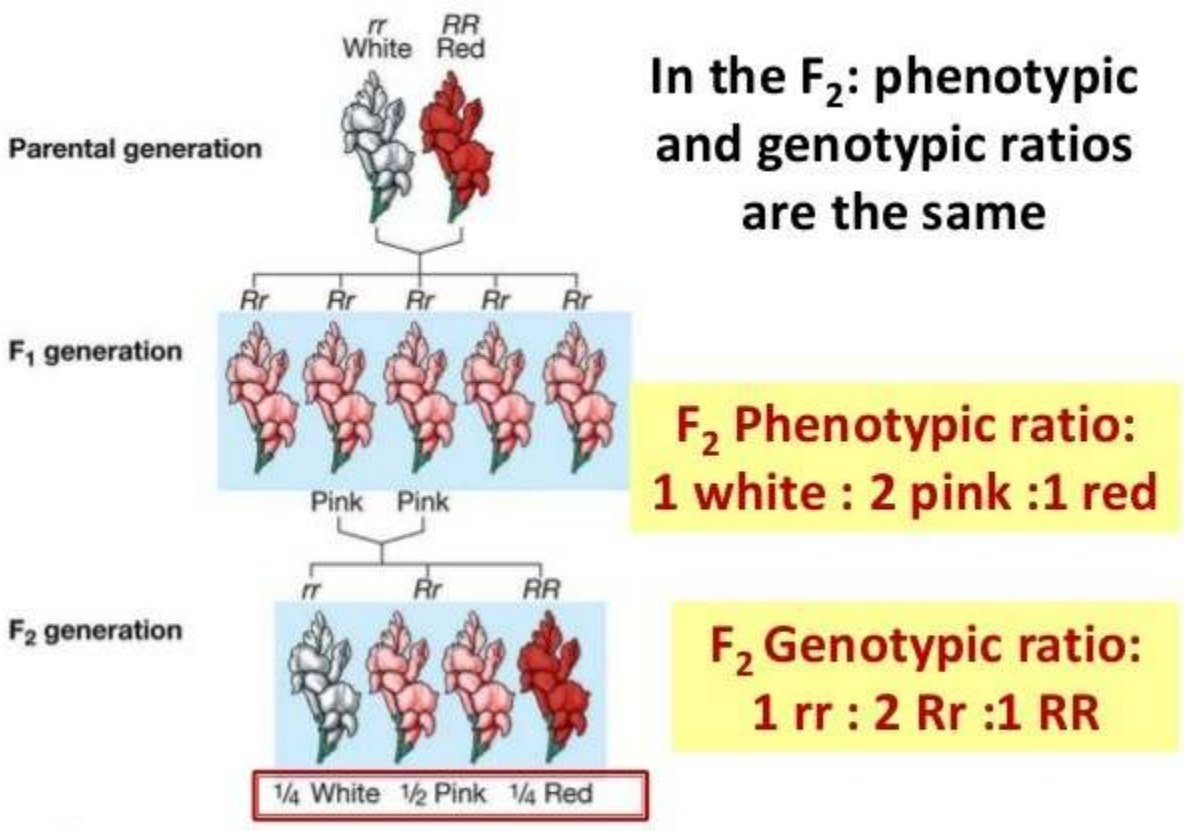
Week 5 Highlights

Deviation from Complete Dominance:

Neither allele at a locus is completely dominant. The heterozygote shows an intermediate phenotype.

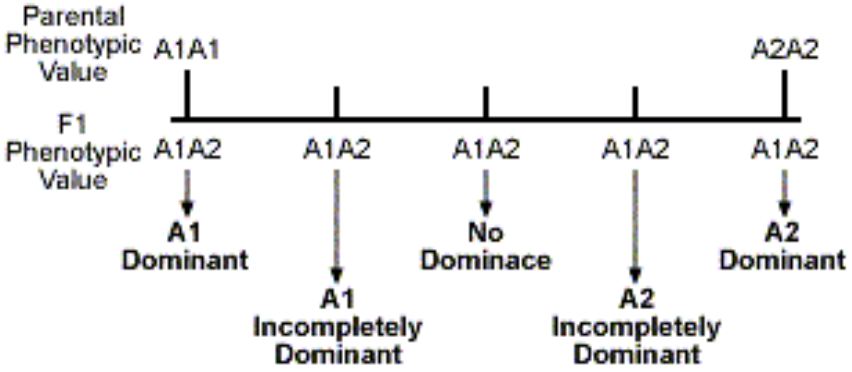
Flower colour:



Various types of dominance:

Over dominance: The heterozygote has a higher value than either of the two homozygotes.

Under dominance: The heterozygote has a lower value than either of the two homozygotes.

