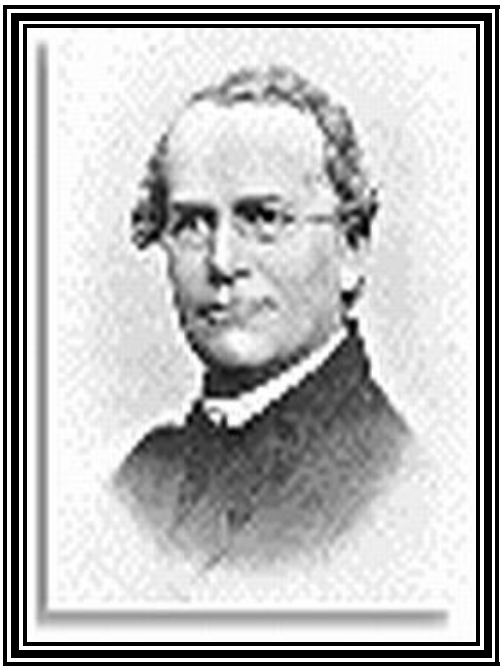
GENETICS

MENDELIAN GENETICS

Mendel's life and work: Gregor John Mendel was born in 1822, to a poor farmer in Heinzen Dorf, in Czechoslovakia. The young Mendel was put to education; though he was-an ardent and sincere student he could not continue his education, because of poverty, so he gave up education and became a priest. As a monk, he had lot of work to do; occasionally he was called to do the job of a stop-gap teachers. His interest *in* science and teaching had led him to Vienna, where he studied Physics, Mathematics and Biology in the local university, His academic career, though not brilliant, his training in PMB was of a great value.



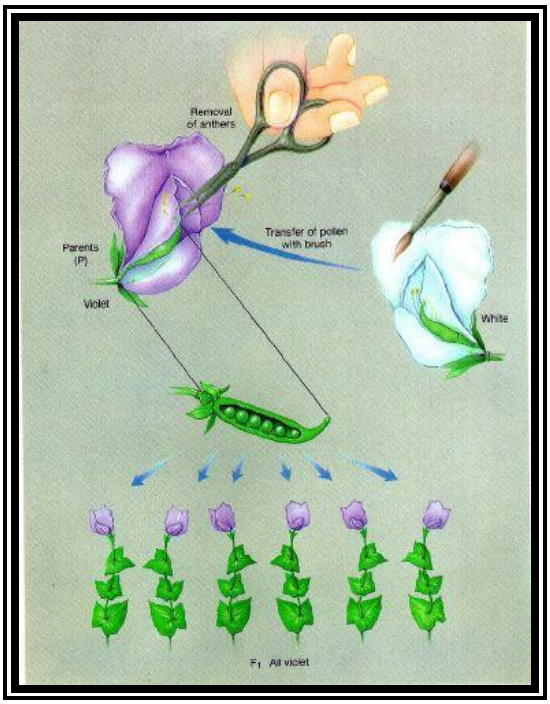
Gregor John Mendel

10.1 Mendel's Results from Monohybrid Crosses

PARENTAL GENERATION PHENOTYPES DOMINANT	RECESSIVE	F_2 GENERATION PHENOTYPES DOMINANT	RECESSIVE	TOTAL	RATIO
Spherical seeds ×	Wrinkled seeds	5,474	1,850	7,324	2.96:1
Yellow seeds ×	Green seeds	6,022	2,001	8,023	3.01:1
Purple flowers ×	White flowers	705	224	929	3.15:1
Inflated pods ×	Constricted pods	882	299	1,181	2.95:1
Green pods ×	Yellow pods	428	152	580	2.82:1
Axial flowers ×	Terminal flowers	651	207	858	3.14:1
Tall stems (1 m) ×	Dwarf stems (0.3 m)	787	277	1,064	2.84:1

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Table 10.1

He used pea plants for pollen transfer and created hybrids.



Hybrid plants in specific ratio.

Upon his return to monastery in Brunn, he took up the teaching profession seriously. But the young Mendel, unsatiated with just teaching, was planning for experimental research. He had neither sophisticated tools nor the laboratory. The backyard of the monastery and garden pea plants has become his laboratory and tools. Paradoxically, he selected garden Pea (Pisum sativum) plants as his experimental materials and collected 36 different varieties, which were different in their phenotypic characters, of which he finally chose seven phenotypic characters, which were distinct and showed clear cut variation. *Ex: for* Height Tall & dwarf, color of the flower violet & white. Position axillary or terminal, color of the pod-yellow and green, shape of the pod-inflated & constricted, shapes of the seed-round and wrinkled, color of the seed-yellow and green. To begin with he grew them separately and allowed them to get self pollinated in successive generation. Finally he selected pure lines of these varieties (Pure line means a plant which on self breeding produces the same kind). Then he grew these varieties of pea plants in separate plots, to prevent cross pollination. When plants grew and started flowering, he cross pollinated the flowers of desired characters for example, he cross-pollinated round seeded varieties with wrinkled varieties; any of the parent plants can be taken as the acceptor. Using tweezers young flowers were opened and the stamens were removed. This process is called emasculation. Then pollen grains were collected from the donor variety and dusted

on to the stigmatic surface of the emasculated flowers, and covered the artificially pollinated flowers with paper bags in order to prevent any foreign pollen contamination. Thus, he crossed Tall with Dwarf, Violet with white, Terminal with Axillary, Round with Wrinkled and so on. These experiments have to be done with care and skill. It is a hard job, but he did it meticulously and spent his time in the field from dawn to dusk. More than any thing else he wrote everything what he did or observed in his diary.

After completing cross pollination work in shortest possible time, he tendered the plants with care and love. The fruits were set, and started to fill. The excitement had grown in him. Probably he would have dreamt of all sorts of variations and combinations of his results of labor. However, when the time came for harvesting, he plucked the ripened fruits, put them in separate bags and tagged them with names and analyzed the results.

Finally he published his findings in a Biological Journal in which he explained - 1) the unit characters, as the factors of inheritance, 2) existence of them in alternate forms called alleles, 3) their transmission through gametes as pure forms, 4) their segregation in equal ratios, 5) their dominance' over recessive traits 6) independent but random assortment of factors, 7) their inheritance in a regular pattern in successive generation in set laws But later lie drifted towards other

experimental materials like Hieralcium (a compositae member) and others. Unfortunately, the materials were unsuitable and the results were quite contrary to the previous findings. He could not get any where. He started to doubt about his own findings and he was a distraught man. He was overburdened; he over worked; in this kind of stress and strains he passed away as any other mortal, a "Great Mortal".

His work, though read and published (Ann. Proceedings of the Natural History society of Brunn, 1866), remained unnoticed or unrecognised for more than 36 years. However, in 1900, three Biologists, Hugo Devries, Tschermak and Correns, while publishing their independent works on inheritance found Mendel's paper and to their surprise, they realized that Mendel had already discovered of what they wanted or considered to be an important discovery. Thus, Mendel's work was rediscovered, since then Mendel's name was etched: 1 H1 the history of experimental biological science in Golden letters as the "Father of Genetics". Mendel was lucky in selecting "the lucky seven characters or phenotypes" in pea plants for one thing and for the other he was a priest, a churchman.

Mendel's Laws of inheritance

Experiments with garden pea plants have made Mendel to lay down some principles of inheritance, which are now called as Mendel's Laws of inheritance; the laws are. -

1. Law of unit characters

Every organism has certain distinct morphological as well as physiological characters. These characters are controlled by specific units of heredity. These were termed as factors. Now they are called as Genes. Genes exist in two alternate forms called alleles. Now it is known that the genes are located in chromosomes. For example, the color of the flower: Some plants produce red flowers and some white flowers. So, the genes responsible for producing red color and white color must be different. As both the genes control the same character namely the color of the flower, they are called alleles or allelomorphs.

2. Law of Purity of gametes

The unit characters or hereditary units are transmitted to their off springs through gametes. During reproduction parents produce gametes which contain all the genes for all the characters of an organism. However, these genes are present in single doses. For example-pea plant may have hundreds of morphological and physiological characters. Among them, if we choose one character, then it is controlled by a particular pair of allelic genes. During reproduction only one gene enters into one gamete, thus gametes contain only one gene for this character. Thus, the gamete is considered as pure and uncontaminated with respect to the said character. The same principle holds good for other characters also.

3. Law of dominance and Law of recessiveness

During reproduction, when a gamete carrying a particular gene fuse with another gamete carrying another gene belonging to the same pair of alleles, only one character is expressed in the off spring. For example, in pea plant when the gamete belonging to tall plant fuses with the gamete carrying 'dwarf' gene, the offspring 'sill have both the genes i.e., Tall as well as Dwarf, but only one is expressed; in this case it is the Tall, character. Though the plant has 'dwarf' gene, only the tall character is expressed because of the dominance of tall character. Such genes are called dominant genes and the other unexpressed genes are called recessive genes; they remain unexpressed with Tall gene, the Tall dominates the other.

In these cases, the morphological character that is expressed, that is visible, is called the Phenotype and the gene that is responsible for the expression of the phenotype is called the Genotype. For example, Tall, character is called the Phenotype and the gene that is represented by a symbol, i.e., T, represents the Genotype. In Genetics, it is a convention to use the capital letter as the symbol of dominant gene; and small letter for the recessive gene. So, T is dominant and this recessive and Tt form a pair of alleles. Furthermore, depending on the type of genes present, they are termed as dominant heterozygous (Tt), dominant homozygous (TT). But the recessive phenotype is

expressed only when both the genes are homozygous recessive (i.e., tt)

4. Law of Segregation

A pair of allelic genes that are present in an organism for a given character, separate or segregate in equal ratios during gamete formation. This segregation is just a chance and there is no choice. For example, when the tall plant which is heterozygous produces gametes, only one (T) of the gene pair goes into one gamete and ('t') to the other. In this process whether T gene goes to this gamete or that gamete is purely a chance process. However, if thousand gametes are produced, 500 of them receive dominant. "T" genes and the rest (500) receive "t" genes. Thus, the segregation is random, but in equal ratios.

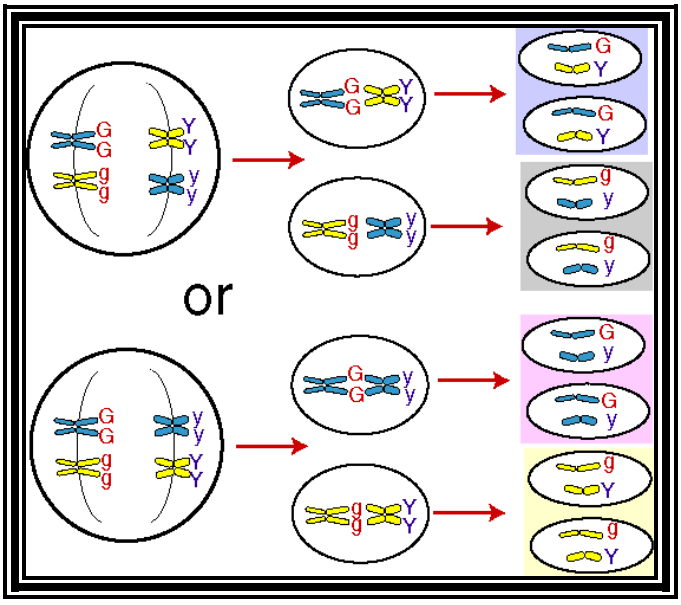


Diagram showing genes of dominant and recessive Characters.

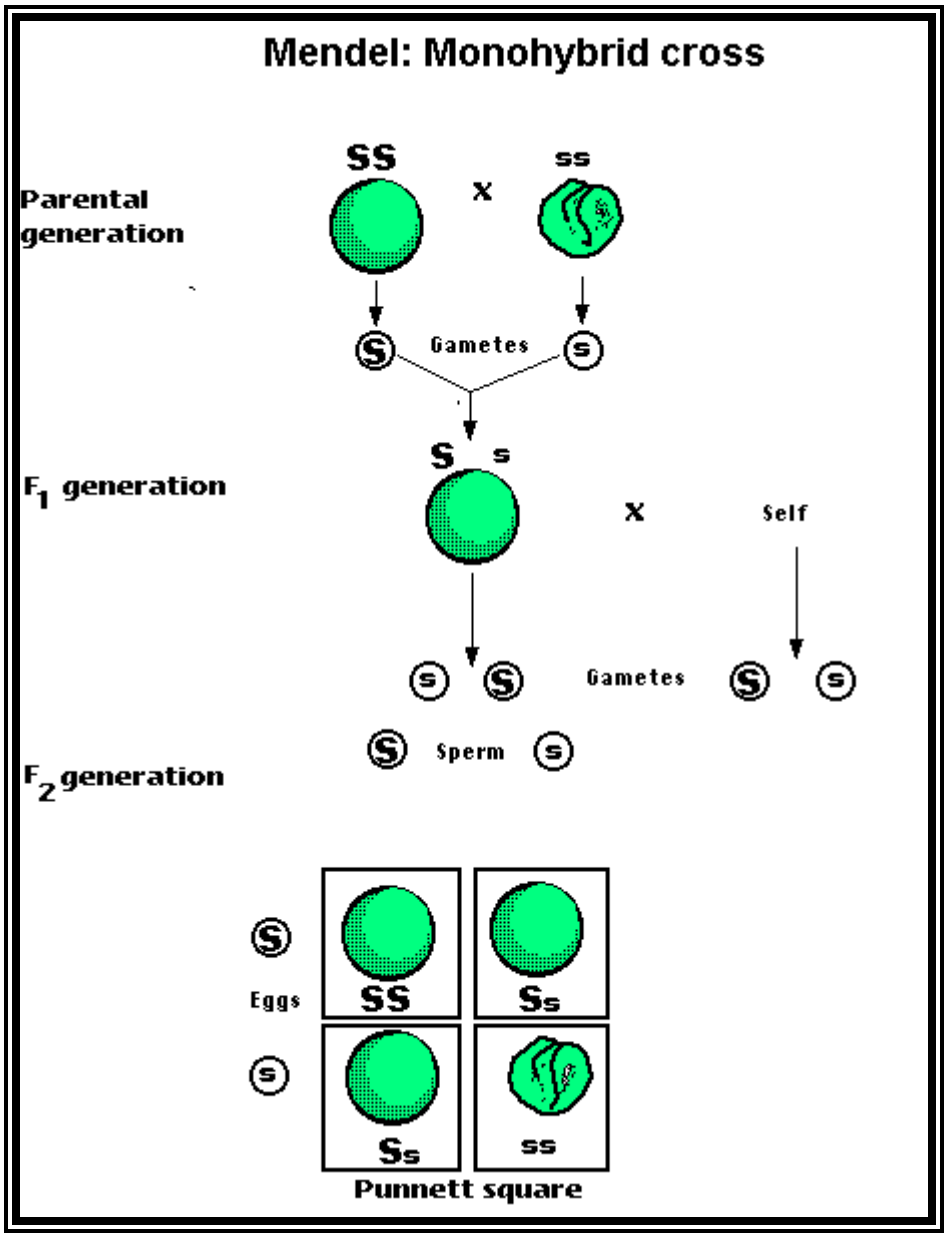
5. Law of Independent Assortment:

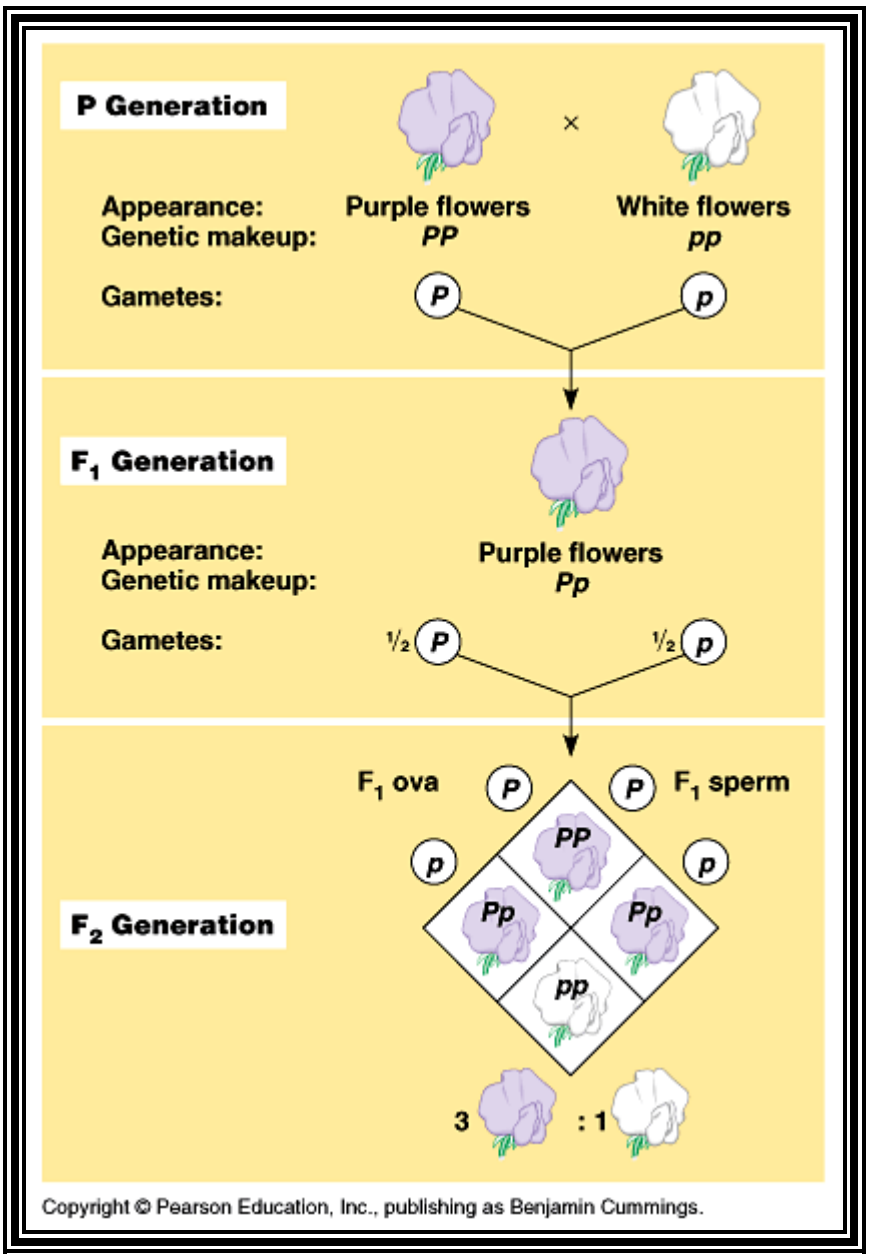
If two or more characters are taken together for observing the pattern of inheritance, different pairs of alleles behave independently and during seggregation, they separate randomly as well as independently. They are not linked 10 each other. This is because different pairs of alleles are located on different pairs of homologous chromosomes. While these genes express they do not influence each other and each of them remains independent and unique.

Monohybrid Cross:

1. One particular character which is controlled by a pair of alleles has been followed to find out the pattern of inheritance.
2. These pairs of alleles are located on a pair of homologous chromosomes. During gametogenesis these homologous pairs separate or segregate in equal ratios and each gamete receives one of the homologue pair, so also the genes. Gametes, with respect to a particular gene are pure, uncontaminated, and uninfluenced. In the FI generation only one character is expressed because of a particular gene, the gene that expresses the character is call dominant gene and the other which remains unexpressed is called recessive gene. Mating of the gametes is purely chance and random and not choice. In the F2 generation the dominant recessive phenotypic characters are expressed in 3:1 ratio, but genotypically the segregation is 1: 2: 1. The

statistical analysis of this type of inheritance is expressed as Monohybrid ratio.





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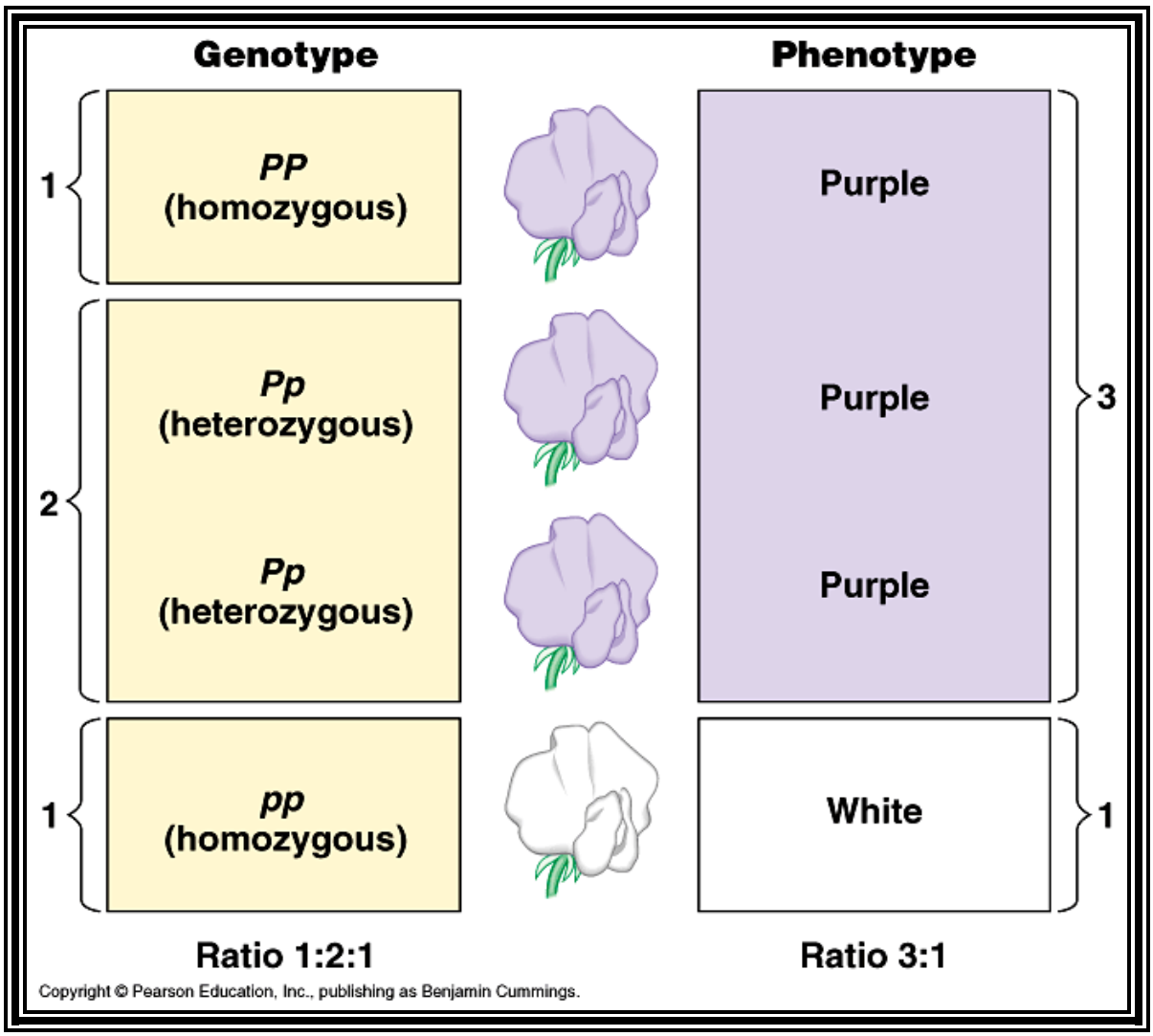


Dwarf - Parent (P)

TT tt -

Genotype

↓ ↓ ↓ ↓ -

Gametes

T T t t

|_____|

↓

Tt F_1

Tall

Selfing

	T	**t**
T	**TT** **Tall**	**Tt** **Tall**
t	**Tt** **Tall**	**tt** **Dwarf**

Tall: Dwarf F_2

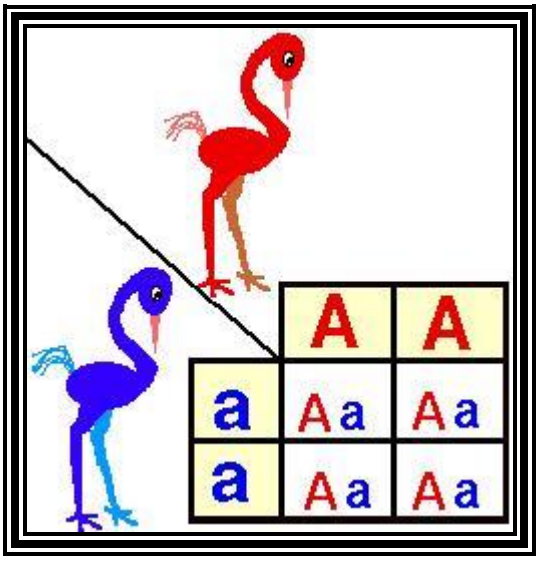
3: 1 **Phenotypic ratio**

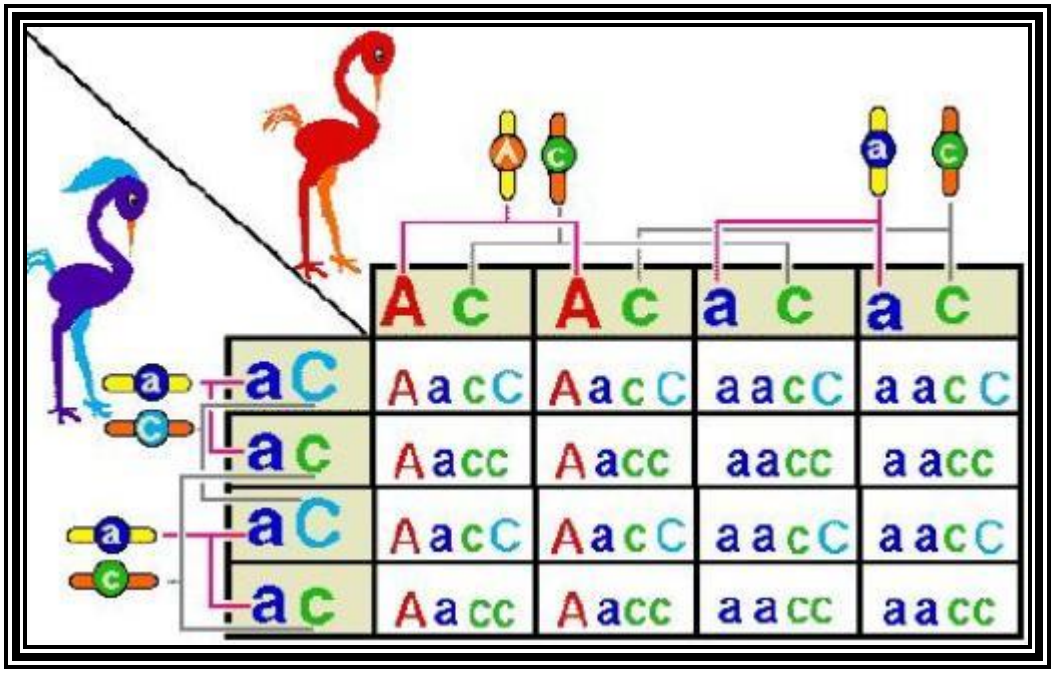
TT: Tt: tt

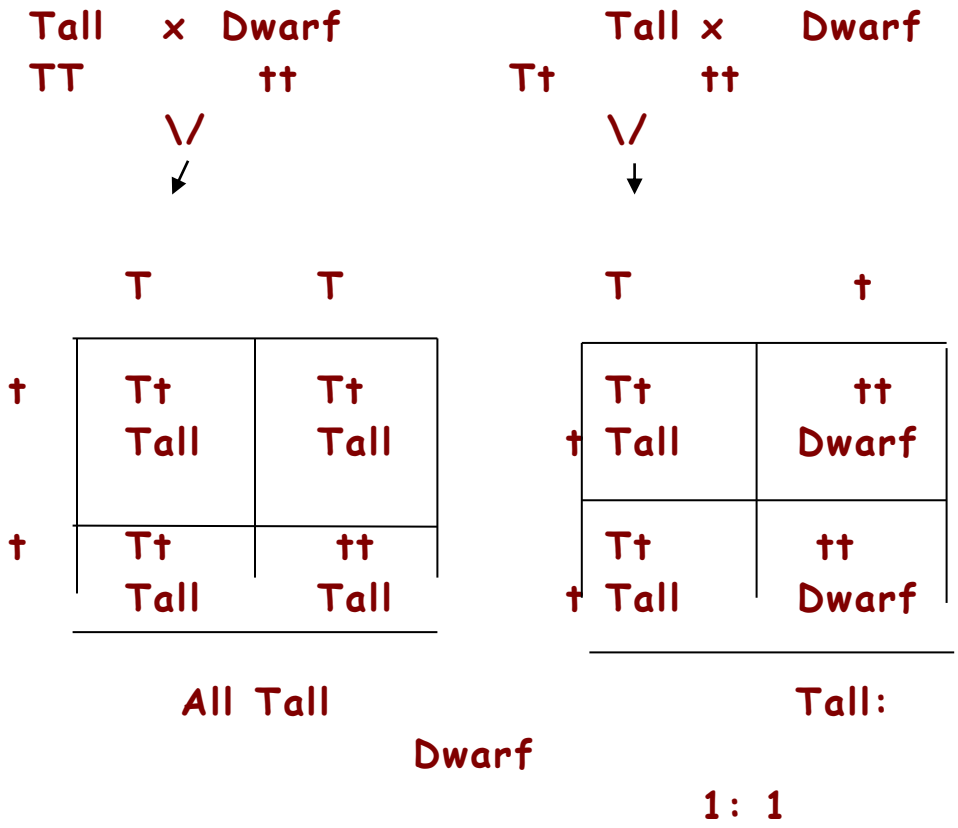
1: 2: 1 **Genotypic ratio**

Test Crossing or Back Crossing: In the case of Dominant Phenotype, by just looking at the morphology, it is difficult to find out" whether the given plant is heterozygous or homozygous for dominance. With regard to recessive, the character is expressed only when both the genes are recessive, thus the Phenotype also indicates the Genotype. In order to find the unknown Genotype of the dominant character, a cross breeding is performed which is called Test crossing or Back crossing. Here the unknown dominant character is crossed with the known recessive character, for example Tall plant (its Genotype is not known) is crossed to dwarf (its Genotype is known). In the cross, if the off springs produced are of both dominant and

recessive in equal ratio, the given plant is heterozygous for the said character. On the other hand, if the offspring's produced are all Tall, then the Tall plant is dominant homozygous. This type of crossing is employed to determine the heterozygosity or homozygosity of a suspected character.





