Big Idea 3: Living systems store, retrieve, transmit and respond to information essential to life processes.

Enduring understanding 3.A: Heritable information provides for continuity of life.

Essential knowledge 3.A.4: The inheritance pattern of many traits cannot be explained by simple Mendelian genetics.

a. Many traits are the product of multiple genes and/or physiological processes.

Evidence of student learning is a demonstrated understanding of the following:

1. Patterns of inheritance of many traits do not follow ratios predicted by Mendel's laws and can be identified by quantitative analysis, where observed phenotypic ratios statistically differ from the predicted ratios.

Genetics

Main Idea: Today we know that inheritance patterns are often more complex than those predicted by Mendelian genetics.

PREFACE

- We know today and Mendel knew himself that his models could not explain all patterns of observed inheritance.

- *We know today that relationship between genotype and phenotype is not always straightforward.*
- *We know that dominant and recessive genes are not always straightforward.*
- *We know that some traits are controlled by more than two alleles.*
- *We know that some genes control multiple traits.*
- *We know that some genes control other the expression of other genes.*

PREFACE

- Although we know that patterns of inheritance extend beyond patterns described by Mendelian models his Law of Segregation and the Law of Independent Assortment hold true and are applicable to even the most most complicated patterns of heredity.

Degrees of Dominance

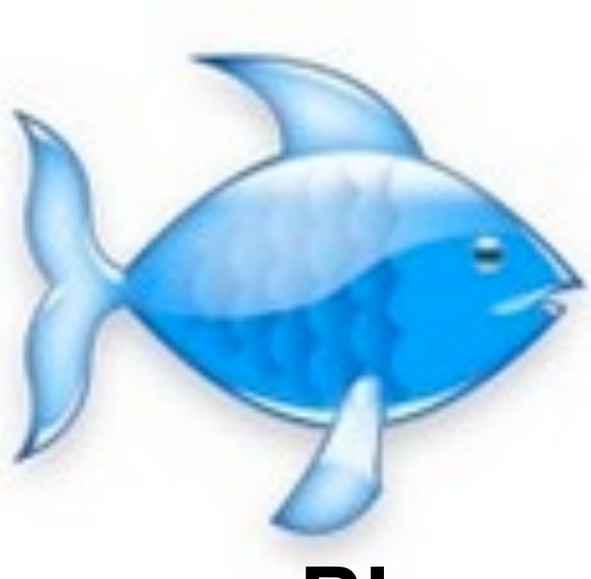
- Alleles can show different degrees of dominance.
- The alleles that Mendel worked with happen to be exhibit **complete dominance**; were the phenotypes of the heterozygous and homozygous dominant are no different.
- In other cases alleles are **incompletely dominant** and In yet in other cases both alleles may be dominant. **Codominance**