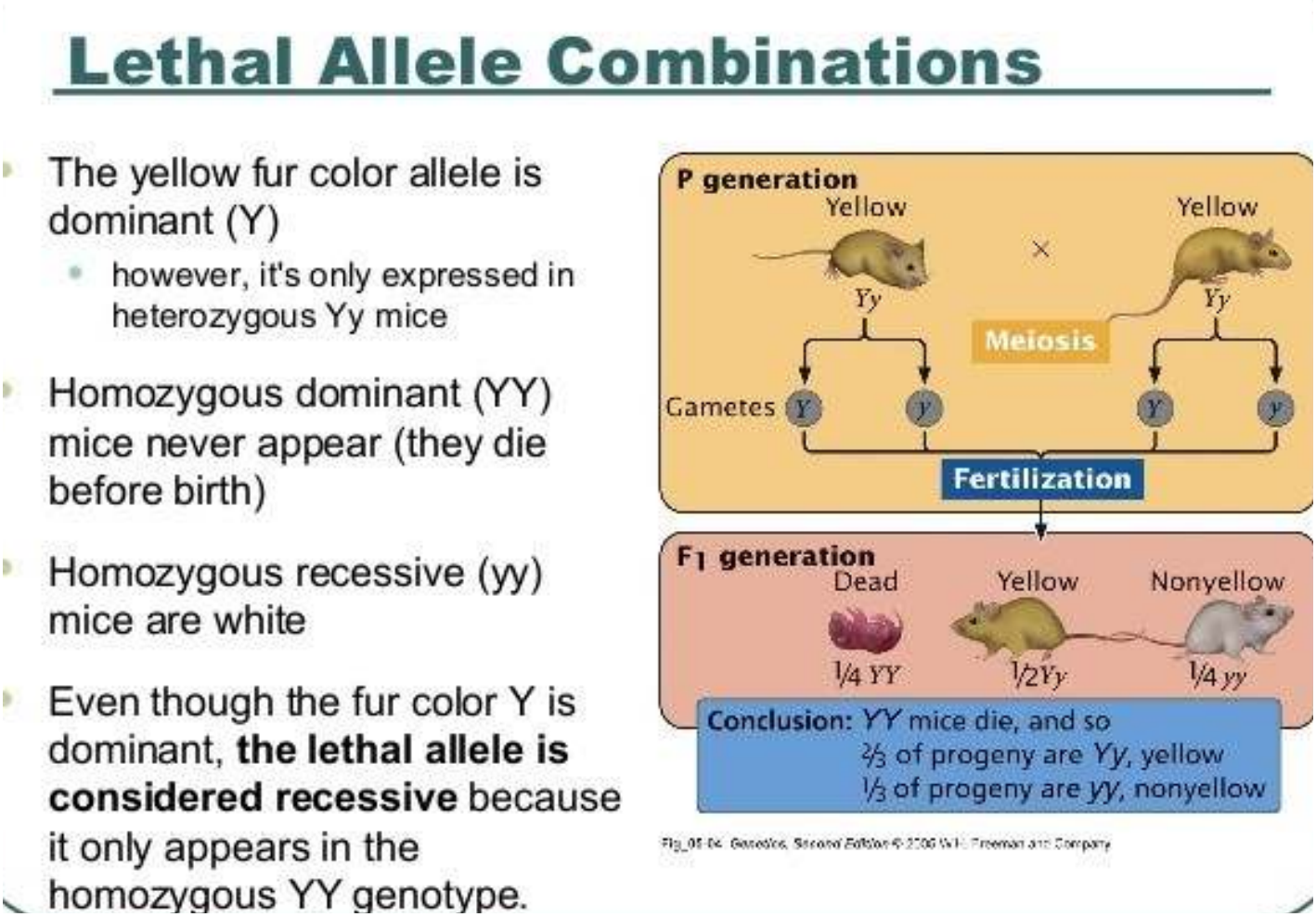


Recessive Lethals:

Cuenot and Baur discovered the first recessive lethal alleles.

These alleles can code for either dominant or recessive characters. However, they do not cause death unless an organism carries two copies of these alleles.

They alter the Mendelian Ratio.



Pleiotropy: One locus affecting more than one trait.

Y is a pleiotropic allele.

Note:

A dominant lethal allele can cause death even in heterozygotes. It can passed on to the next generation only if it’s phenotypic expression occurs after the onset of reproduction.

Multiple Alleles

An individual has two copies of each gene, so can only have two alleles of any gene, but there can be more than two alleles of a gene in a population. An example of this is blood group in humans. The red blood cell antigen is coded for by the gene I (for isohaemaglutinogen), which has three alleles I^A, I^B and I^o. (They are written this way to show that they are alleles of the same gene.) I^A and I^B are codominant, while I^o is recessive. The six possible genotypes and four phenotypes are:

Phenotype (blood group)	Genotypes	antigens on red blood cells	plasma antibodies
A	I^AI^A, I^AI^o	A	anti-B
B	I^BI^B, I^BI^o	B	anti-A
AB	I^AI^B	A and B	none
O	I^oI^o	none	anti-A and anti-B

The cross below shows how all four blood groups can arise from a cross between a group A and a group B parent.

phenotype	group A		x		group B		
genotype	I^AI^o				I^BI^o		
gametes	I^A or I^o				I^B or I^o		
fertilisation	♂gametes: I^B, I^o / ♀gametes: I^A → I^AI^B, I^AI^o / I^o → I^BI^o, I^oI^o						
genotype	I^AI^B		I^AI^o		I^BI^o		I^oI^o
phenotype	group AB		group A		group B		group O
ratio	1	:	1	:	1	:	1

Other examples of multiple alleles are: eye colour in fruit flies, with over 100 alleles, and human leukocyte antigen (HLA) genes, with 47 known alleles.

Epistasis: Gene Interaction and Phenotype Effects

(https://www.nature.com/scitable/topicpage/epistasis-gene-interaction-and-phenotype-effects-460/)

By: Ilona Miko, Ph.D. (Write Science Right)
Citation: Miko, I. (2008) Epistasis: Gene interaction and phenotype effects. Nature Education 1(1):197

Epistasis describes how gene interactions can affect phenotypes.

In his dihybrid crosses with pea plants, Gregor Mendel simultaneously examined two different genes that controlled two different traits. For instance, in one series of experiments, Mendel began by crossing a plant that was homozygous for both round seed shape and yellow seed color (*RRYY*) with another plant that was homozygous for both wrinkled seed shape and green seed color (*rryy*). Then, when Mendel crossed two of the F_1 progeny plants with each other (*RrYy* × *RrYy*), he obtained an F_2 generation with a phenotypic ratio of 9:3:3:1, as summarized in Table 1.

Table 1: Phenotypes and Genotypes in Mendel's F_2 Generation

Proportion	Genotype	Phenotype
9/16	*R_Y_*	Round, yellow
3/16	*R_yy*	Round, green
3/16	*rrY_*	Wrinkled, yellow
1/16	*rryy*	Wrinkled, green

In this dihybrid cross, each gene locus had an independent effect on a single phenotype. Thus, the *R* and *r* alleles affected only the shape of the seed and had no influence on seed color, while the *Y* and *y* alleles affected only seed color and had no influence on seed shape. In this case, there were two separate genes that coded for two separate characteristics.