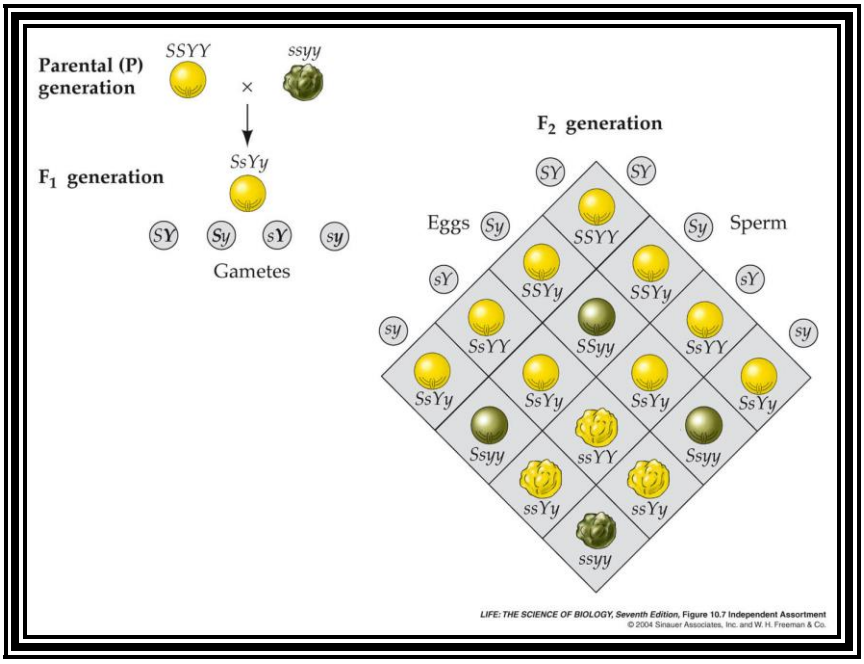


Dihybrid Cross

1. In this case the inheritance of two different characters is studied simultaneously. Two characters are controlled by two different pairs of alleles which are located on two different pairs of homologous chromosomes. These genes do not interact or influence each other. During reproduction only one gene of each pair of alleles enters with gametes, thus the purity of the gametes is

maintained. During gametogenesis, the two different pairs of alleles separate ill equal ratios, but they assort randomly but in dependently. The expression of genes in the FI plants obeys the law of dominance. They do not influence or interact in expressing their respective characters. In the F2 generation the phenotypic ratio will be 9:3:3:1.

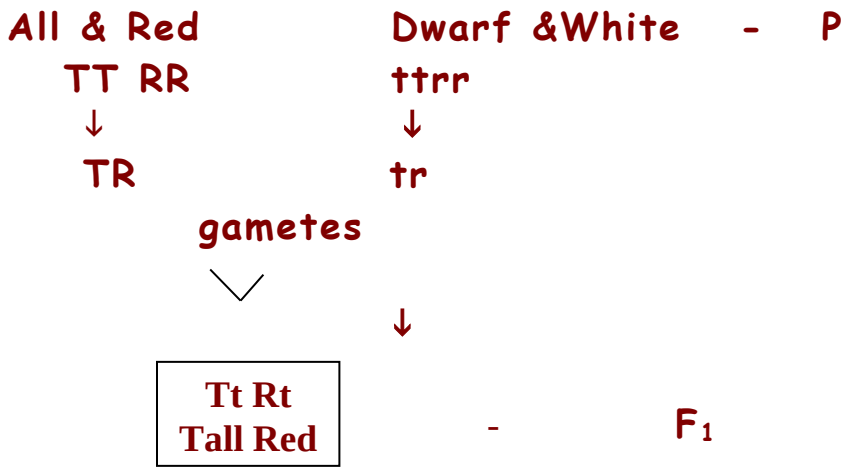
2.



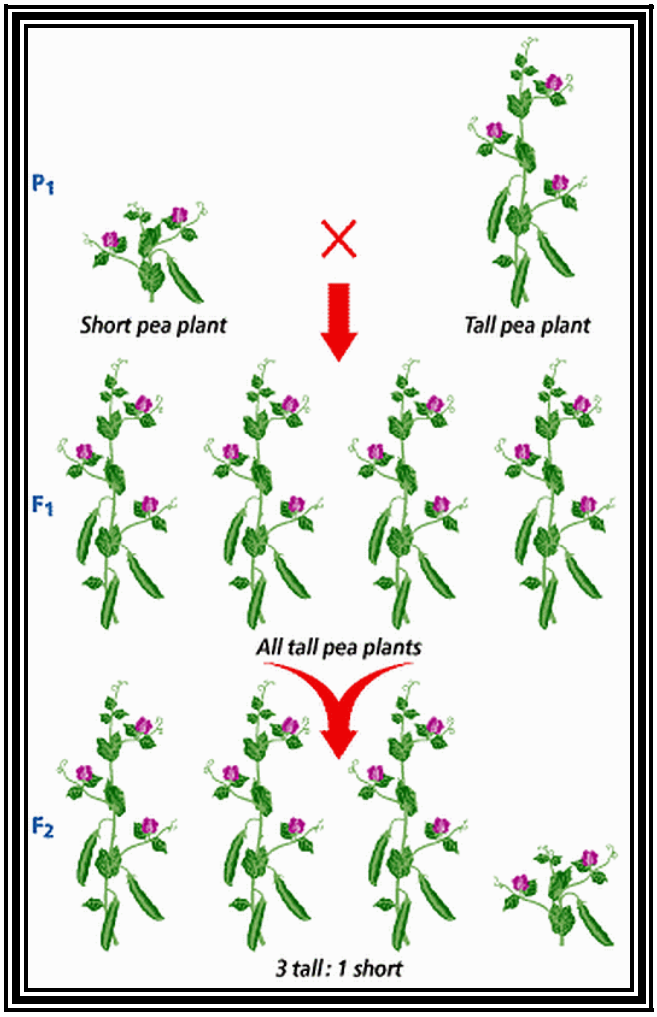
Expression Dihybrid genes

When Mendel studied these characters together, he was very fortunate for all the seven characters chosen were controlled by seven pairs of alleles and luckily, they were located on seven different pairs of homologous chromosomes He did not know about this fact. If any two different pairs of alleles were to

present on the same pair of chromosomes his conclusion would have been different.



As both the FI progeny have the same Genotype the probability of the gene combination is equal, because chromosomal segregation is random. Here 4 different combinations are possible. Thus 4 different types of gametes are produced in each of these individuals. Again, the fusion between the gametes is 150 a chance, hence each of them has equal chance to meet the other. Thus, the permutation-combination value is 16. This can be expressed in the form of a Checker Board.



Tall Red Tall Red

Tt Rr Tt Rr

↓ ↓ ↓ ↓ ↓ ↓ ↓

↓ ↓ gametes

TR Tr tR tr

TR Tr tR tr

TR Tr tR

tr

	TTRR Tall Red	TTRr Tall Red	TtRR Tall Red	TrRr Tall Red
TR				
	TTRr Tall Red	TTrr Tall White	TtRr Tall Red	Ttrr Tall White
Tt				
	TtRR Tall Red	TtRr Tall Red	TtRR Dwarf Red	tt Rr Dwarf Red
tR				
	TtRr Tall Red	Ttrr Tall White	tt Rr Dwarf Red	tt rr Dwarf White
tr				

TallRed:TallWhite:DwarfRed:Dwarf White

9: 3 :3:1

If the F1 hybrids are crossed to completely recessive plants, which is also called as Test Cross, the segregation is still equal.

Tt Rr x tt rr

↓

tR tr

	TtRr Tall Red	Ttrr Tall	tt Rr Dwarf	tt rr Dwarf
tr				

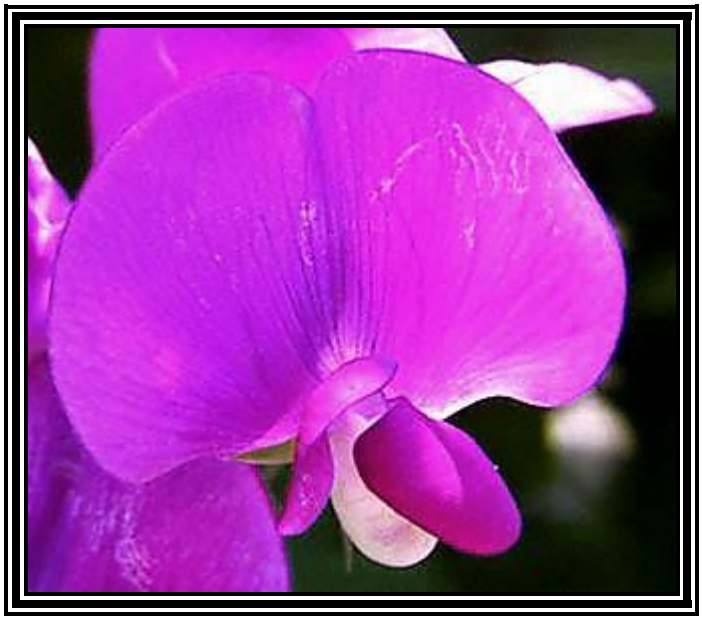
	White	Red	White

These test-crosses can be used for any given number of characters provided they show independent assortment; otherwise they show different results.

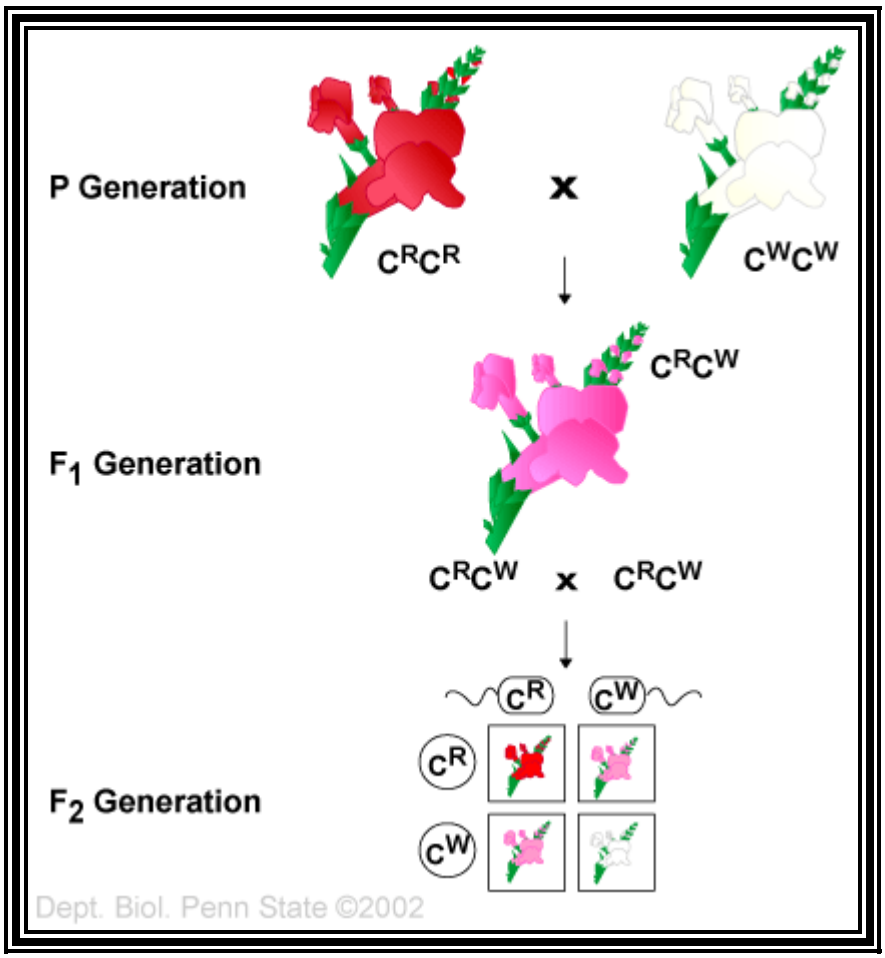
Partial Dominance

Mendel's studies were restricted to few characters, where a particular gene's expression is complete and over-bearing. The expression of single dominant gene in a heterozygous form is so complete, that it is rather difficult to distinguish the dominant homozygous from dominant heterozygous condition. Such gene expressions constitute complete dominance. But in some cases, the expression of the gene is not complete and in heterozygous condition it shows incomplete or intermediate type of expression. In the case of Mirabilis jalapa (4 o'clock plant) when red flowering plant is crossed to white (Recessive), the F1 that is produced has neither red color nor white color in the flower, but expressed as an intermediate character i.e., pink color of the flower. The careful observations of pigmentation reveals that floral petals contain a mosaic of white and red patches, as if equal amount of red and white color is mixed. If such F1 plants are selfed the Phenotypic expression of F2 generation is 1:2:1 (Red: Pink: White) which is same as the genotypic ratio [RR

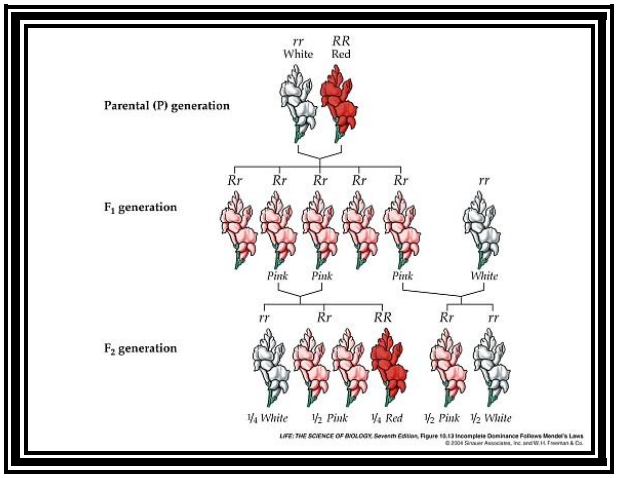
(1): Rr(2):rr(1)]. This type of partial dominant inheritance is more a qualitative type; such a type of intermediate or partial dominant inheritance is also found in the case of eye color in Drosophila melanogaster, feather color in fowls etc.