Codominance

Red

C^RC^R

X



Blue

C^BC^B

Red & Blue

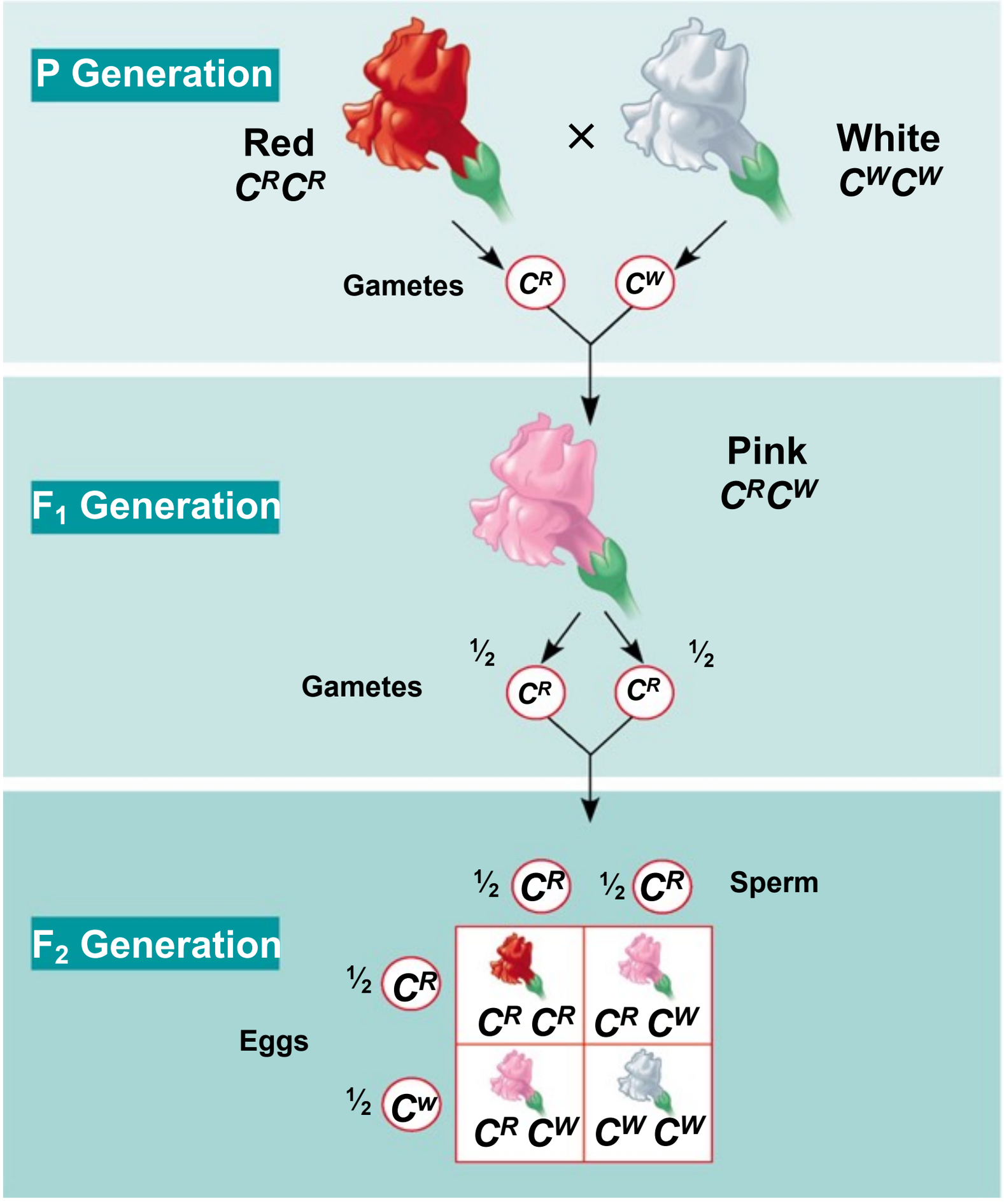
C^RC^B

Red & Blue

C^RC^B

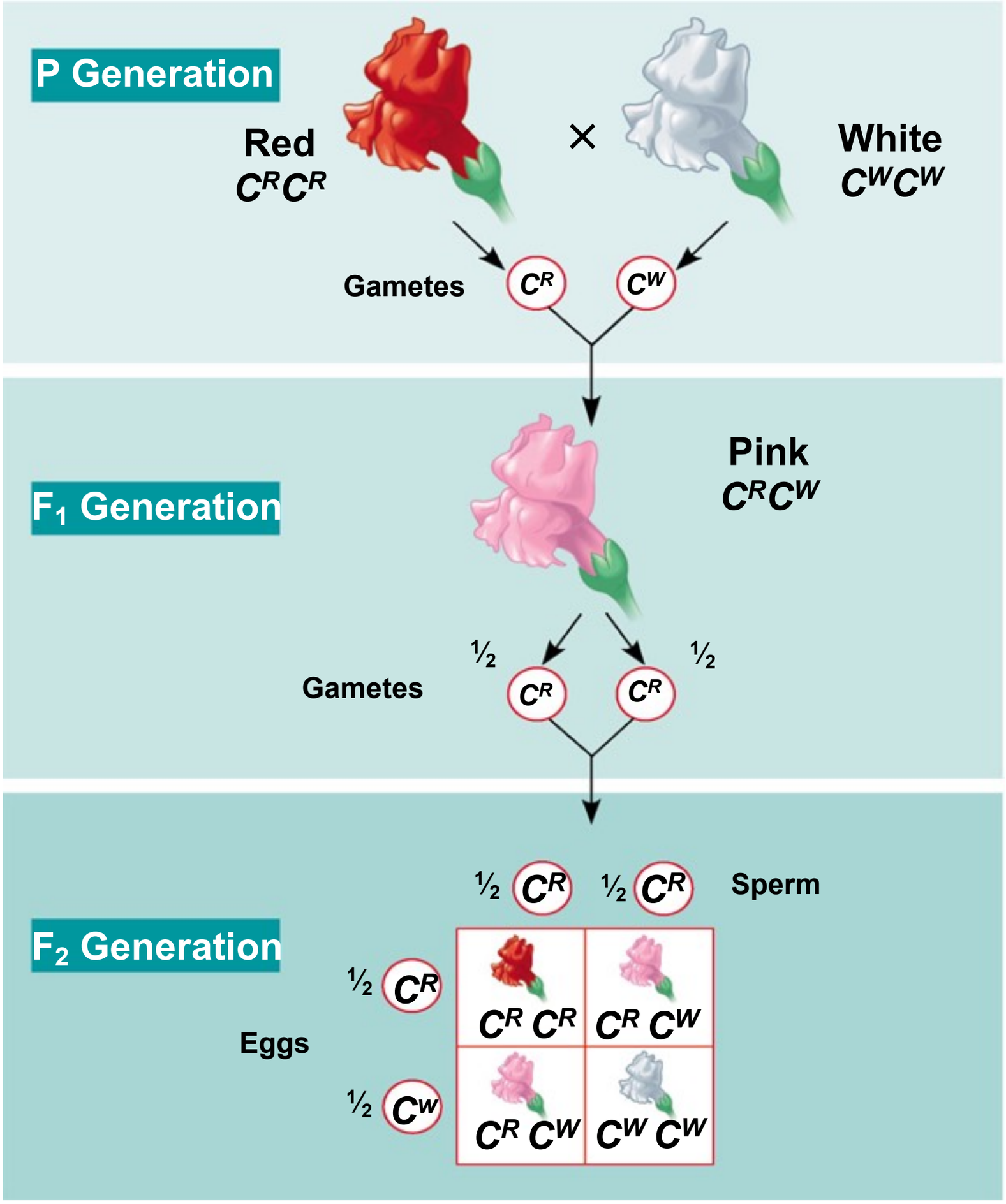
Notice the change in symbolic representation, now we must use all capital letters to show that recessive alleles do not exist and we use superscripts to differentiate between the two

Incomplete Dominance



Incomplete Dominance

This looks like the blending hypothesis! Why does this not support that idea?