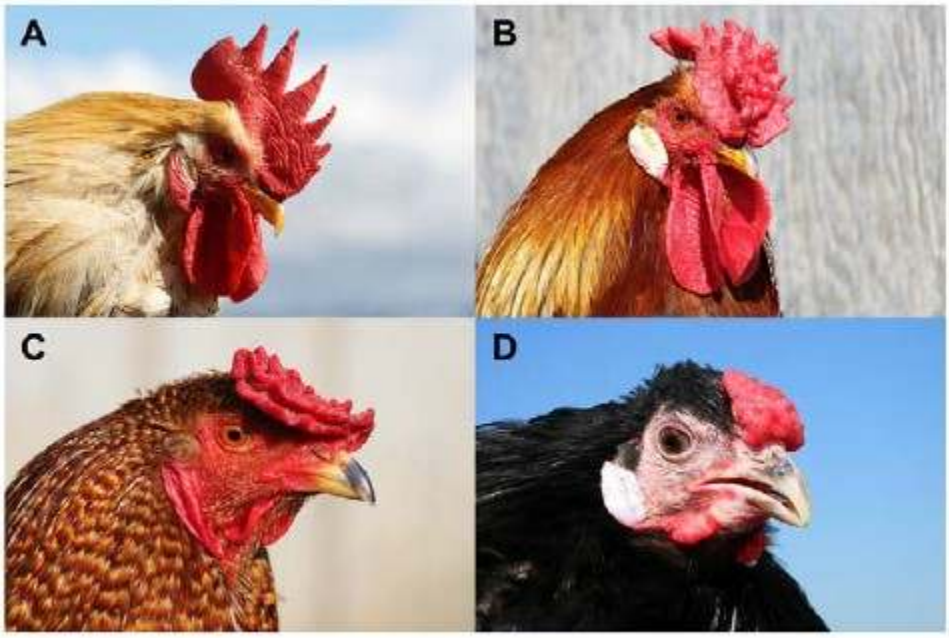
But what happens when two different loci affect the same characteristic? For instance, what if both of the loci in Mendel's experiment affected seed color? When two genes are involved in the outcome of one characteristic, a dihybrid cross involving these genes can produce a phenotypic ratio very different from 9:3:3:1. Under these circumstances, there are more than two gene products affecting the same phenotype, and these products may have complex hierarchical relationships. **Any time two different genes contribute to a single phenotype those genes are said to be epistatic.**

Although some researchers have attempted to categorize all digenic (two-gene) epistatic interactions with specific names, those classification schemes are seldom used today. One reason that they have fallen out of favor is that terms such as "dominant" and "recessive" are best used to describe the effects of alleles of single genes. Furthermore, epitasis is not restricted to the interactions of only two genes. Rather, epistasis occurs in all of the following scenarios:

- Whenever two or more loci interact to create new phenotypes
- Whenever an allele at one locus masks the effects of alleles at one or more other loci
- Whenever an allele at one locus modifies the effects of alleles at one or more other loci

Epistasis is an interaction at the phenotypic level of organization. The genes that are involved in a specific epistatic interaction may still show independent assortment at the genotypic level. In such cases, however, the phenotypic ratios may appear to deviate from those expected with independent assortment.

Comb Pattern in Fowls (Bateson and Punnett):

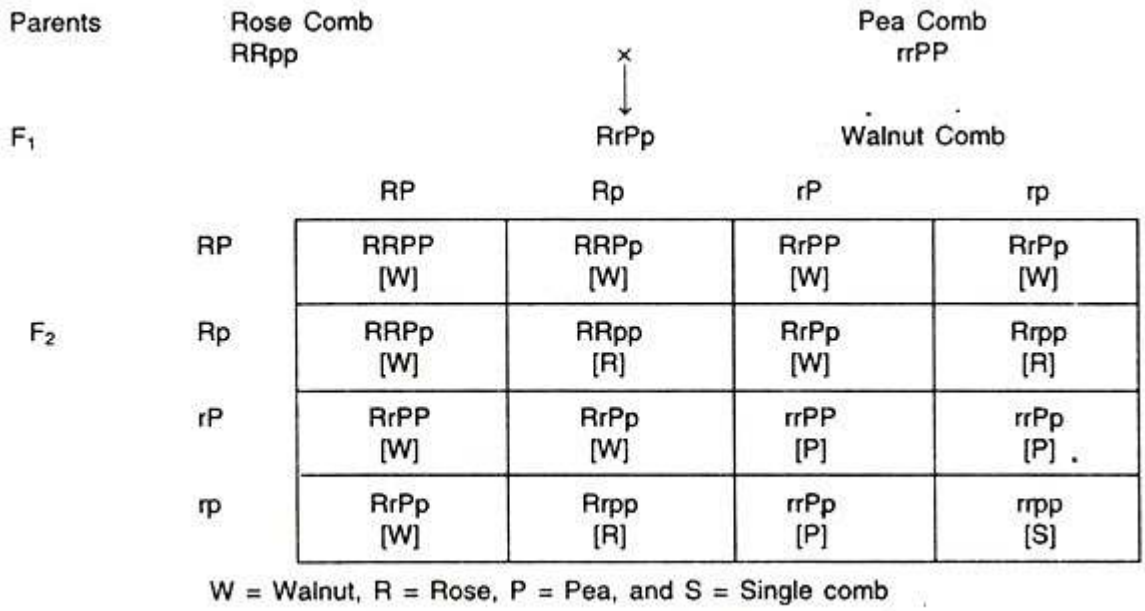


A) Single Comb

B) Rose Comb

C) Pea Comb

D) Walnut Comb



At R locus, R is dominant to r.

At P locus, P is dominant to p.

The loci are independently assorting.

Genotype	Ratio	Phenotype
R__P__	9	Walnut
R__pp	3	Rose
rrP___	3	Pea
rrpp	1	Single

Note: Extra reading for those of you whoa re intersted:

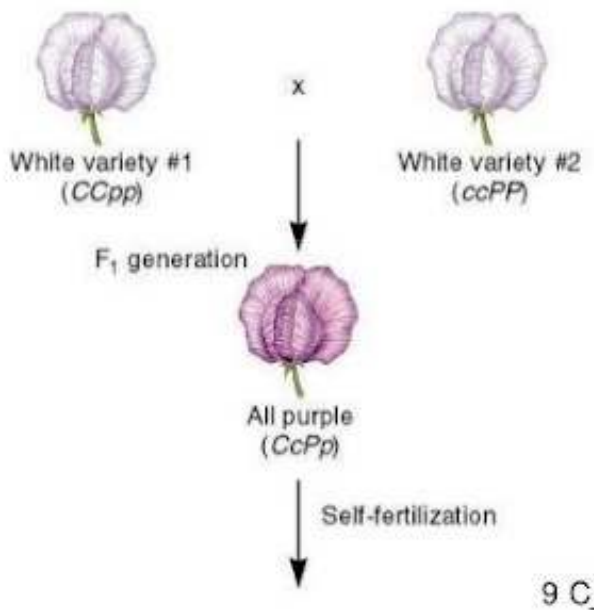
(Imsland et al (2012). The Rose-comb Mutation in Chickens Constitutes a Structural Rearrangement Causing Both Altered Comb Morphology and Defective Sperm Motility. PLoS genetics. 8. e1002775. 10.1371/journal.pgen.1002775.)

