yellow	9
RRYy	2		
RrYy	4		
RRyy	1	round, green	3
Rryy	2		
rrYY	1	wrinkled, yellow	3
rrYy	2		
rryy	1	wrinkled, green	1

Extending these results to more than 2 loci yields the following table.

	monohybrid	**dihybrid**	**trihybrid**	**n-hybrid**
F_1 gametic genotypes	2	4	8	2^n
proportion of homozygous recessives in F_2	1/4	1/16	1/64	$(1/2^n)^2$
number of different F_2 phenotypes given complete dominance	2	4	8	2^n
number of different genotypes	3	9	27	3^n

IMPORTANT : Mendel also demonstrated that the alleles are unchanged in the passage from one generation to the next. At the time of Mendel's discoveries, the general feeling was that traits were blended in the offspring and the modified allele (blended alleles) were then passed to subsequent generations. Mendel showed that the traits are passed as discrete particles (round or wrinkled) and are not changed when passed from generation to the next. This particulate nature of inheritance also supported Darwin's theory of natural selection in that now selection could operate to change the frequency of alleles while not changing the allele itself.

Exceptions to Mendelians laws

Co-dominance:

Alleles can also be codominant in that the alleles are expressed equally and completely in the phenotype as in the heterozygote who expresses both A and B antigens (for example, AB blood group in humans).

1. there are two alleles I^A I^B
2. genotypes — phenotypes

genotypes	phenotypes
$I^A I^A$	A blood
$I^B I^B$	B blood
$I^A I^B$	AB blood

e.g. sickle cell anemia

1. two alleles Hb^a (normal), Hb^s
2. genotypes — phenotypes

genotypes	phenotypes
Hb^aHb^a	normal
Hb^aHb^s	normal
Hb^sHb^s	sickle cell anemia

1. At the molecular level, the traits are codominant as both types of hemoglobin are produced in equal amounts by a heterozygous person.
2. However, at the organismal level, Hb^a is dominant to Hb^s, Hb^aHb^a is normal, Hb^aHb^s is essentially normal, and Hb^sHb^s is sickle cell anemia.

Incomplete dominance : means one allele is incompletely dominant over another allele

In snapdragons,

P RR (red) x rr (white)

F1 Rr x Rr (pink)

F2	RR	Rr	rr
	red	pink	white
	1	2	1

- At the organismal level, the red allele is incompletely dominant over the white allele
- However, at the molecular level the alleles are codominant in that pink is caused by 1 allele (red) coding for a functional protein that produces red pigment and by 1 allele (white) coding for a non-functional protein that does not produce any red pigment. Thus only half the amount of red pigment is produced and a pink flower is the result.

Thus dominance and recessiveness are due to the relative expression of the alleles at the organismal level, but at the molecular level most allelic pairs are likely to be codominant.

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In 1903, Sutton and Boveri noted that the transmission of chromosomes from one generation to the next paralleled the transmission of genes from generation to generation

They proposed the **Chromosome Theory of Heredity** which states that the chromosomes are the carriers of the genes. As there are many more loci/genes in an organism, it follows that a single chromosome has many loci.

Sex Determination

In dioecious species (separate sexes) there are several means to determine sex. The chromosomes involved in sex determination are called sex chromosomes. All other chromosomes are called autosomal chromosomes or autosomes. Although sex chromosomes provide the most common means of sex determination, it is not the only mechanism.

- In bees, males are haploid (n) while females are diploid (2n)
- Sex may be determined by a single allele or multiple alleles as in some wasps
- By environmental factors as in some turtles, these have indeterminate genetic sex-determining mechanisms. The temperature at which the eggs are incubated determines the sex of the turtles. In some species, warm nests yield mostly males and cool nests yield mostly females. In other species of turtles this is reversed.
- The autosomes occur in homologous pairs with each chromosome possessing one copy (allele) of each gene. Segregation and reassortment lead to the pattern of inheritance that we have seen so far, which is called Mendelian inheritance. The sex chromosomes may be genetically distinct thus homologous pairs may not exist and this leads to inheritance patterns that are different from autosomal inheritance.

There are three basic types of chromosomal mechanisms

1. **XX-XY :** in which females are homomorphic XX and males are heteromorphic XY.This is found in mammals including humans and some insects including Drosophila.

   In humans, females have 23 homomorphic pairs and males have 22 homomorphic pairs plus a heteromorphic pair. During meiosis, females produce only one kind of gamete all having one X chromosome. Males produce two kinds of gametes, one with an X and the other with a Y chromosome. Females are homogametic and males are heterogametic.

2. **ZZ-ZW** system in which females are heteromorphic ZW and males are homomorphic ZZ. This occurs in birds, some fishes, and moths. It is essentially the opposite of XY in mammals.

3. **XX-XO** system in which females have 2 X chromosomes. Males have only 1 X and no additional sex chromosomes.This occurs in many species of insects. This was the first sex determining mechanism discovered, and the sex determining chromosome was named the X in 1905. Gametes of males have either an X chromosome or no sex chromosome.

   Sex determination in the XY system is the most studied because it is found in humans and Drosophila. Whether the X chromosome or the Y chromosome determine the sex, it varies from species to species. In Drosophila, the greater the number of X chromosomes relative to the autosomes, the more likely the individual will be female.

phenotype	chromosomal complement	Ratio between X chromosome and autosomal sets
normal female	XX + 2N autosomes	1.00
normal male	XY + 2N autosomes	0.50
metafemale	XXX + 2N autosomes	1.50
metamale	X + 3N autosomes	0.33
intersex	XX + 3N autosomes	0.67

Sex balance theory or genic balance theory states that the X chromosome determines the sex of the individual and that sex is a dosage phenomena, where the ratio of the amount of the X relative to the autosomes determines the sex.

The sex balance theory was assumed to apply to other XY systems, including humans. However, cytologic evidence (chromosomal studies) of mice and humans showed that

1. XO were female (Turner)
2. XXY were male (klinefelter)

Which is opposite of what the sex balance theory would predict. All males have at least one Y and all females have no Y's, regardless of the number of X's. The reason is that on the Y chromosome, there is a gene that causes an undifferentiated gonad to become a testis. This gene is called the sex determining region Y (sry) . Its mode of action is basically to control a number of other genes that effect the development of the sexual characteristics.

X-linked Inheritance

In animals with XY sex determining mechanism, the X chromosome has many loci, many that have nothing to do with sex as such. The Y is usually smaller and possesses fewer loci that are not the same loci as that on the X chromosome. Thus females that have the same allele at a locus on the X chromosome are homozygous. Different alleles would be heterozygous. Males, because they have only one X, are hemizygous and can have only one allele at a locus. Because of this, one copy of a recessive allele will be expressed in the phenotype in males.

In sex-linked inheritance, crosses are not reciprocal. The X-linked pattern is called the criss-cross pattern of inheritance because fathers pass the trait to daughters who pass it on to sons.

Sex-limited traits are traits that are autosomally inherited, and they are expressed in one sex, but not in the other. Some examples include sexually dimorphic plumage in birds, milk yield in mammals, antlers in deer, beards in humans.

Sex-influenced traits appear in both sexes but more so in one sex than another. Male pattern baldness in humans is an example. The male hormone testosterone is needed for full expression of baldness. Because of this hormone difference, the allele for baldness behaves as a dominant trait in males (expressed when heterozygous), but behaves as a recessive allele in females (must be homozygous to be expressed)