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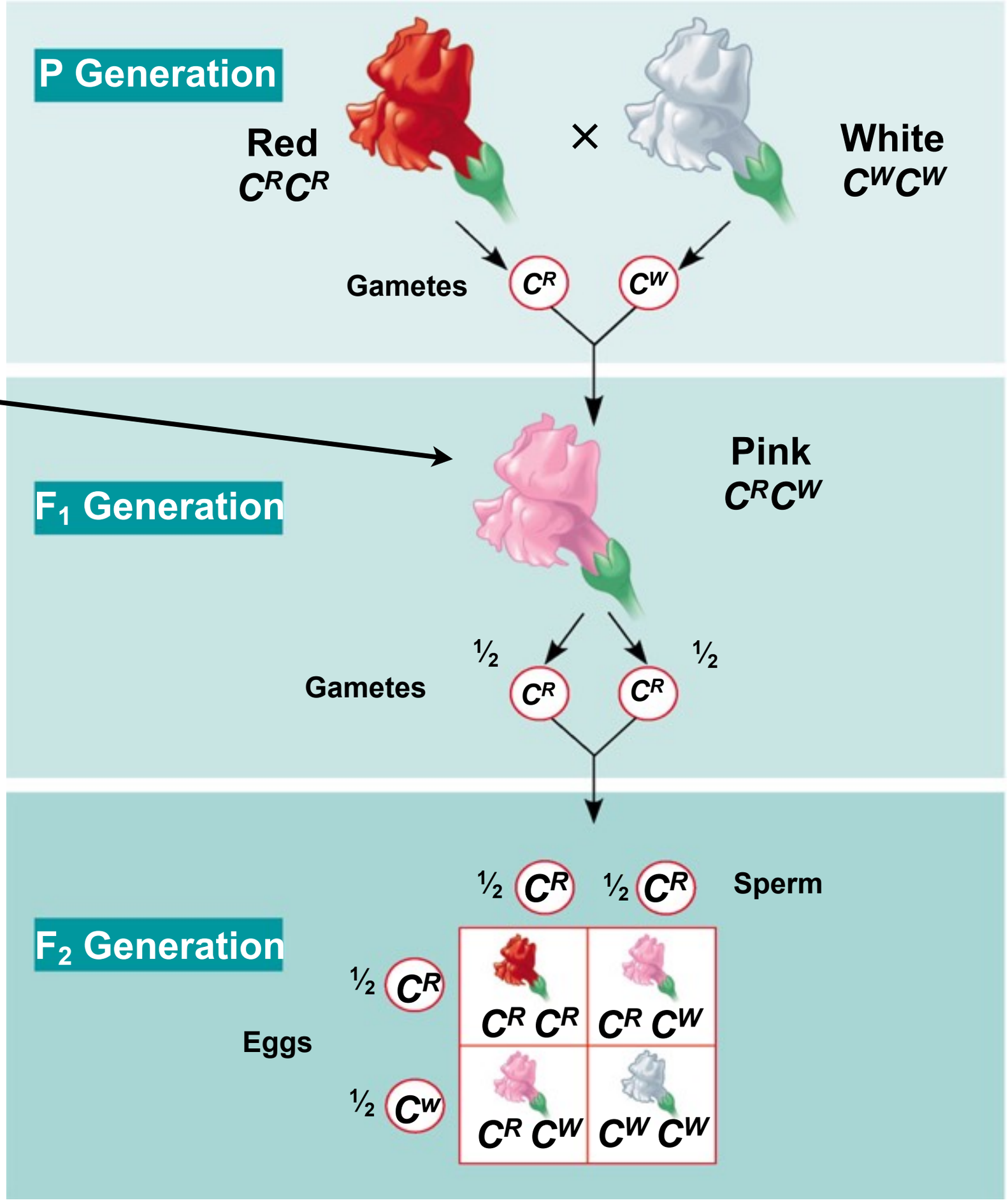
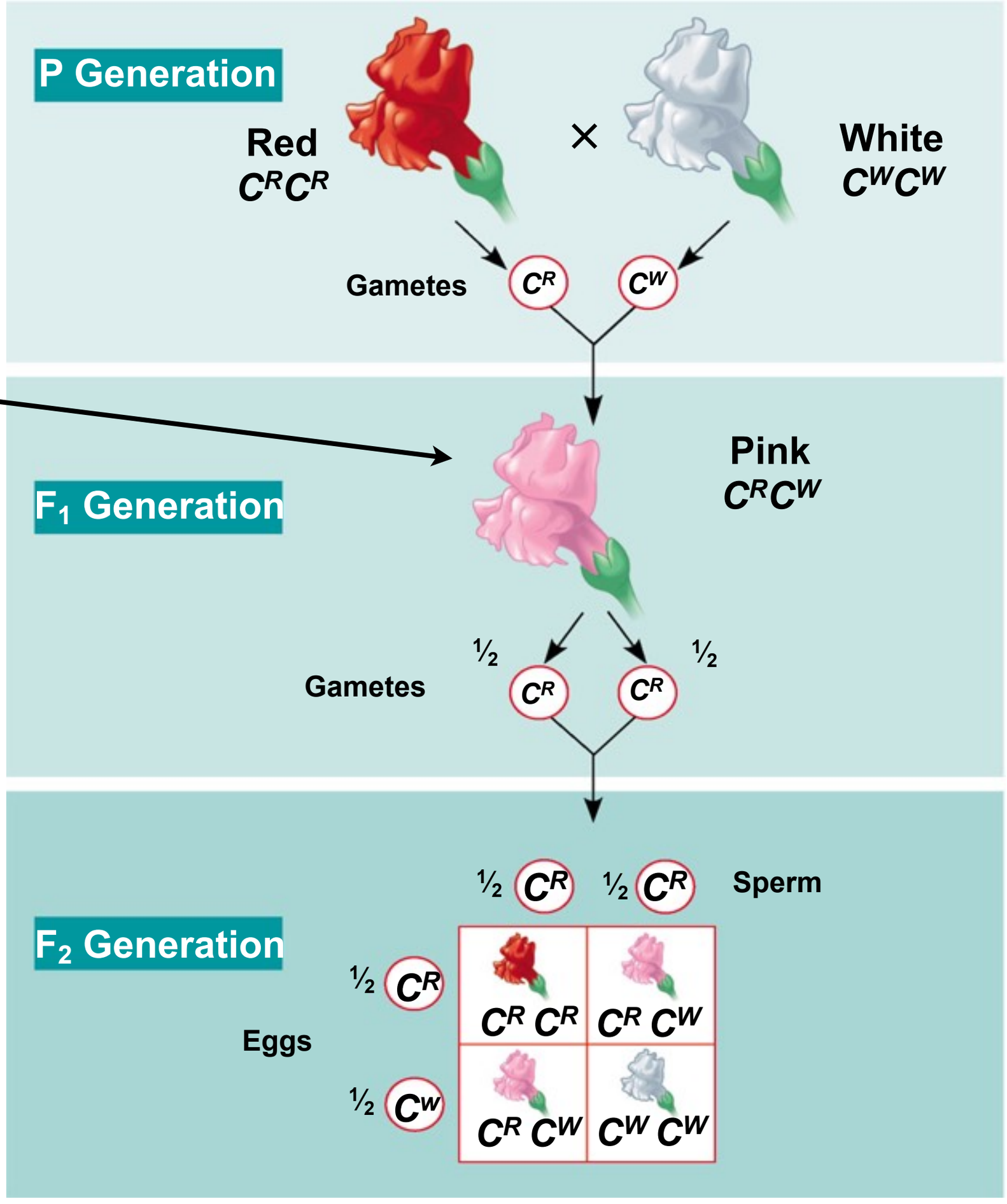