Flower Colour Production in Sweet Pea (*Lathyrus odoratus*): Bateson and Punnett

Sweet pea (*Lathyrus odoratus*)

(Sweet Pea is different from garden pea used by Mendel)

Complementary Genes (9:7 Ratio)



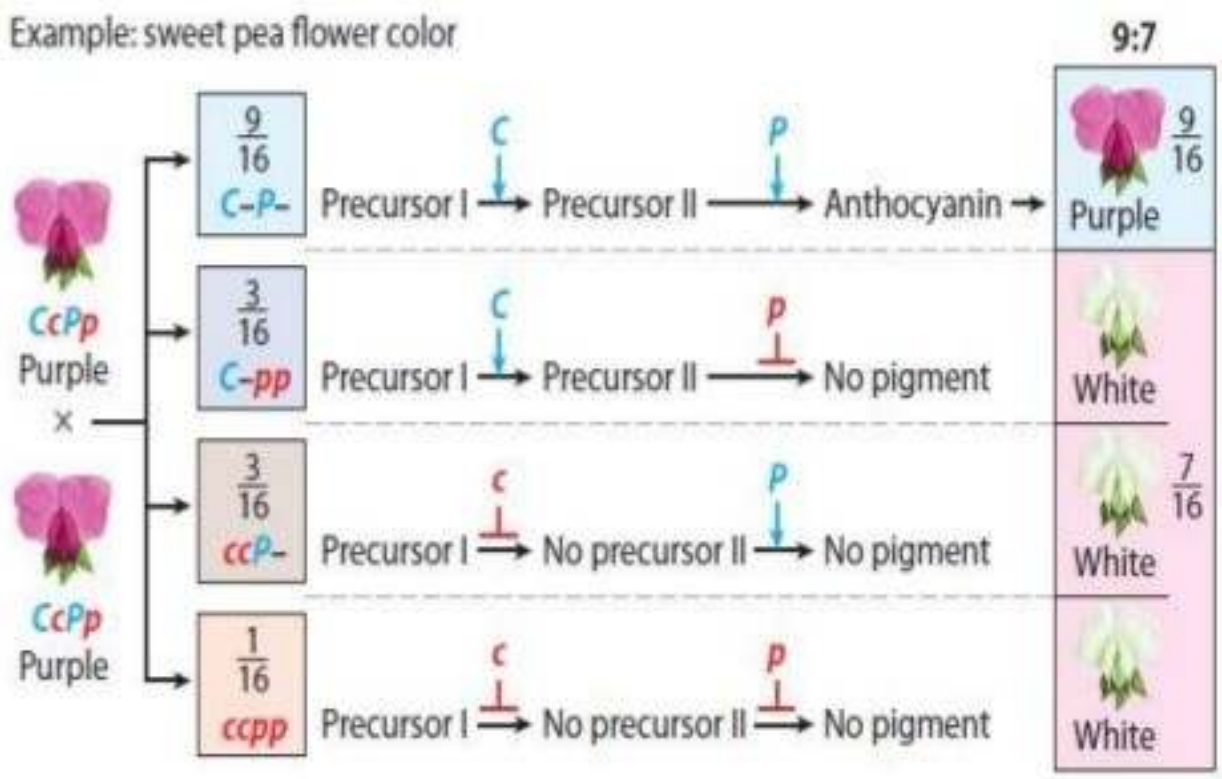
	CP	Cp	cP	cp
CP	CCPP Purple	CCPp Purple	CcPP Purple	CcPp Purple
Cp	CCPp Purple	CCpp White	CcPp Purple	Ccpp White
cP	CcPP Purple	CcPp Purple	ccPP White	ccPp White
cp	CcPp Purple	Ccpp White	ccPp White	ccpp White

9 C_P_ : 3 C_pp :3 ccP_ : 1 ccpp

purple white

Many years after Bateson first described this 9:7 phenotypic ratio in pea plants, researchers were finally able to determine the two genes responsible for it (Dooner *et al*., 1991). These genes control flower color by controlling pea plant biochemistry, in particular that related to pigment compounds called anthocyanins. In peas, there is a two-step chemical reaction that forms anthocyanins; gene *C* is responsible for the first step, and gene *P* is responsible for the second. If either step is nonfunctional,

then no purple pigment is produced, and the affected pea plant bears only white flowers. The dominant *C* and *P* alleles code for functional steps in anthocyanin production, whereas the recessive *c* and *p* alleles code for nonfunctional steps. Thus, if two recessive alleles occur for either gene, white flowers will result.



❖ **C** and **P** products controlling different steps of anthocyanin synthesis pathway . Since anthocyanin production requires the action of the product of **C** as well as the product of **P** , both step must be successfully completed for anthocyanin production and deposition in flower petals .

Petal colour in Primula (Malvidin Production in Primula):

(Sometimes called Dominant Suppression Epistasis. Yields 13:3 ratio)

In the *Primula* plant, the pigment malvidin creates blue-colored flowers. Synthesis of malvidin is controlled by gene *K.* A dominant K allele yields the pigment while a recessive k allele does not yield pigment. The production of this pigment can be suppressed by a dominant *D* allele, which is found at completely different locus. A recessive d allele at this locus does not suppress the expression of the pigment.