Phenotypic Color


P Generation
x
C^RC^R
C^WC^W
F_1 Generation
C^RC^W
C^RC^W x C^RC^W
F_2 Generation
C^R
C^W
C^R
C^W
Dept. Biol. Penn State ©2002

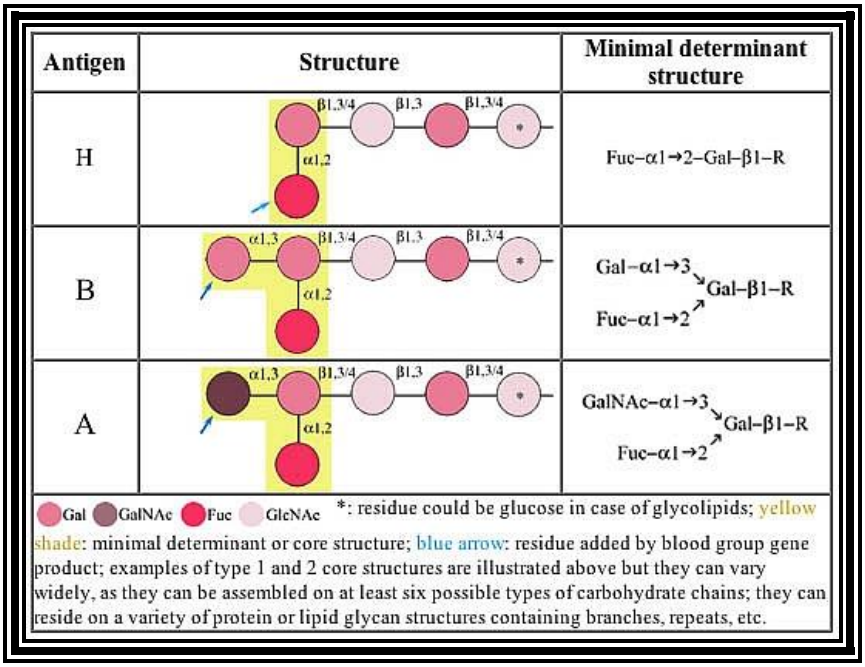
1: 2: 1


rr White
RR Red
Parental (P) generation
Rr Rr Rr Rr Rr
rr
F1 generation
Pink Pink Pink White
rr Rr RR Rr rr
F2 generation
¼ White ½ Pink ¼ Red ½ Pink ½ White

1:2;1

MULTIPLE ALLELES

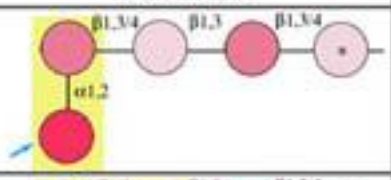
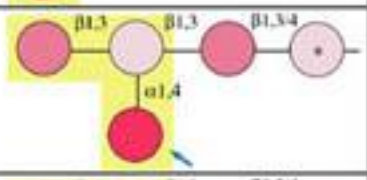
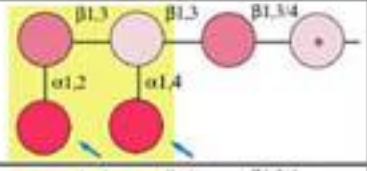
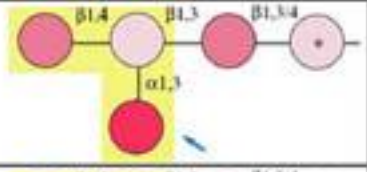
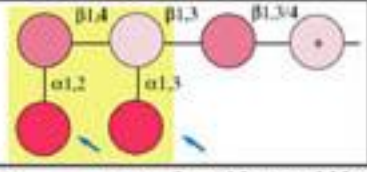
A gene responsible for a particular function, in course of time it may undergo a mutation and bring about a change in its function, hence in its phenotype. In a Population, it is possible that a wild type of gene may undergo mutation, resulting in multiple forms of the same gene. The phenomenon of gene existing in different forms is called multiple allelism or gene polymorphism. Such genes effect or affect the phenotype in various ways. However, these genes may exhibit recessive, dominant or co dominant condition with the wild type gene.



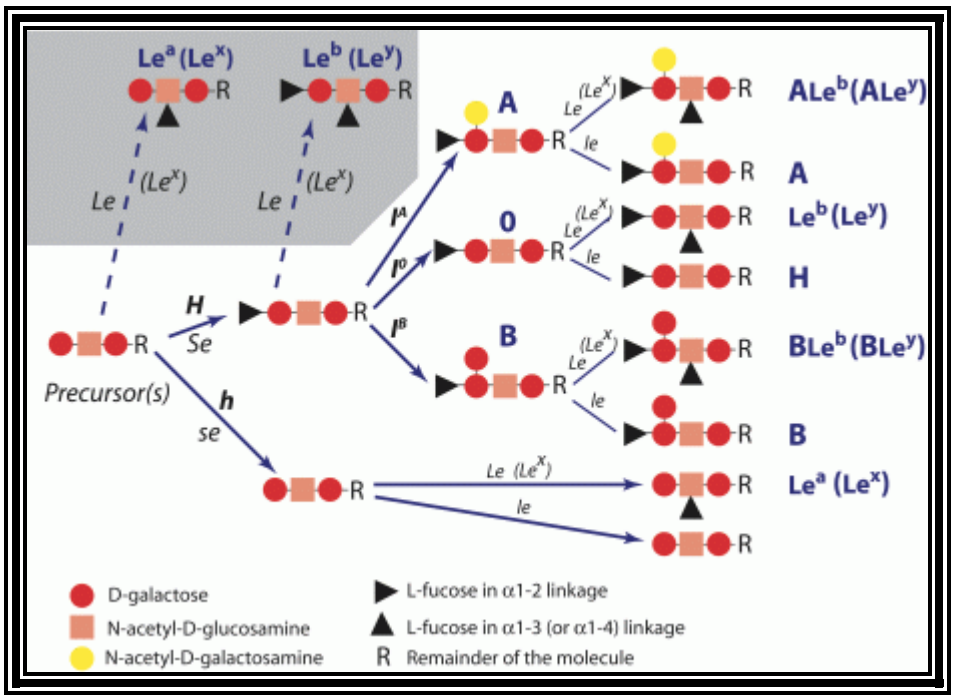
The existence of such multiple forms of genes in a population is not an uncommon feature, and the classical example is blood groups in human beings. Investigations in this regard have shown the presence of different types of blood groups, Rh^+ Rh^- and A.B.O. groups. Particularly A B O blood group is of immense importance. For it is extensively used in blood transfusion in the case of accidents, severe anemia, or surgery etc. Landsteiner was the first to identify such blood groups. The variation in the blood groups is because of the membrane proteins of red blood cells (erythrocytes).

Some of the membrane proteins get glycosylated (addition of sugars) differently thus they produce various types of blood groups. Persons belonging to A blood group contain A type of glycosylated protein in the membrane of erythrocytes. (Similarly, "B" and the "0" type). These physiological phenotypes due to the presence of A. B and 0 genes. The genotype of human beings may fall into any of the following types; AA, BB, 00, AB, AO or BO.

Identification of the blood group types is very essential for blood transfusion, because, if by chance or mistake, blood of A type is given to B type person or vice-versa, the man who gets such blood type dies because of agglutination or aggregation of blood cells. This aggregation is due to antigen-antibody reaction.

Phenotype	Structure	Minimal determinant structure
H		Fuc–α1→2–Gal–β1–R
Le^a		Gal–β1→3 GlcNAc–β1–R Fuc–α1→4
Le^b		Fuc–α1→2–Gal–β1→3 GlcNAc–β1–R Fuc–α1→4
Le^x		Gal–β1→4 GlcNAc–β1–R Fuc–α1→3
Le^y		Fuc–α1→2–Gal–β1→4 GlcNAc–β1–R Fuc–α1→3

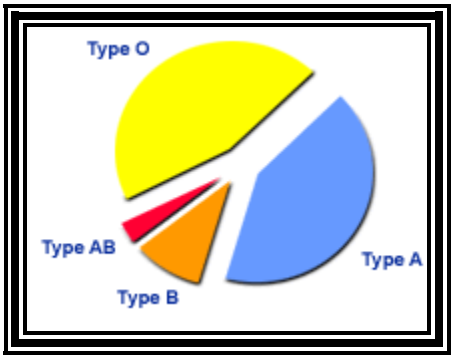
Gal GalNAc Fuc GlcNAc *: residue could be glucose in case of glycolipids; yellow shade: minimal determinant or core structure; blue arrow: residue added by blood group gene product;examples of type 1 and 2 core structures are illustrated above but they can vary widely, as they can be assembled on at least six possible types of carbohydrate chains; also they can reside on a variety of protein or lipid glycan structures containing branches, repeats, etc.



Lewis and ABO blood group antigens;

A substance or substances, like proteins and polysaccharides etc., when injected into a human being, elicit or induce the synthesis of a class of serum proteins which react with the injected proteins and immobilize them. The substance that induces the synthesis of serum proteins is called an antigen (Agglutinogen) and the protein that is produced in response to antigen is called antibody (Agglutinin). It is a unique feature, that human beings are endowed with a capacity to produce specific antibodies against innumerable antigens. Basing on this property of interaction between antigen and antibody, vaccines have been developed to combat various disease causing organisms like smallpox, tuberculosis, plague, cholera, polio and recently Copox; etc, recently vaccine, against cancer also have been

developed. Using antigen - antibody reactions blood types in human being s ca n be identified.



A-AB-A and O,

Identification of Blood Groups:

It is always good to have our blood typed. Under emergency condition, it will be easier for doctors to perform blood transfusion without delay. In hospitals and other clinics, detecting the blood groups particularly, A, B and 0 types Rh + and Rh- and MN & S has been made very easy. The testing for the blood group can be performed any where if some basic facilities are available.

Blood type of cells	Genotype	Antibodies made by body	Reaction to added antibodies	
			Anti-A	Anti-B
A	I^AI^A or I^Ai^O	Anti-B		
B	I^BI^B or I^Bi^O	Anti-A		
AB	I^AI^B	Neither anti-A nor anti-B		
O	i^Oi^O	Both anti-A and anti-B		

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 10.14 ABO Blood Reactions Are Important in Transfusions

Identification of blood types

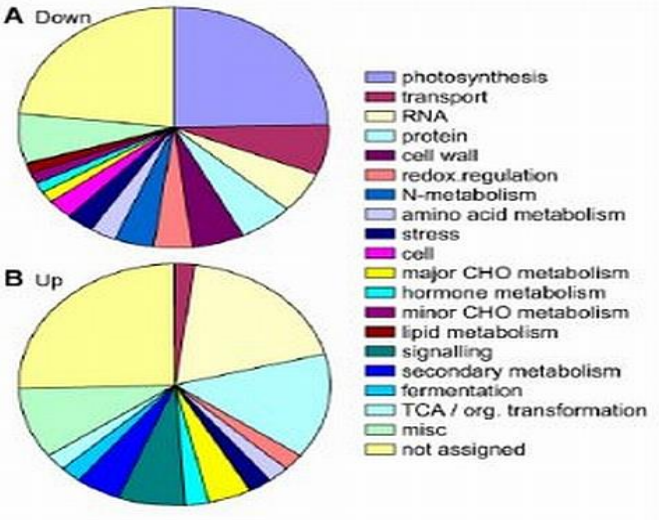
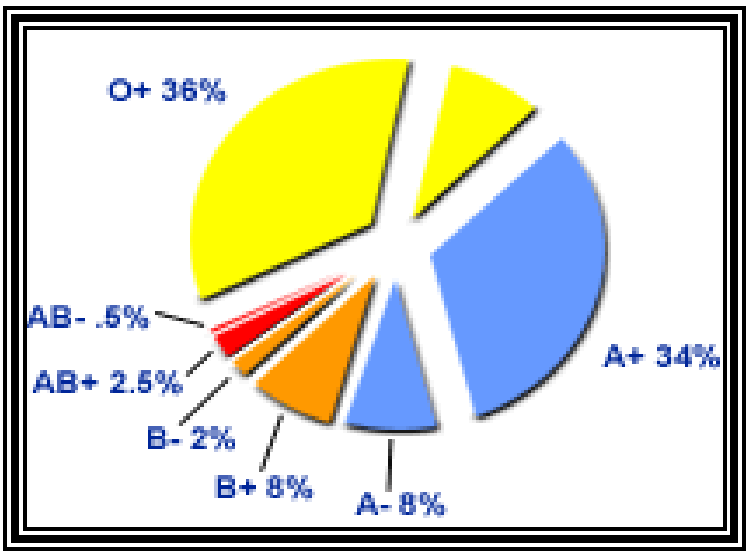


Figure 3. Function of genes affected by Glc independent of the genetic background. Biological functions of genes that are down-regulated (A) or up-regulated (B) in all three RILs (RIL 45, RIL 232, and RIL 310) are shown according to the The Institute for Genomic Research ontologies (see Supplemental Table S1 for list of genes).



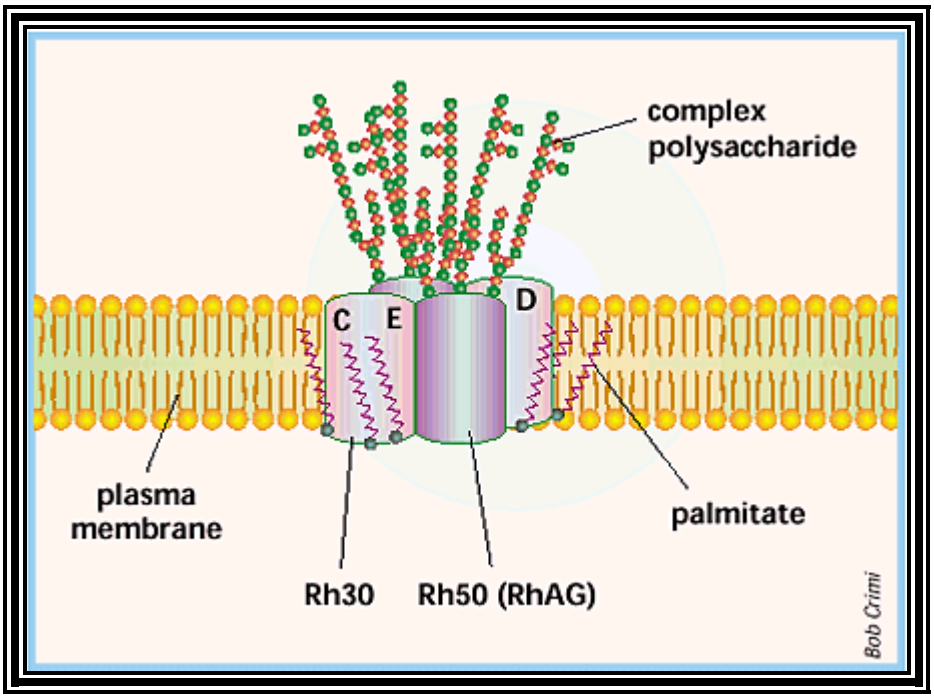
The best and surest way to detect is to have antiserum or antibodies against A, B, O, Rh^+ and Rh^- antigens. Antibodies can be prepared by isolating antigens like A, B and Rh + and the same if injected intradermally to an unimmunized Rabbit or Goat, the recipient reacts to the antigens and produces immunoglobulin proteins called antibodies against the said antigens. After second booster dose of antigen, antibodies can be collected by bleeding the animal. The blood obtained thus contains a variety of proteins; but the Immunoglobulins can be separated from the others by selective salt precipitation and column chromatographic procedures. Such purified antibodies against A, B, Rh^+ antigens can be stored in deep freezers for a long time.