Dominant Suppression Epistasis

Example: Malvidin production in Primula (anthocyanin giving blue flower)

KKDD *Non blue* x kkdd *Non blue*

↓

F1 KkDd *Non Blue*

F2	KD	Kd	kD	kd
KD	KKDD	KKDd	KkDD	KkDd
Kd	KKDd	KKdd	KkDd	Kkdd
kD	KkDD	KkDd	kkDD	kkDd
kd	KkDd	Kkdd	kkDd	kkdd

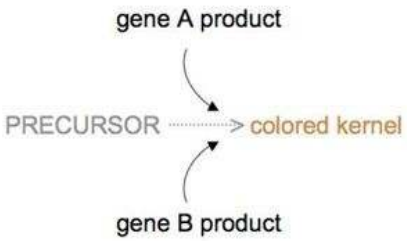
Malvidin production controlled by dominant allele at K locus but the pathway is blocked by a dominant allele at the suppressor locus D

Produces a 13 : 3 ration, like feather colour in chickens

Kernel Colour in Wheat: (Duplicate Genes)

Cross between two wheat plants with coloured kernels and of the genotype AaBb yields the following results-

Genotype	Phenotype	Enzymatic Activites	
9 A_B_	Colored Kernels	Functional enzymes from both genes	15
3 A_bb	Colored Kernels	Functional enzymes from A genes	
3 aaB_	Colored Kernels	Functional enzymes from B genes	
1 aabb	White Kernels	Non Functional enzymes from both genes	1



Genes don't always have to act in opposition to each other for an interaction to be epistatic, however. Sometimes, two genes that each have the same role in protein production can substitute for each other.

The mechanism by which wheat kernel color is determined is an example of duplicate gene action. In wheat, kernel color is dependent upon a biochemical reaction that converts a precursor substance into a pigment, and this reaction can be performed with the product of either gene *A* or gene *B*. Thus, having either a dominant *A* allele or a dominant *B* allele produces color in the kernel, but a lack of either allele (that is homzygous recessive at both A and B locus- aabb) will produce a white kernel.

Fruit Colour in Squashes:

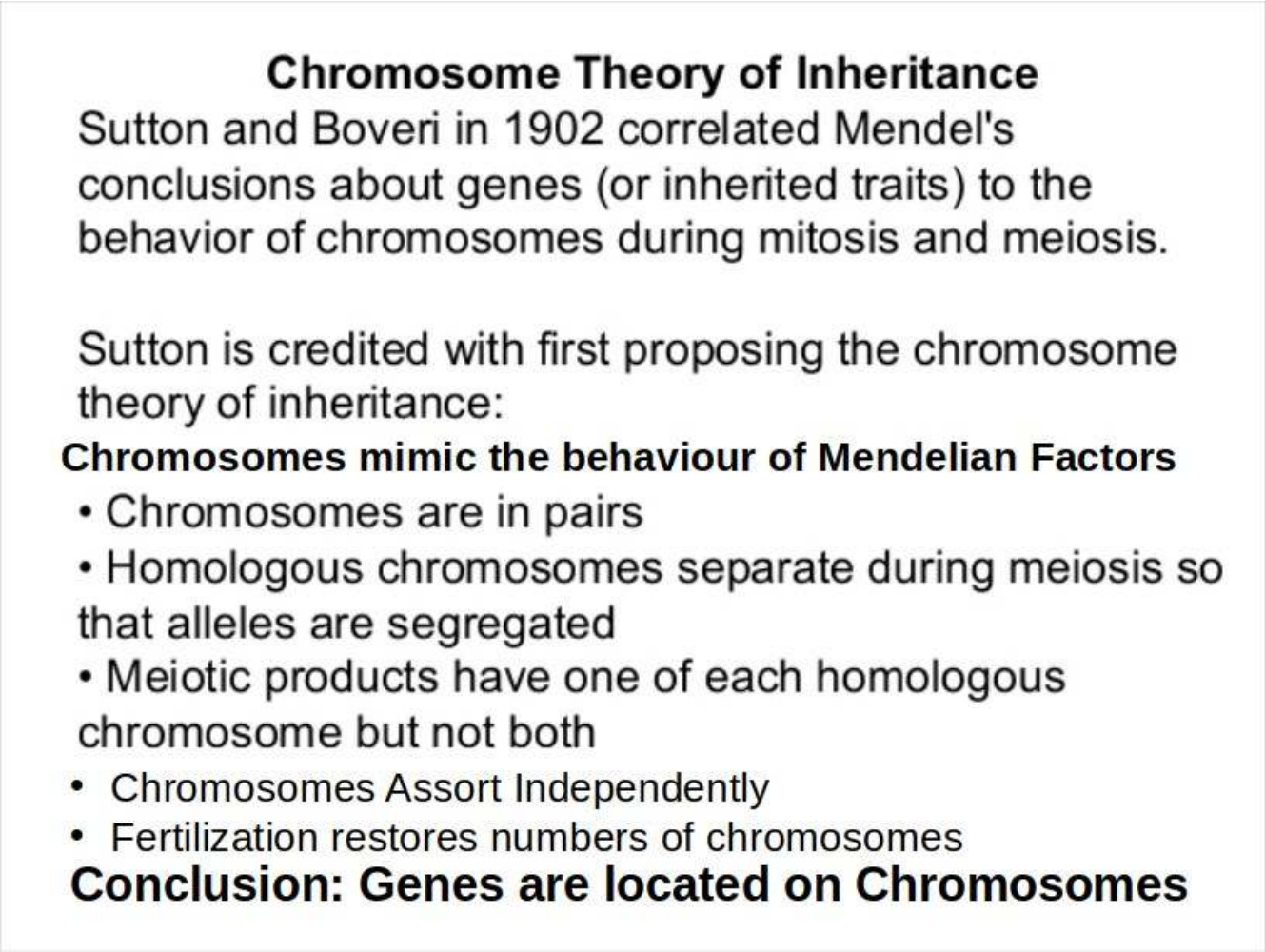
At one locus, dominant W=No colour and recessive *w*=colored. At the second gene yellow is dominant to green, and the symbols used are *G*=yellow, *g*=green. If the dihybrid is selfed, three phenotypes are produced in a 12:3:1 ratio. The following table explains how this ratio is obtained.

Genotype	Fruit Color	Gene Actions
9 *W_G_*	White	Dominant W allele negates effect of *G* allele
3 *W_gg*	White	Dominant W allele negates effect of *g* allele
3 *wwG_*	Yellow	Recessive w allele allows yellow allele expression
1 wwgg	Green	Recessive w allele allows green allele expression

Today, scientists know that Mendel's predictions about inheritance depended on the genes he chose to study. Specifically, Mendel carefully selected seven genes that affected seven different traits. However, unlike the phenotypes that Mendel considered, the majority of phenotypes are affected by more than one gene. Indeed, most of the characteristics of organisms are much more complex than the characteristics that Mendel studied, and epistasis is one source of this complexity. Epistasis can occur in a variety of different ways and result in a variety of different phenotypic ratios, as illustrated in Table below.

Examples of Digenic Epistatic Ratios

Ratio	**Description**	**Name(s) of Relationship (Used by Some Authors)**
9:3:3:1	Complete dominance at both gene pairs; new phenotypes result from interaction between dominant alleles, as well as from interaction between both homozygous recessives	Not named because the ratio looks like independent assortment
9:4:3	Complete dominance at both gene pairs; however, when one gene is homozygous recessive, it hides the phenotype of the other gene	Recessive epistasis
9:7	Complete dominance at both gene pairs; however, when either gene is homozygous recessive, it hides the effect of the other gene	Duplicate recessive epistasis
12:3:1	Complete dominance at both gene pairs; however, when one gene is dominant, it hides the phenotype of the other gene	Dominant epistasis
15:1	Complete dominance at both gene pairs; however, when either gene is dominant, it hides the effects of the other gene	Duplicate dominant epistasis
13:3	Complete dominance at both gene pairs; however, when either gene is dominant, it hides the effects of the other gene	Dominant and recessive epistasis
9:6:1	Complete dominance at both gene pairs; however, when either gene is dominant, it hides the effects of the other gene	Duplicate interaction
7:6:3	Complete dominance at one gene pair and partial dominance at the other; when homozygous recessive, the first gene is epistatic to the second gene	No name
3:6:3:4	Complete dominance at one gene pair and partial dominance at the other; when homozygous recessive, either gene hides the effects of the other gene; when both genes are homozygous recessive, the second gene hides the effects of the first	No name
11:5	Complete dominance for both gene pairs only if both kinds of dominant alleles are present; otherwise, the recessive phenotype appears	No name



Sex- Linked Inheritance (X-Linked Inheritance): T H Morgan

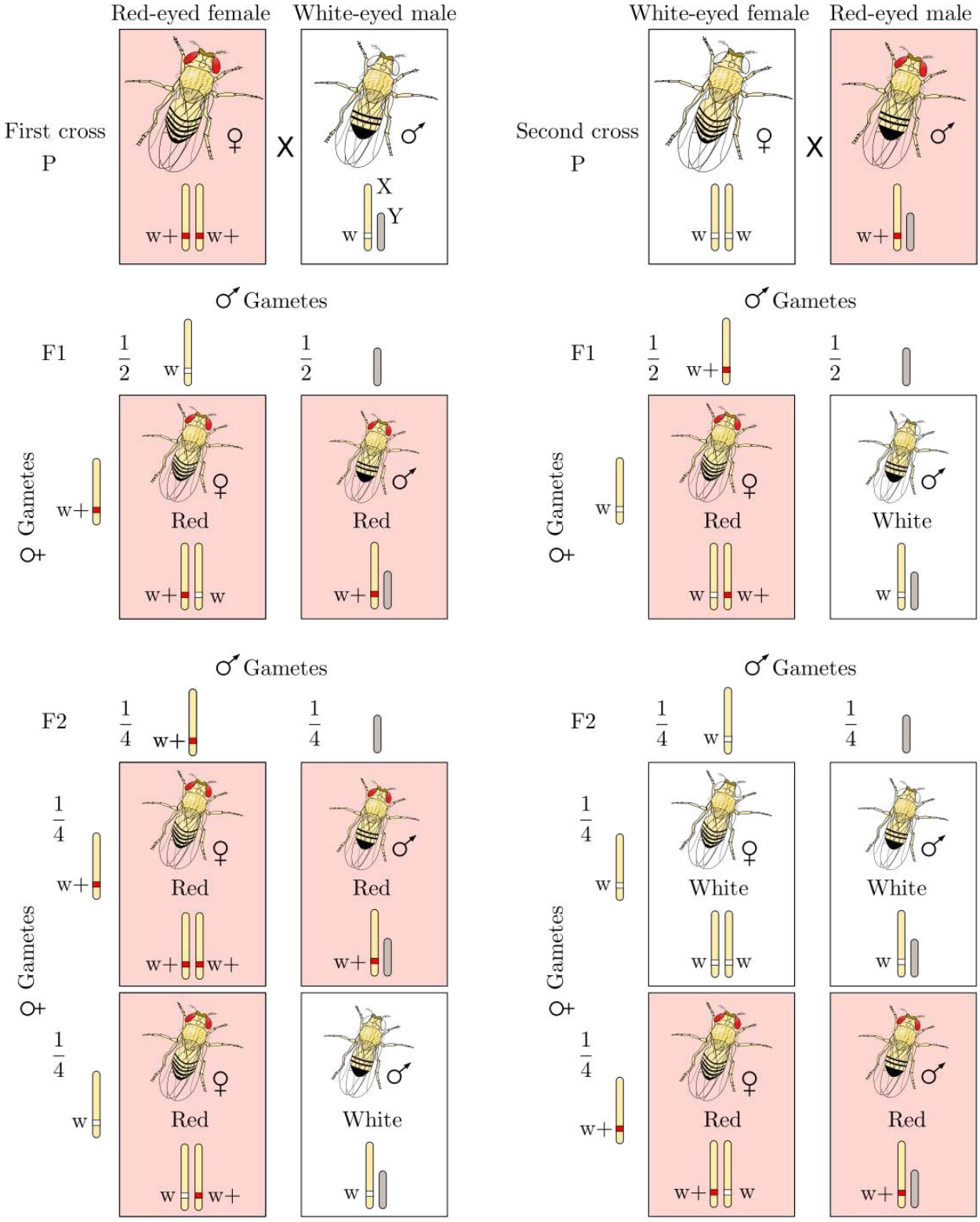
Inheritance of white eye colour in *Drosophila melanogaster*

In the crosses below, w+ represents dominant, red eye colour allele and w represents the recessive white eye colour allele.