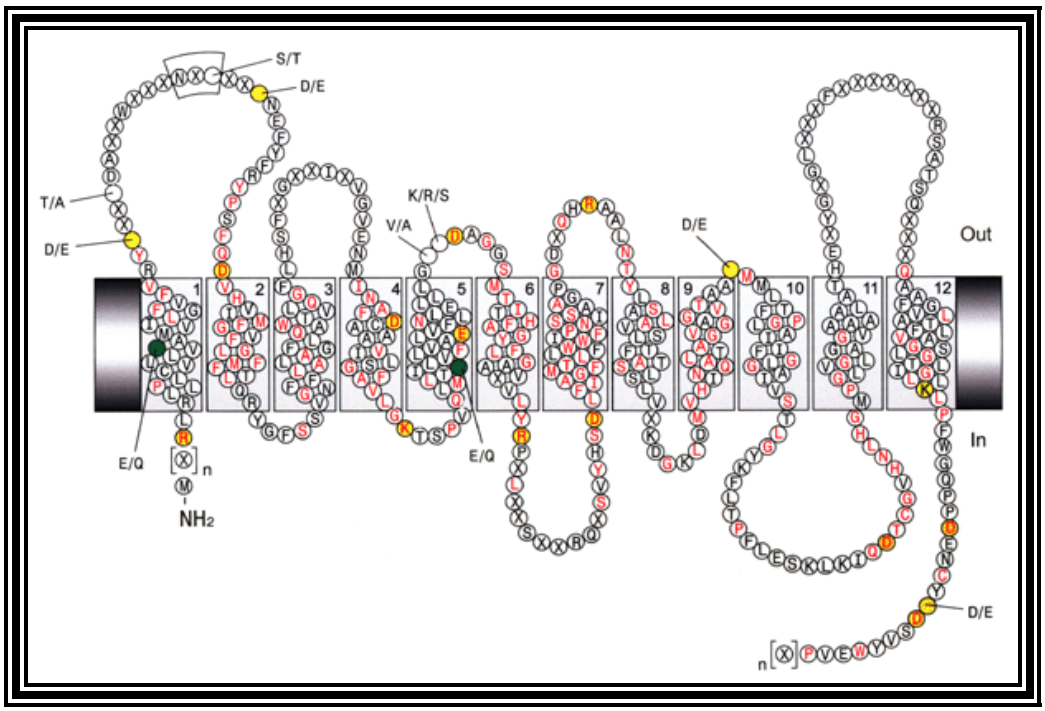
When testing for an unidentified blood type, few drops of blood are taken out of the person and same is applied on to four clean micro slides. Then a drop of dilute antibodies against A, B, O and Rh^+ should be added all to the blood on the micro slides. With

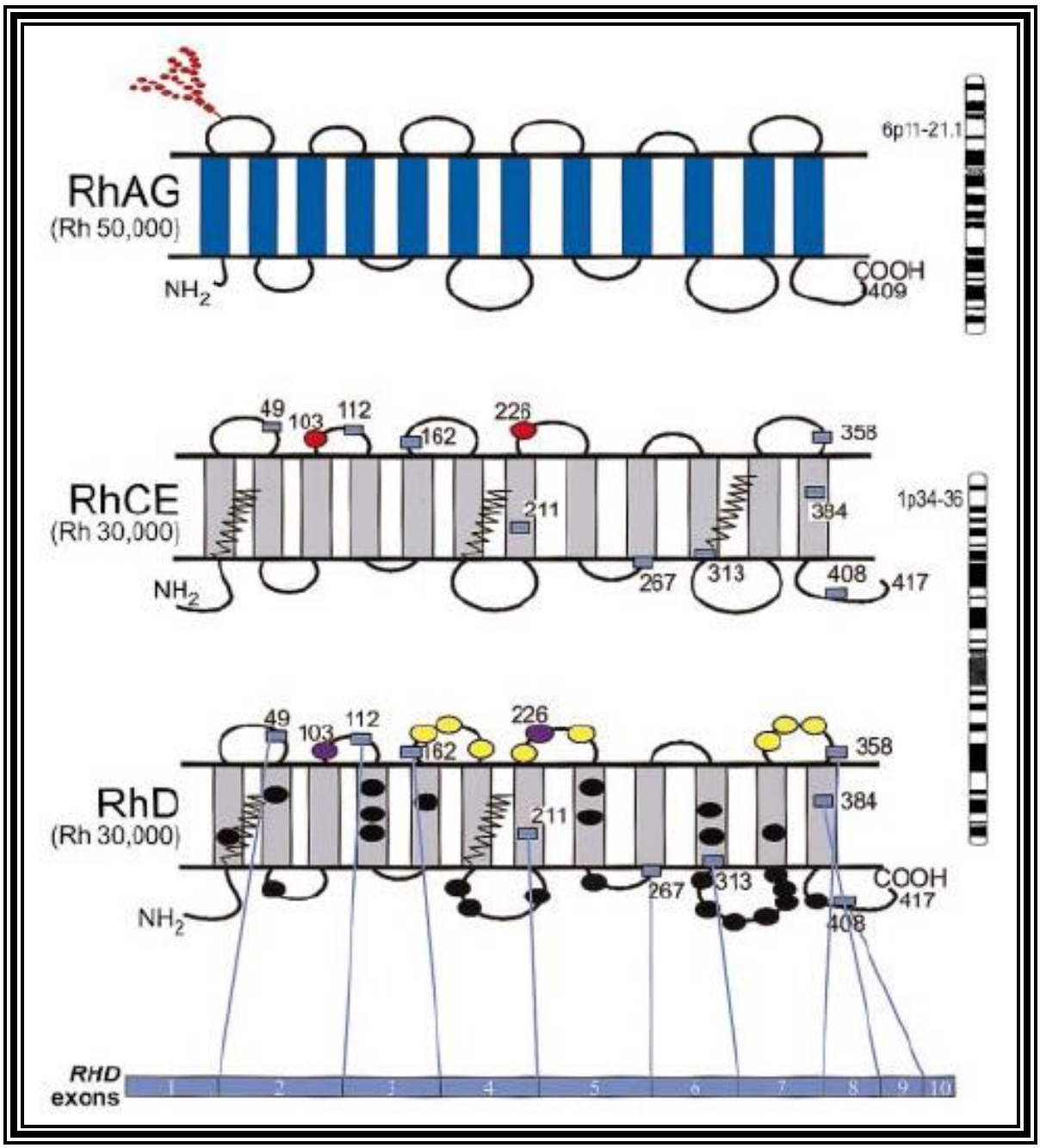
the help of the needle the two should be mixed. Allow the antibodies and antigens to react for some time, and later the blood smears can be viewed thro ugh the microscope. Wherever cell aggregation or agglutination is observed, the blood type can be identified as A +, B' AB' Rh+. If agglutination is not found the blood of a person can be identified as A- (0), B-(O). O and Rh (-). The principle of detection is simple. The antibodies raised against pure antigens, have certain specific regions in their protein, which recognize the antigens and they interact with them resulting in the binding between the two. When the blood of an untyped person is mixed with pure antibodies, the antigens present on the erythrocytes or blood cells interact with the antibodies and bring about aggregation of cells. If aggregation is detected in a particular serum, say A serum, the blood type can be identified as A. On the contrary if the blood cells do not agglutinate with A serum, but do so with B serum, then the blood type can be said to be as B. On the other hand, if the blood cells of that person show agglutination against both the A & B serum, it can be said that the blood group of that man is AB. Notwithstanding this, if there is no reaction against any of the A or B sera, it can be concluded hat the blood is of 0 type.

With regard to Rh+, if the blood cells get agglutinated against Rh+ serum, the person is Rh-, if not he is Rh+ negative Rh-, Similarly any type of blood can be detected, if one possesses the right type of antibodies Fig. 66.

Blood cells of untyped persons	Antibodies against			Conclusions
	A	B	Rh+	
1	+	-	+	A type and Rh +
2	-	+	-	B type and Rh -
3	+	+	-	AB type and Rh -
4	-	-	+	O type and Rh +
5	+	+	+	AB type and Rh +
6	-	-	-	O type and Rh -

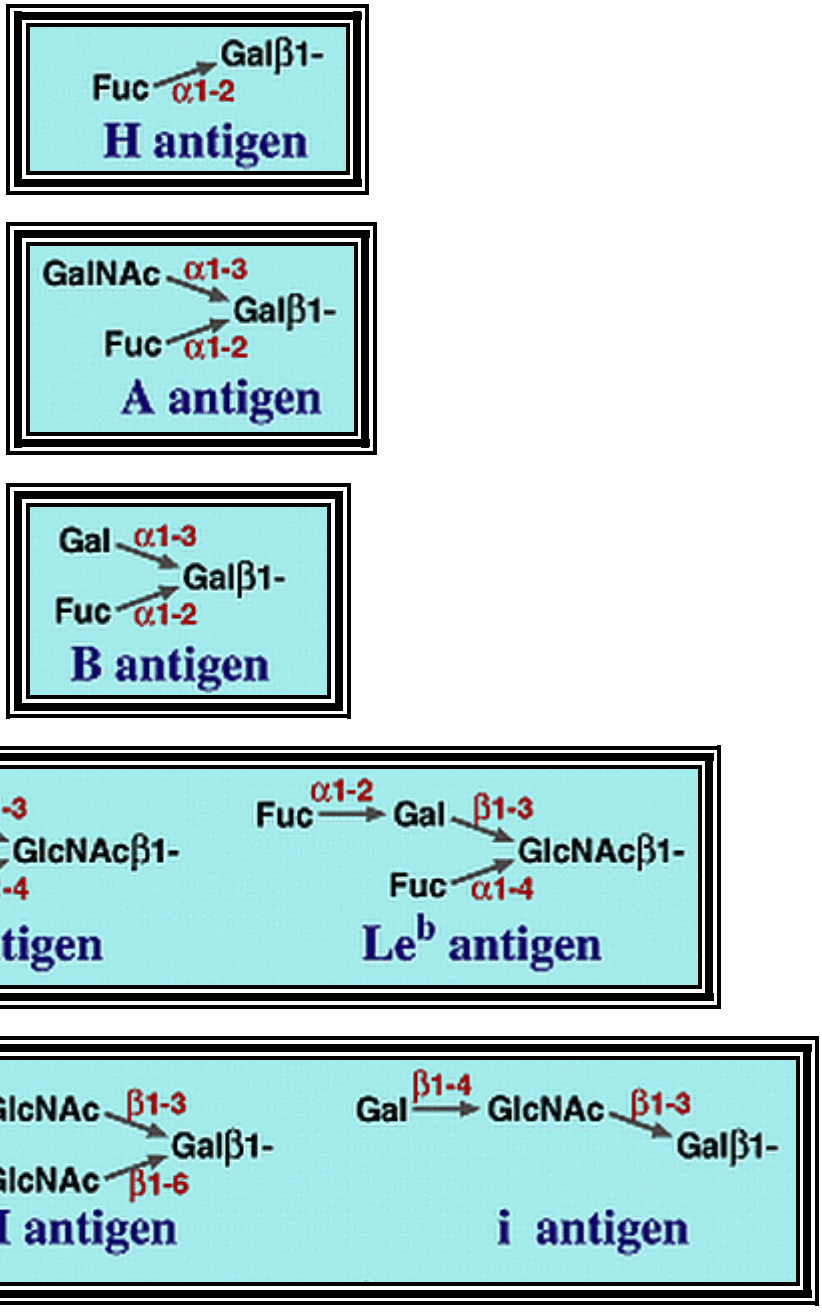


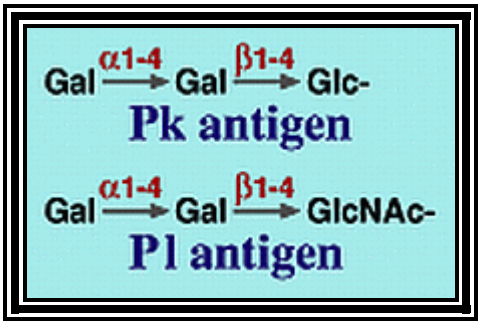

S/T
D/E
T/A
D/E
K/R/S
V/A
D/E
Out
In
E/Q
E/Q
D/E
NH2
1
2
3
4
5
6
7
8
9
10
11
12

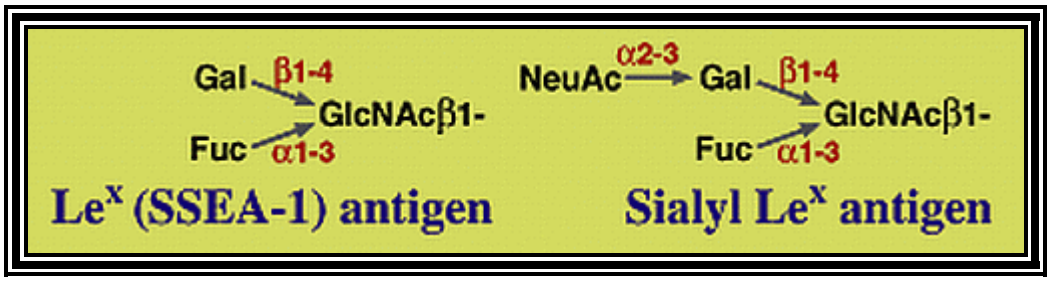


Similar to ABO type there are other characters which are controlled by multiple alleles. In humans MNS series have 20 multiple alleles, Kell series have 6 and Rh series have 30 or more alleles. Another significant aspect of blood group genotype is co-

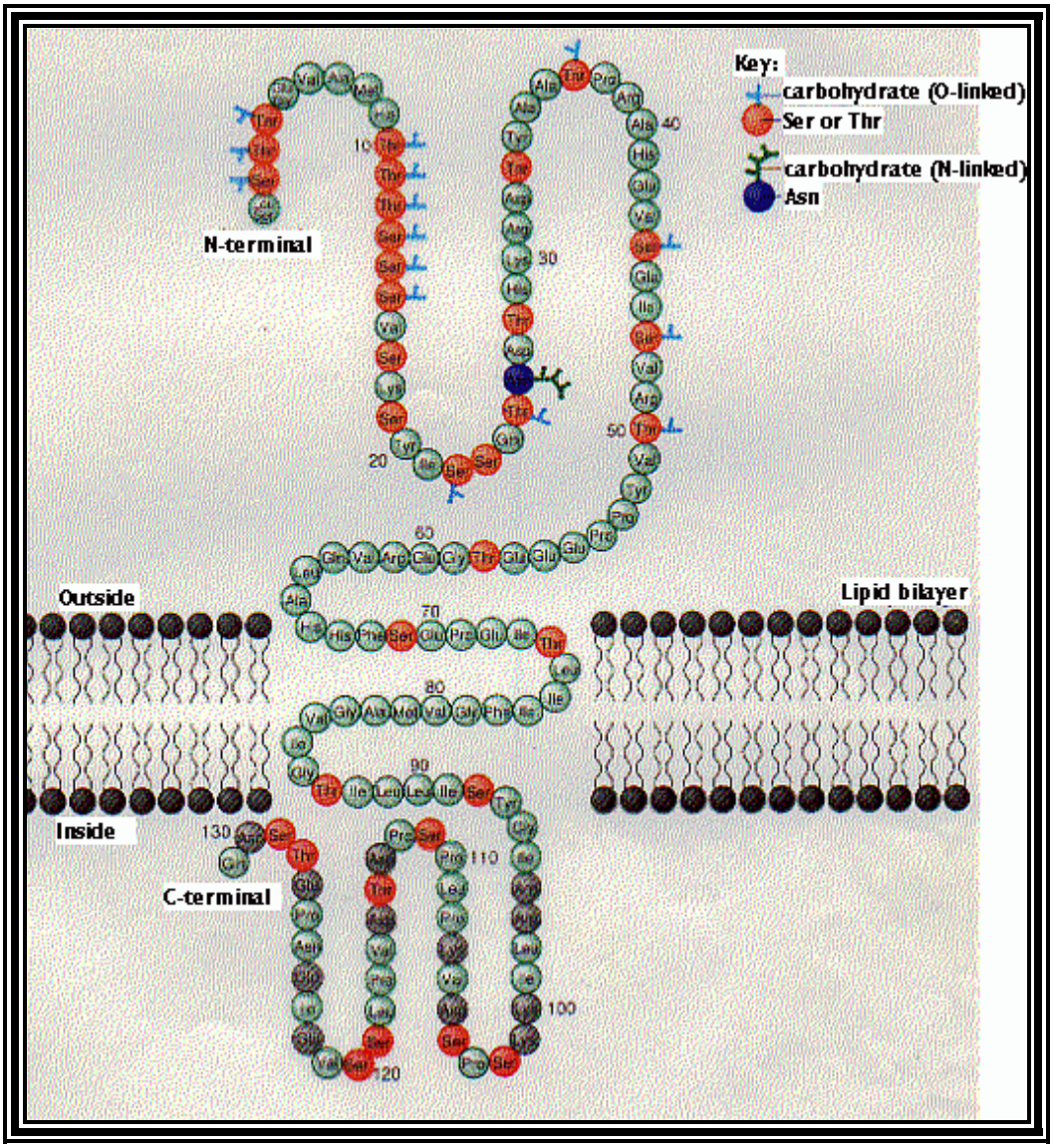
dominance, where both the genes express their character equally without affecting the phenotypic character of the blood-Ex. A and B genes express their antigens equally and both remain in the same man without any interaction or modification.

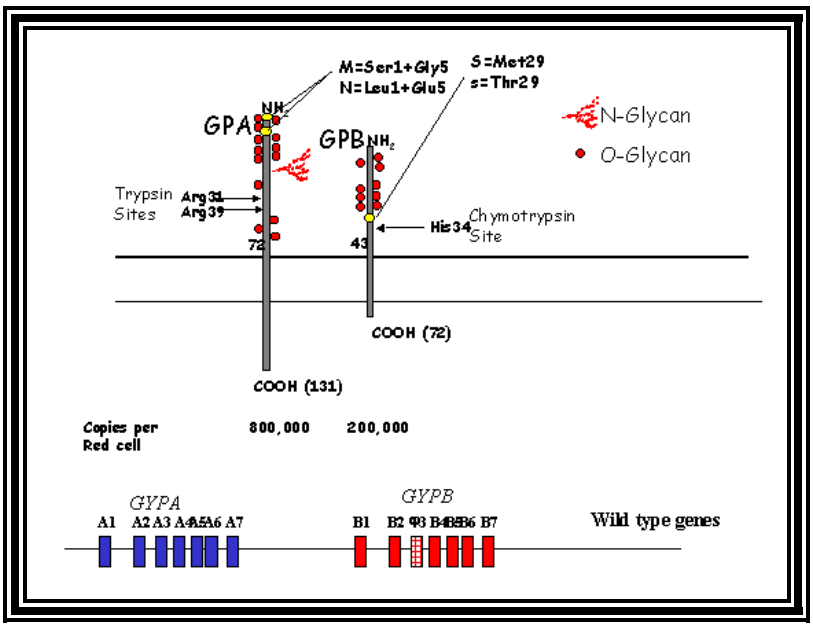


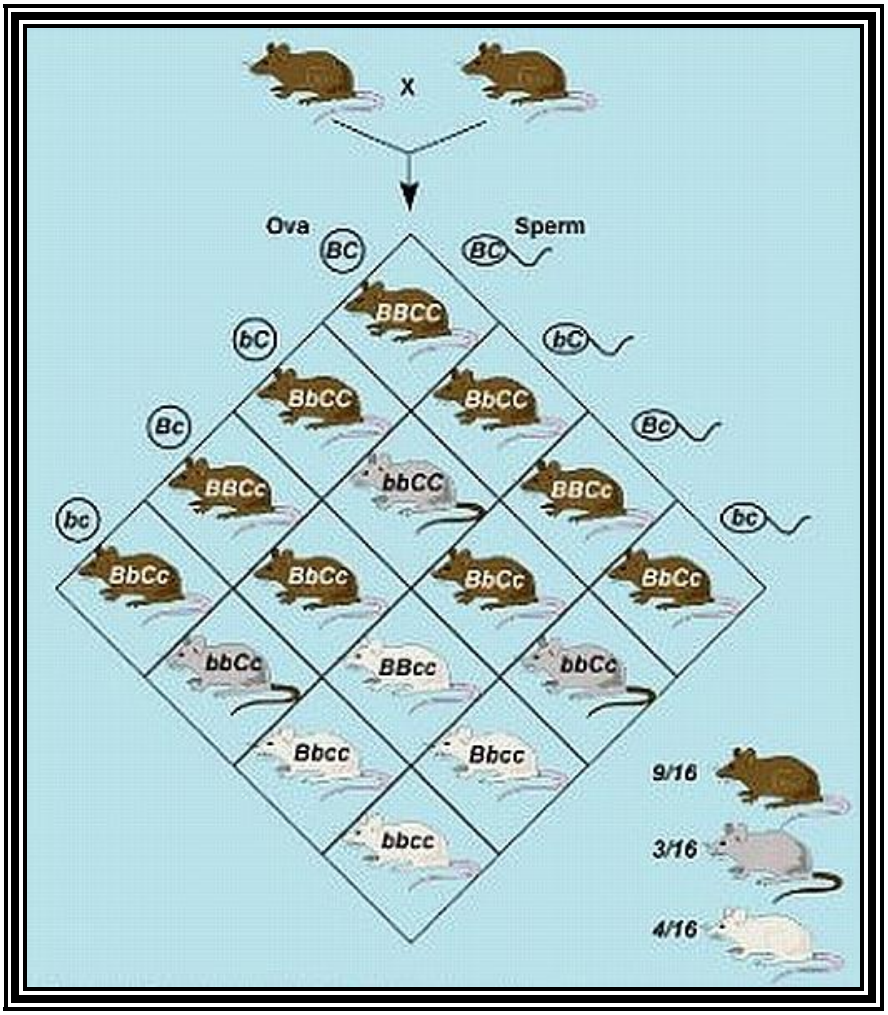

Gal α1-4 Gal β1-4 Glc-
Pk antigen
Gal α1-4 Gal β1-4 GlcNAc-
P1 antigen


Gal β1-4
GlcNAcβ1-
Fuc α1-3
Le^x (SSEA-1) antigen
NeuAc α2-3 Gal β1-4
GlcNAcβ1-
Fuc α1-3
Sialyl Le^x antigen

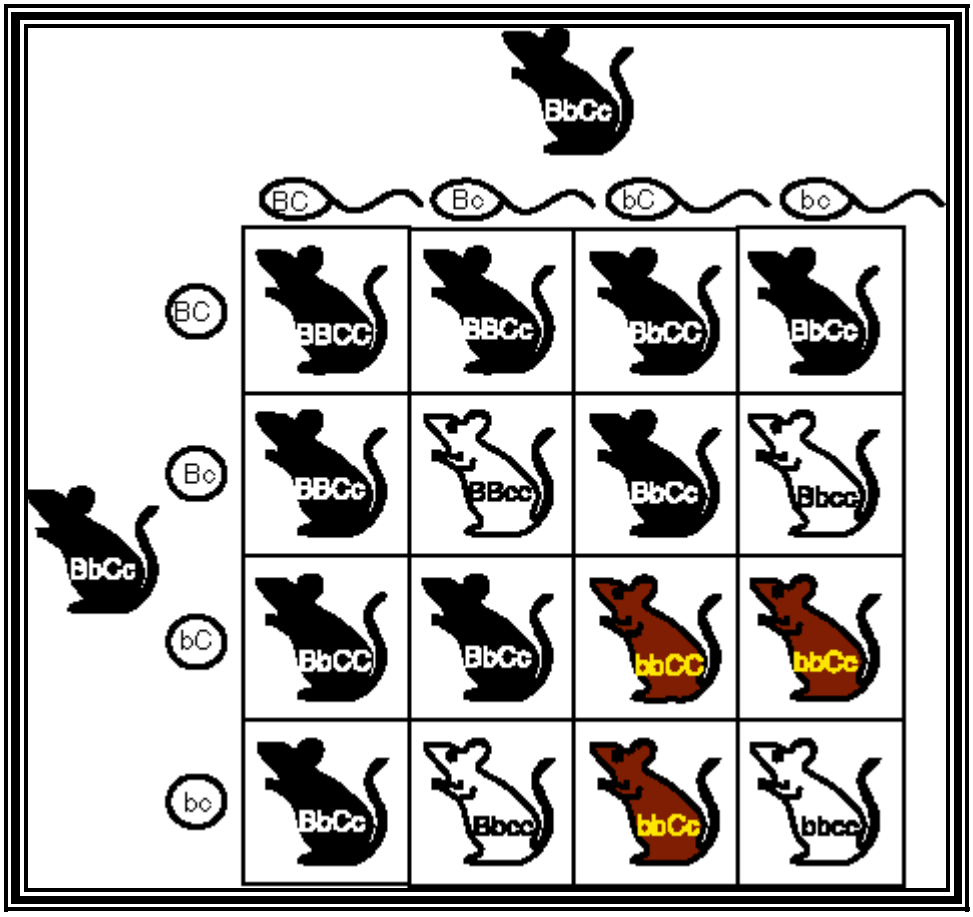

Gal α1-4 Gal β1-4 Glc-
Pk antigen
Gal α1-4 Gal β1-4 GlcNAc-
P1 antigen

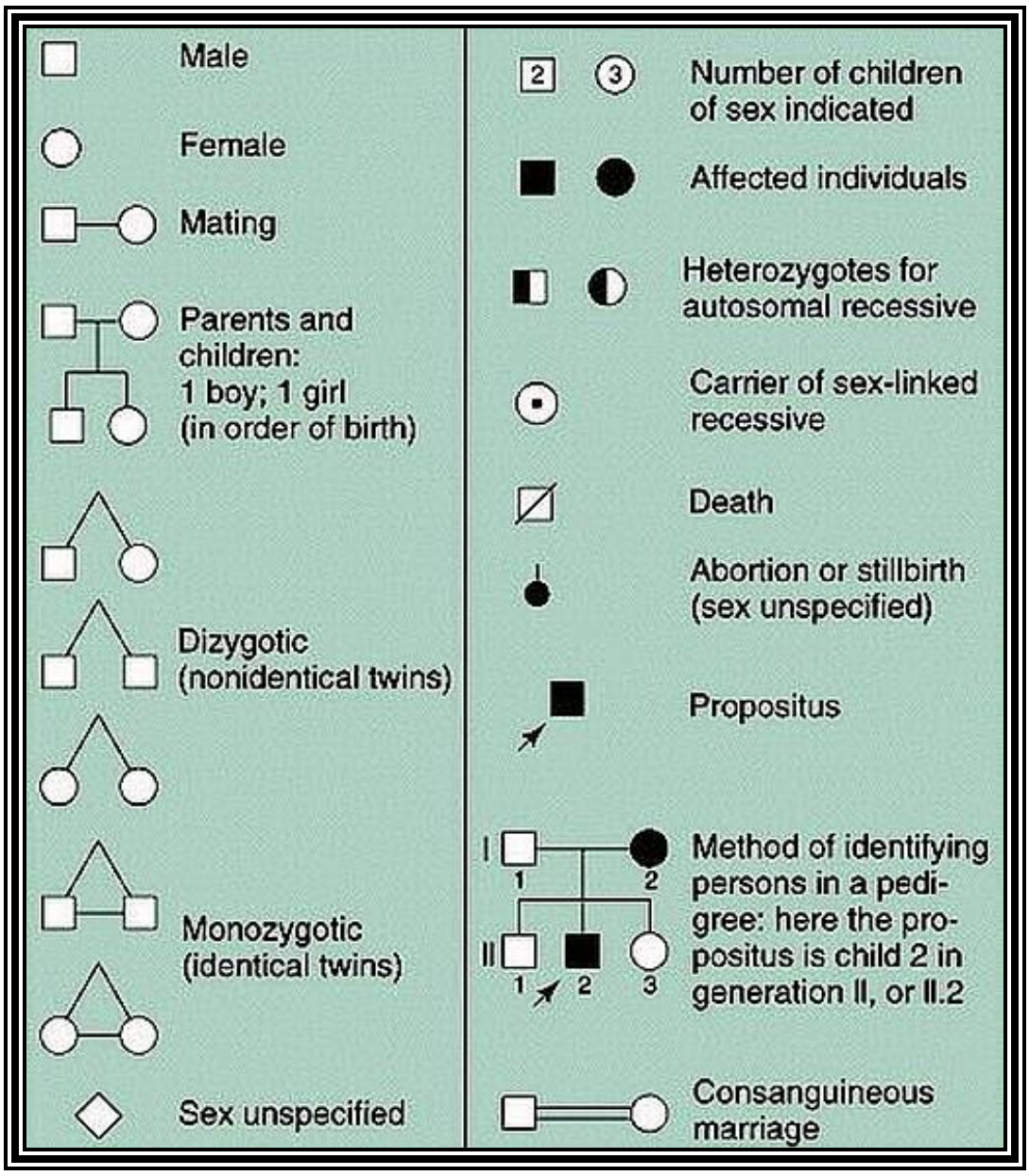

Key:
carbohydrate (O-linked)
Ser or Thr
carbohydrate (N-linked)
Asn
N-terminal
Outside
Lipid bilayer
Inside
C-terminal