(https://www.nature.com/scitable/topicpage/thomas-hunt-morgan-and-sex-linkage-452/)

One day in 1910, American geneticist Thomas Hunt Morgan peered through a hand lens at a male fruit fly, and he noticed it didn't look right. Instead of having the normally brilliant red eyes of wild-type *Drosophila melanogaster*, this fly had white eyes. Morgan was particularly interested in how traits were inherited and distributed in developing organisms, and he wondered what caused this fly's eyes to deviate from the norm. Morgan's fly lab at Columbia University was already in the habit of breeding *Drosophila* so that the researchers there could observe the transmission of genetic traits through successive generations, so Morgan chose to do a simple breeding analysis to find out more about white eyes. Little did Morgan know that, with this white-eyed fly, he was about to confirm the chromosome

theory of inheritance. In doing so, Morgan would also be the first person to definitively link the inheritance of a specific trait with a particular chromosome.



Morgan found several deviations from Mendel’s results-

The reciprocal crosses yielded different results.

In the second cross above, the F1 males and females showed different phenotypes.

In the F2 of both crosses, the observed ratio was different from teh expected Mendelian ratio (that is, both males and females of F2 should show a 3:1 ratio of dominant to recessive phenotype). So how was the white eye character inherited?

Therefore, Morgan hypothesised that the white eye allele was on the X chromosome and was recessive to the red eye allele. This clearly explained the pattern of inheritance. **Thus Morgan was teh first person to definitively link the inheritance of a particular character to the inheritance of a particular chromosome. Thus he provided the first clear evidence for the Chromosomal Theory of inheritance.**

Inheritance of Sex Chromosomes in *Drosophila melanogaster*:

In order to understand Morgan's experiments aimed at answering this question, it is first helpful to review the pattern of sex chromosome inheritance in fruit flies.

In *Drosophila melanogaster*, normal males have XY chromosomes while normal females have XX chromosomes.

Note that males have only one X chromosome, which means that the male phenotype is not reflective of a dominant or recessive trait, but rather, it is merely reflective of the only sex chromosome that the male fly carries. Geneticists refer to the state of the male genotype (with only one X chromosome) as hemizygous. For x-linked characters, males are **Hemizygous**. Whatever the allele on the X chromosome of a male, it will be expressed.

When a female fly (denoted *XX*) is crossed with a male fly (denoted *XY*), their offspring will be 50% female and 50% male.

Inheritance of sex chromosomes in *D. melangaster*

		Male Gametes	
		X	*Y*
Female Gametes	*X*	*XX*	*XY*
	X	*XX*	*XY*

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Note: This is merely describing how sex chromosomes are inhertited ie., passed on from parents to offspring. This does not mean that XX determines female sex and XY determines male sex.

In Drosophila melanogaster, sex is determined by X chromosome, Autosome ratio. Assume the following values for chromosomes-

One X chromosome = 1, one entire set of autosomes, A = 1, Y chromosome = 0.

Any individual with a X chromosome to Autosome ratio of 0.5 is a male while an individual with a ratio of 1 is a female.

Chromosomes	Ratio	Sex
XY, AA	(1+0)/(1+1) = 0.5	Male, fertie
XO, AA	(1+0)/(1+1) = 0.5	Male, sterile
XX, AA	(1+1)/(1+1) = 1	Female, fertile
XXY, AA	(1+1)/(1+1) = 1	Female, fertile

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The Importance of Morgan’s discovery:

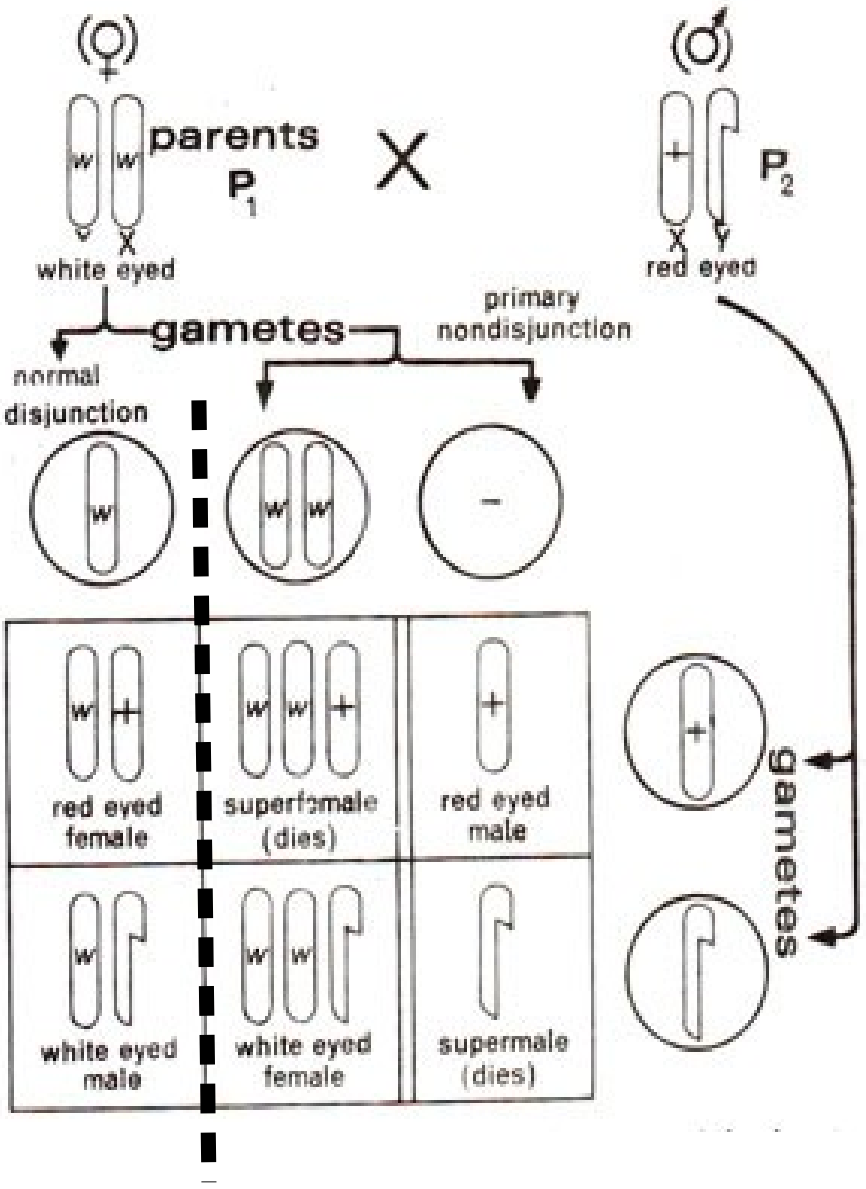
Morgan's conclusion—that the white-eye trait followed patterns of sex chromosome inheritance—was at once very specific and very grand. A few years prior to these test crosses, Mendelian ideas of inheritance had been enthusiastically discussed by many researchers in the context of new findings about chromosomes. Indeed, after observing meiotic reductive divisions and correlating them to chromosome counts in male and female offspring, cytologists Walter Sutton, Nettie Stevens, and E. B. Wilson had all promoted the idea that sex was determined via chromosome based inheritance. Morgan, however, had long resisted the idea that genes resided on chromosomes, because he did not approve of scientific data acquired by passive observation. Furthermore, Morgan was not convinced that traits couldn't morph into new forms in an organism based on the blending of parental contributions, an idea leftover from pre-Mendelian scientists. Morgan was sure that Wilson and the other researchers who promoted the chromosome theory of inheritance were looking for an easy answer as to how independent assortment occurred in gamete formation, because he believed they ignored counterevidence in the face of excited conviction. In fact, he thought that the concept of genes was at best an invention intended to link the mysterious paths of chromosomes and discontinuous inheritance patterns. Morgan formalized his derision in a well-known publication (Morgan, 1909), wherein he called for a more experimental approach to the understanding of inherited factors and insisted that germ plasm should not be cast aside as a putative carrier of inherited traits.