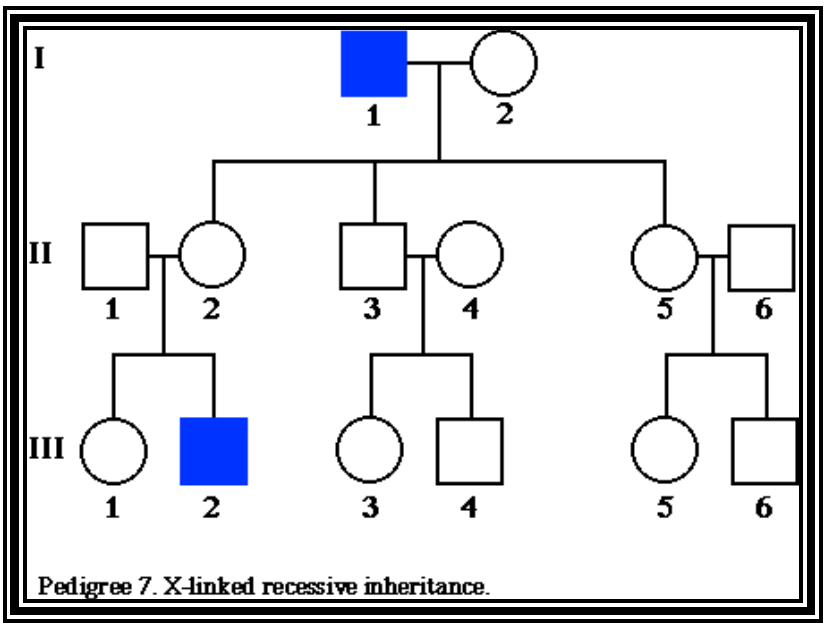

M=Ser1+Gly5
N=Leu1+Glu5
S=Met29
s=Thr29
GPA
GPB
NH2
N-Glycan
O-Glycan
Trypsin Sites
Arg31
Arg39
His34
Chymotrypsin Site
72
43
COOH (72)
COOH (131)
Copies per Red cell
800,000
200,000
GYPA
GYPB
A1 A2 A3 A4 A5 A6 A7
B1 B2 B3 B4 B5 B6 B7
Wild type genes


X
Ova
Sperm
BC
bC
Bc
bc
BBCC
BbCC
bbCC
BBCc
BbCc
bbCc
BBcc
Bbcc
bbcc
9/16
3/16
4/16

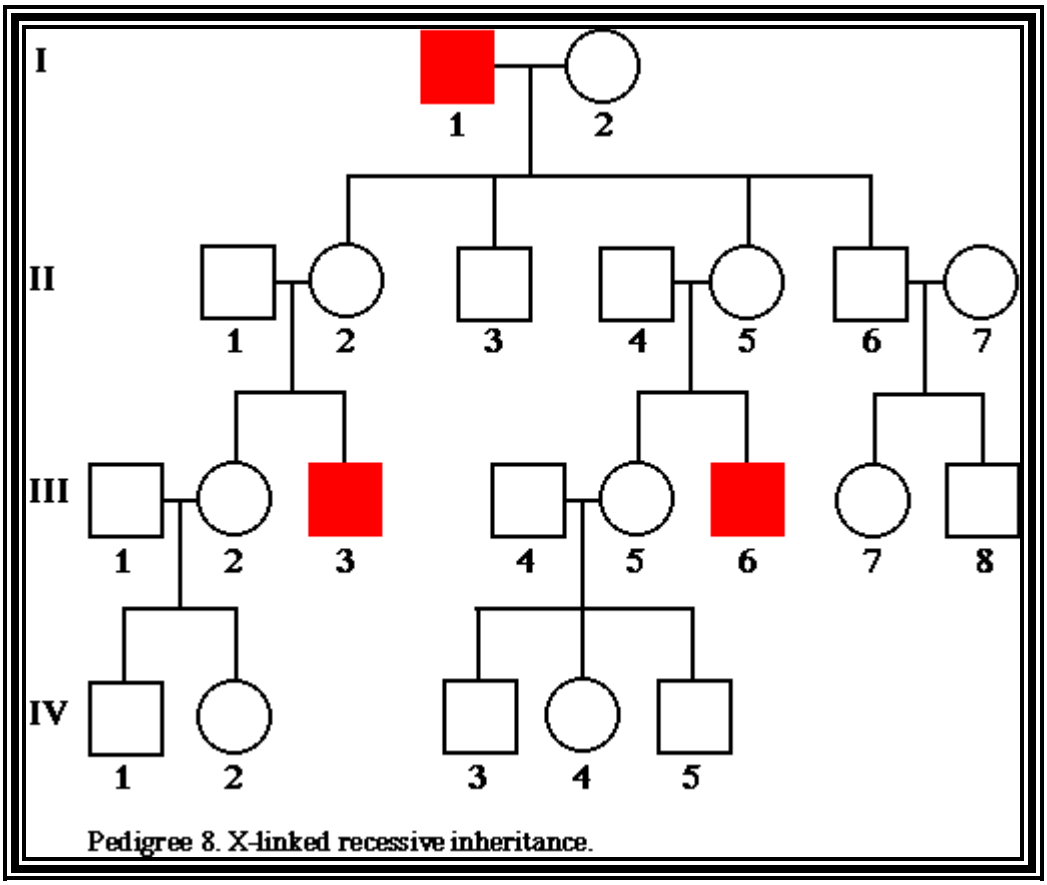
Epistasis: One gene, which is independent of the other, capable of suppressing the expression of the other gene; but it is not recessive.




Male
Female
Mating
Parents and children:
1 boy; 1 girl
(in order of birth)
Dizygotic
(nonidentical twins)
Monozygotic
(identical twins)
Sex unspecified
2
3
Number of children of sex indicated
Affected individuals
Heterozygotes for autosomal recessive
Carrier of sex-linked recessive
Death
Abortion or stillbirth (sex unspecified)
Propositus
I
1
2
II
1
2
3
Method of identifying persons in a pedigree: here the propositus is child 2 in generation II, or II.2
Consanguineous marriage



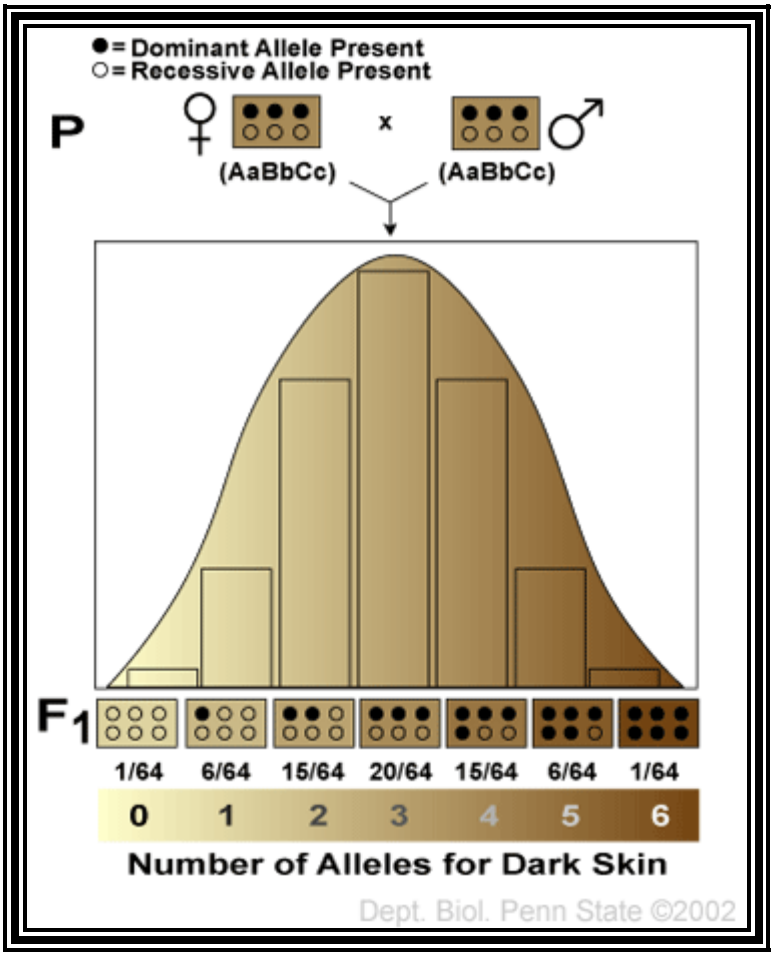
Pedigree 7. X-linked recessive inheritance.



Pedigree 8. X-linked recessive inheritance.

Multiple gene inheritance:

A particular phenotypic character is controlled not by a single gene but many act on the same character. This type of inheritance is called multiple factor inheritance and quantitative. Examples- skin color.



Quantitative inheritance.

Sex determination and sex-linked inheritance:

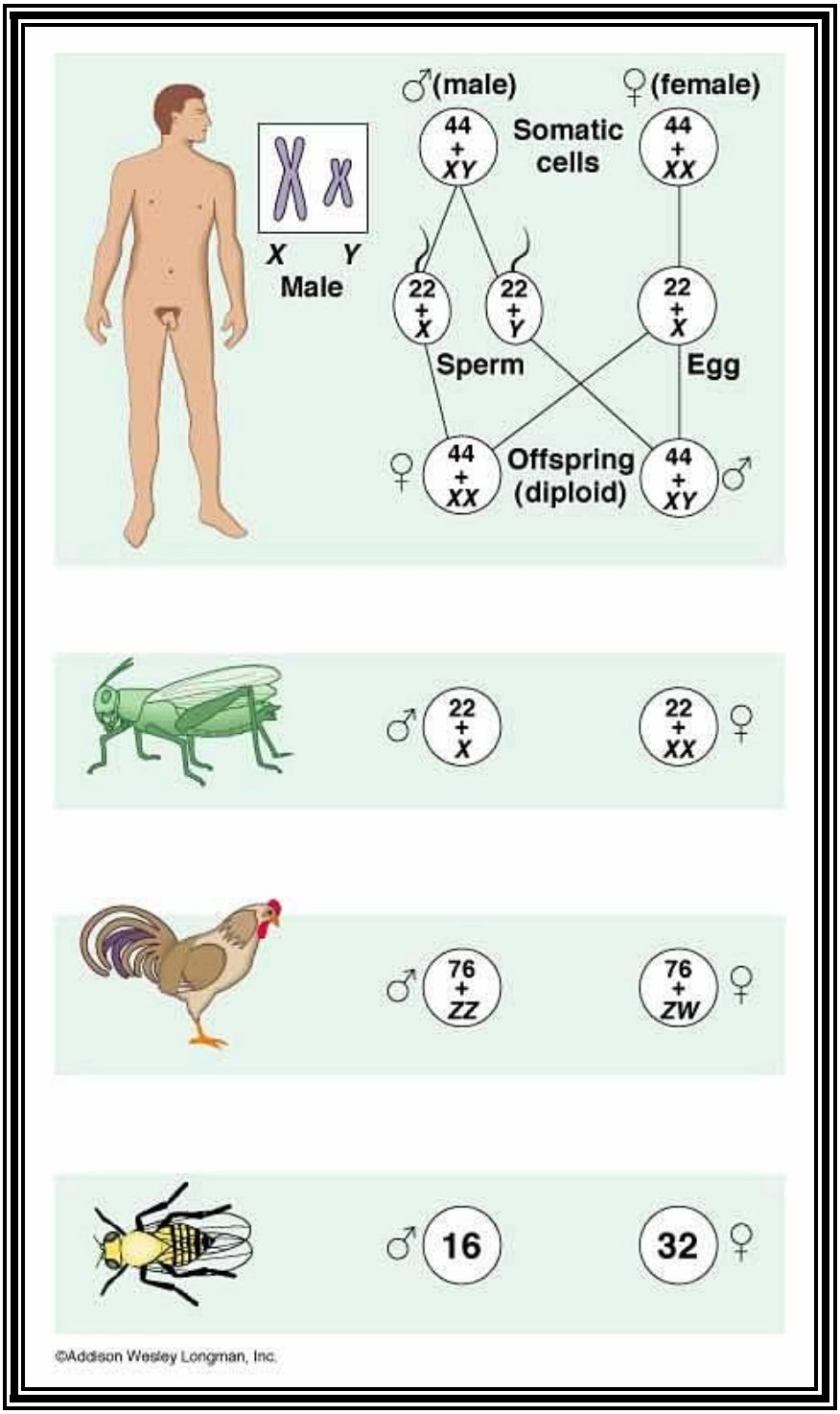
Organisms with morphological sex difference as males and females, the sex of each of them is generally determined by sex chromosomes, which contain sex determining genes. Those chromosomes which determine sex of an organism are called sex chromosomes and other chromosomes are autosomes. In human being there totally 2n = 46 chromosomes, of which 44 are called autosomes and the other two are called sex chromosomes, where they constitute two types, one is called X chromosome and the other is called Y chromosome. A male individual contains, 2n=44A + XY and the Y is male determining chromosome, but the female contains 2n=44A + XX, where X is female determinant. This rule of XX and XY differs in different systems.