Interestingly, within a year of this public criticism of chromosome theory, Morgan set out to test the idea of inherited chromosomal factors using *Drosophila*. Because Morgan was particularly interested in experiments designed to test hypotheses, he turned to the fly system to maximize data acquisition over short periods of time. Soon after launching these experiments, Morgan saw his white-eyed fly peering back at him through his hand lens. Then, many crosses later, Morgan became convinced by his own empirical evidence that traits could in fact be passed on in the same manner predicted by the inheritance of sex chromosomes. Morgan never looked back, and he developed a huge following of accomplished students over the next few decades. Indeed, for his work with *Drosophila*, Morgan was awarded the Nobel Prize in 1933.

Additional Experiments by Calvin B Bridges on the inheritance of White eye colour in Drosophila:

Bridges, repeated Morgan's experiment with white eyed flies. When he crossed White eyed females with Red eyed males, most of the times he obtained the expected results. However, at a frequency of about one in 2000, the same cross gave him white eyed females and red eyed males as F1 progeny. This was un expected. After a lot of research, Bridges explain this result based on the non-disjunction of X chromosomes in the white eyed female parent.

Additionally, in D. Melanogaster, XO is a sterile male while XXY is a fertile female (see above for explanantion). Therefore, Bridges hypothesisised that teh white eyed F1 female was the XXY type. He obtained proof for this by staining the Oogonial cells of the female and observing the chromosomes.

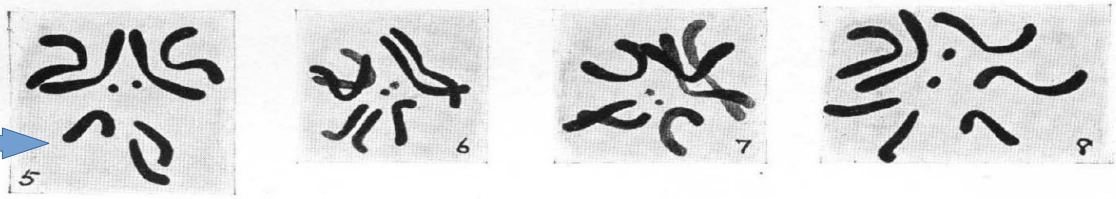


CALVIN B. BRIDGES, NON-DISJUNCTION AND THE CHROMOSOME THEORY

Chromosomes from Normal (XX) females

Chromosomes from XXY females

Y Chromsome



Dosage Compensation

For most autosomal genes, both the alleles are expressed in organisms. Therefore, both males and females have the same “dosage” of autosomal gene products. However for X linked genes, in many animals (with XX-XY system of chromosomes), males have a lower dosage compared to females.

Therefore, there needs to be Dosage Compensation for X linked genes.

Y is gene poor and hence dosage compensation seems not to be important for Y linked genes.

Dosage compensation can occur in two ways (1) Over expression of teh male X chromosome (Drosophila males) or (2) inactivation of the extra X chromosome in females (Mammals).

X- Chromosome inactivation can be (a) Biased (for example, in marsupials, the paternal X is always shut down) or (b) Random (true placental mammals- Eutheria).

Random X inactivation:

During embryonic development in females, at a particular time, one of the two X chromosomes (paternal or maternal) is Randomly chosen and inactivated. Once this decision has been made by a cell, all the subsequent cells in this lineage will shutdown the same X chromosome.

Thus, ON AN AVERAGE, a female eutherian mammal will have paternal X inactivated in 50% of her cells and maternal X inactivated in the other 50%. Please nte that there is a wide variation possible around this expected percentage. That is to say that in some females or in some tissues of given female, one type of X chromosome may have been predominantly inactivated puely by chance while in another female or tissue, this percentage might be quite different.

Thus females are Mosaics with respect to X linked gene products *ie*., some of their cells transcribe paternal X while some others transcribe maternal X chromosome.

An example of such mosaicism is Calico cat whcih is characterised byrandom patches of red and black based colours. All calico cats are females. No two calico cats have identical patches.

The inactivated X chromosome in the females can be seen a s a darkly staining body with in the nucleus of cells. This was first observed by Barr and Bertram. Mary Lyon identified these bodies as the inactivated X chromosomes. These bodies are called “Barr Bodies”. The process of X chromosome inactivation is also called Lyonisation.

Note: In a female, only one X chromosome is kept active. All other chromosomes are converted into Barr bodies. Thsi means that a person with XXX genotype will have two Barr bodies, an XXY individual in Humans will be phenotypically a male (Klienfelter syndrome) but will have a Barr body etc.