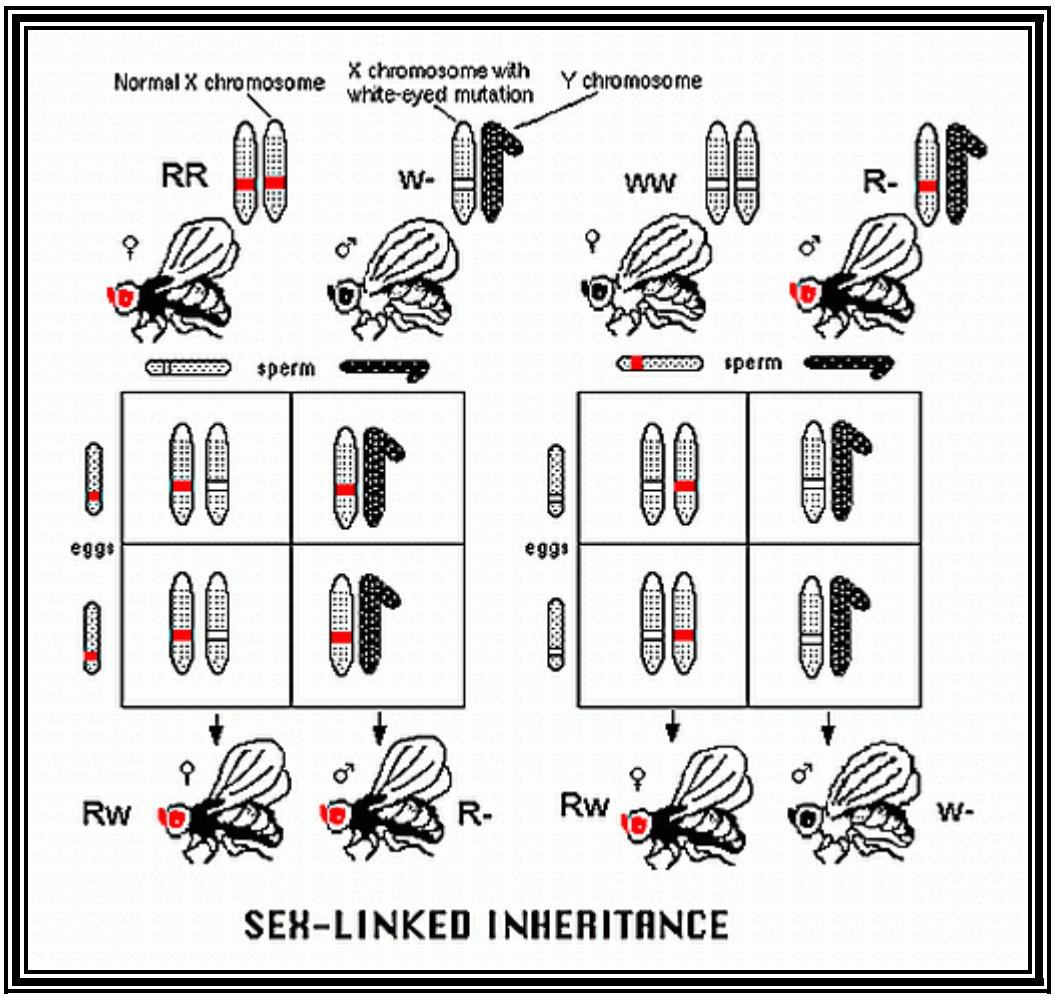
A majority of plants and animals exhibit sexual mode of reproduction. Some of them are bisexual (hermaphrodites) and some of them are unisexual. In higher animals unisex is a predominant feature, where male and female sexes arc distinguished by characteristic structural and functional features. Even many plants exhibit this kind of sexual dimorphism.

Sex chromosomes and Autosomes:

Cytogenetic studies, in the past fifty years or so, have established that the sex of on organism, in its early development is determined by special chromosomes called Sex chromosomes or Allosomes such as X and Y.

All other chromosomes are called Autosomes (A). All unisexual animals including Insects, Fishes, Frogs, Birds and mammals including human beings show XY mechanism of sex determination. Even some unisexual plants like Melandrium, Coccinia, Sphearocarpus etc. show X/Y mechanism. However, certain variations are also found.


♂(male)
♀(female)
44 + XY
Somatic cells
44 + XX
X Y
Male
22 + X
22 + Y
22 + X
Sperm
Egg
♀ 44 + XX
Offspring (diploid)
44 + XY ♂
♂ 22 + X
22 + XX ♀
♂ 76 + ZZ
76 + ZW ♀
♂ 16
32 ♀
©Addison Wesley Longman, Inc.



(1) Sex determination in human beings:

The diploid number of homos sepians is 46. In females, 2n = 44 A + XX is the chromosomal pattern, but in males 44A + XY is the chromosomal composition.

The X chromosome in males is euchromatic (genetically active) and Y chromosome .is completely heterochromatic; assumed to be genetically inactive. In fact, it is now established that the male determining gene is

located in Y chromosomes and the female determining gene on X chromosomes.

There are cases where the chromosomal composition in certain patients was found to be 44A + XO i.e. one of the sex chromosome is missing and the sex is female. In another case 44A + XX shows male sex. This is because, in the first case me Y chromosome is completely missing. So the X chromosome determines the sex of an individual as female. But in the second case (44A + XX), a segment of Y chromosome containing male determining gene(s) is somehow translocated to one of the X chromosomes. In this special case, in spite of the absence of Y chromosome the sex of the patient was male, because the translocated segment of Y chromosome contained sex determining gene. This clearly establishes it is XX and XY combination that ultimately determines the female & male sexes respectively. The same is true with many higher animals and also some plants.

Out of two X chromosomes in females one is euchromatic and the other is total heterochromatic and it appears as a bar body in females. In males the Barr body is absent If by chance a Barr body is identified in males, then his chromosomal composition is 44A + XXY, and it is an abnormality.

But in birds 2A + ZZ determines male sex and 2A + ZW determines female sex.

2. Sex determination in Drosophila: In Drosophila, mosquitoes and other dipterans insects, the sex determination is by XX and XY mechanism, but

with a difference when compared to the sex determination of human beings. Its 2n number is 8. If 2n = 6A +XX-it is female. If 2n = 6A+XY then it is male. But if an insect has 2n = 6A with only one X chromosome, then the insect develops as a male. This is due to the balance between autosomal number and sex chromosomes; here male sex is determined in spite of the absence of Y chromosomes.

6A+XX = Female 6A 4- XXY = Super female

6A+XY = male 6A + XYY = Super male

6A L XO = Male

Molecular mechanism of sex determination in Drosophila has been more or less elucidated. The genes involved in the processes are sXl, dsXl and few other related genes. The alternate splicing of the said gene transcripts plays a significant role in determining the sex of the organism at an early stage of tissue differentiation.

3. Sex determination in Honey bees: In honey bees, the queen bee lays eggs and the worker bees collect honey. The queen bee is always diploid and it alone is capable of laying eggs. If the eggs fertilize with a sperm, the animal develops into females. On other hand if the haploid egg remains unfertilized, it develops into a male donor bees or slave bees.

4. Sex determination in bacteria: In bacteria, males are slightly bigger in their cell size than their female counterparts. The male sex of bacteria is

determined by the presence of an episomal containing fertility factor. If the said factor is absent, then the bacteria act as female.

SEX LINKED INHERITANCE

Similar to Autosomes, sex chromosomes particularly X & Y chromosomes also carry expressible genes.

As sex chromosomes determine the sex of an organism, the genes found on sex chromosomes, as a linkage unit, also express their phenotype which is restricted to a particular sex of an organism. Such type of inheritance and expression limited to only one or the other combinations of sex chromosomes is called sex linked inheritance. So certain characters are inherited to either female or male sexes.

X-linked characters: Certain characters like color blindness, hemophilia muscular dystrophy in human beings, red and white eye color in Drosophila melanogaster; and black and barred plumage in poultry are some of the examples of sex linked, specifically X linked characters.

Y-linked characters: The Y chromosome also contains many genes in human beings but they don't express. Even if expressed, it is difficult to identify. But recent investigations do indicate that Y chromosomes also carry genes which express only under certain intracellular environment A gene for hypertrichosis i.e., hairs on external pinna, male sex determining factor, HLA

- antigen and overall height controlling factors have been assigned to Y chromosomes.

PATTERN OF SEX-LINKED INHERITANCE:

E.g., Color blindness:

Persons having color blind trait cannot distinguish red color from the green color. This character is controlled by a receive gene called "c". The normal wild type is "C" gene. These genes arc located on X chromosomes. If the female is heterozygous for this character i.e., "Cc", her color sensitivity is normal. On the other hand, if she is homozygous for color blind genes "cc" she is color blind. On the other hand, if a male carries a "c" gene on X chromosome; he is color blind; it is because the Y chromosome docs not carry any normal allelic and it is genetically inactive.

Criss-Cross inheritance: If the female, heterozygous (Cc) for color blind gene, marries a normal male, (CY), the probability of getting female to male children is 50:50. Among males, 50% will be color blind and other 50% normal. But all the females will be normal Follow the diagrammatic representation below.

Instead, if a heterozygous (carrier) female (Cc) marries a color-blind male CY: 50% of the females and 50% of the male children will be color blind and other male and female children are normal.

The same pattern of sex-linked inheritance is also found with respect to hemophilia gene.

SEX INFLUENCED CHARACTERS:

Not all phenotypic characters expressed in females or males show sex-linked inheritance. For example, in human species, beard, moustache, hair development on the chest, voice cracking, masculinity etc., are restricted to males. Similarly, non development of beard, moustache, chest hairs, non cracking of voice and development of breast etc are restricted to females. The above said characters, restricted to a particular sex, are expressed not at the early childhood but manifested at the adolescent stage. Such character's arc called sex influenced or secondary sexual characters.

The genes responsible for the expression of such characters are not found on sex chromosomes. However, the expression of such characters is under the influence of sex hormones and the age. Even masculinity and feminism are secondary sexual features.

Another good example is milk production in cattles. The genes responsible for milk production are present in both males and females, but they are expressed only in females because the female hormones influence the genes to produce milk.

Sex limited characters: Development of horns mostly in male sheep, formation of characteristic comb and feathers in male cocks and baldness mostly in male humane are actually sex-limited characters.

GENETIC DISEASES

Heritable disorders are called Genetic diseases and they arc often lethal. Such disorders go unnoticed in plants, but in higher animals, especially in human beings, these diseases arc of great concern to the mankind. One should note that not all congenital diseases arc heritable; some of them arc acquired due to pathogens.

Genetic diseases are due to mutations. They may be induced or spontaneous. Mutation in single genes (point mutations) or changes in the chromosomal structure (aberrations) or in number (ploidy) leads to variations in the morphology and function. Some of these changes are inherited to off springs. The genetic diseases may express at birth itself or later.

In fact, Garrod and Landsteiner were responsible for the discovery of inborn errors in human beings. Since then, a large number of such diseases have been identified and the details of such diseases have been studied at the biochemical level and also at the molecular l~3Vel. The recent innovations in the field of genetic engineering technology have provided tools and techniques to identify such genetic disorders. In fact, in many western countries like Great Britain, West Germany, France and USA, facilities are

available in many medical centers, for genetic screening and genetic counseling.

Some of the genetic diseases known to man are color blindness, Hemophilia, Phenylketoneuria, Alkaptonuria, Albinism, Tyrosinosis, Brittle bone, Autoimmunity, Sickle cell anemia, Genetic dwarfism, Huntington's chorea, Erythroblastasis faetalis, Turner's syndrome, Down's syndrome, Klienfelter's syndrome, Thalassemia, Glactosemia, Diabetes, Alzheimer's disease etc. Even families prone to heart disease. Alcoholism has been traced to genetic disorders.

Phenylketoneuria: This disease is caused by point mutations. In this case the enzyme responsible for the conversion of phenylpyruvate to hydroxypyruvate is inactive; hence phenylpyruvate accumulates in the body. The result is the mental disorder and such persons are called Phenylketoneuria idiots. However, this disease can be kept under control by providing the substrates in the diet.

Alkaptonuria: This is another genetic disease caused by the disorder of enzymes responsible for converting Homogentistic acid to acetoacid. Because of this, patient's urine turns blue black as it comes in contact with air. This disorder also manifests in mental malfunctions. Again this disease can be controlled by feeding the patient with a diet containing the substrate.

Turner's syndrome: This is a chromosomal disorder is due to the loss of one X chromosome (2n = 44A + X). Patients exhibit deformities like enlarged genitals, short stature, and webbed neck, broad shield like chest, under developed breasts, uterus and ovaries. Their mental behavior is like idiots. They are female individuals and their life span is short. There is no cure.

Klienfelter's Syndrome: The disease is caused by the presence of one extra X chromosome along with the normal XY chromosomes, (2n = 44A + XXY). The person afflicted with this kind of disease are males; long legged, develop female type of breasts, voice docs not crack, beard and chest hairs do not develop. In this case also there is no permanent cure.

Down's syndrome: Persons have one extra autosome (21st autosome). The chromosomal constitution is 2n = 44A + 21stA + XY. The person is male and exhibit mental disorders. Peculiar foldings of eyelids, short stature, stubby hands and feet, malformation of heart etc., these patients arc also called as Mongoloid idiots. There is no cure for this disease.

Huntington chorea: This disease expresses only at later stage of the life, say around 45-60 years of age. They suffer from extreme body tremors due to single gene defect this is also due to cavitations in the brain, which causes neural disorders.

Diabetes mellitus: In most of the cases, this disease is expressed at the age of 45-50 years. The sugar level of blood rises very high due to the absence of functional insulin molecules or the insulin fails to stimulate sugar

uptake by cells. High levels of blood sugar causes disorders in the body and in extreme cases patients go through comatic stage from which they may not recover at all. However, by proper intake of insulin one can lead a normal life. This affliction is global phenomenon, nearly 20- 30 percent of the developed countries have one or the other type of Diabetes; namely Diabetes-1 and Diabetes-2; where the former is juvenile and the later is an adult disease.

Hemophilia: Hemophilia is often called bleeding to death disease. In normal humans a cut leading to bleeding stops with clotting of the blood. But in hemophiliacs, the defective gene does not produce clotting factor that is why they bleed to death. In hemophiliac there arc some variations, such as .external and internal bleeding. This disease is not autosomal linked, but sex linked.

Sickle cell anemia: This disease is very common in black -population of Africa. The normal hemoglobin gene produces functional oxygen carrying hemoglobin protein. In a mutant (just one amino acid substituted) the hemoglobin is rendered non functional. In homozygous both genes are not functional. Hence the RBC cells collapse for the lack of sufficient oxygen, and the cells show sickle shape. People from this disease suffer from the lack of sufficient oxygen, and often gasp for the breath. But the heterozygous persons though show symptoms, they are immune against malarial infection.

Alzheimer*s disease: This disease manifests at old age and the diseased people suffer from forgetfulness ex, misplacing the key, leaving the key

some place is not the disease, but having the key if one fails to unlock with the key is a clear manifestation of the disease. This has been attributed to single gene.

Persons suffering from such genetic diseases should go through proper diagnosis and treatment. This can be done through proper genetic counseling. Though there are no permanent cures, at least by proper care and precautions they can be maintained till they die a natural death.

Duchene Muscular Dystrophy: A membrane protein is involved in muscle contraction. Mutation in this gene can cause abnormality in muscle contraction. It is X-linked