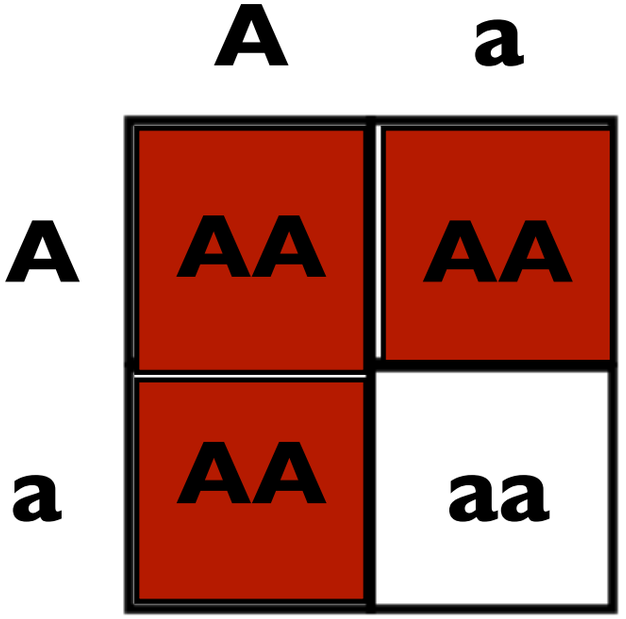
Incomplete Dominance

This looks like the blending hypothesis! Why does this not support that idea?

If the blending hypothesis were correct all F2 offspring would be pink, instead red and white both reappear.

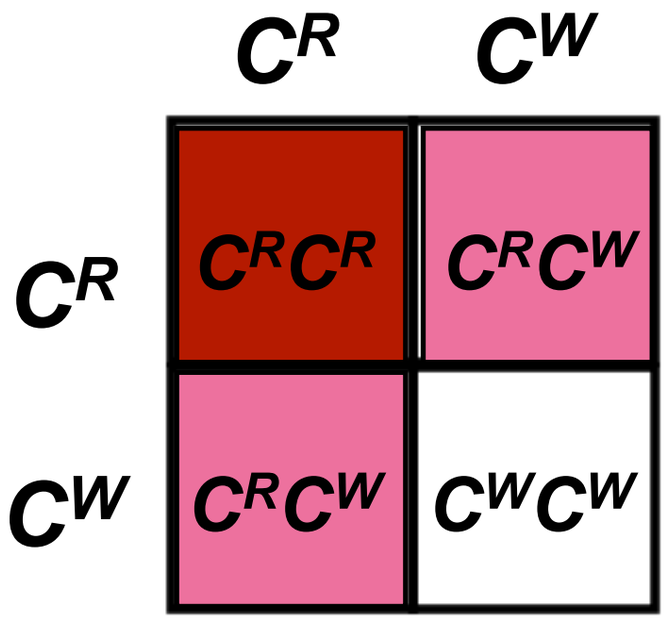


Comparison of Degrees



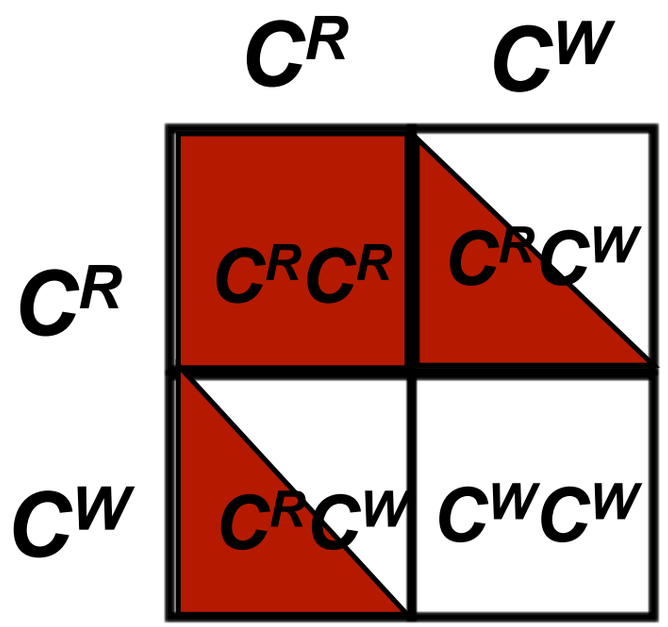
Genotype- 1:2:1
Phenotype- 3:1

Complete Dominance



Genotype- 1:2:1
Phenotype- 1:2:1

Incomplete Dominance



Genotype- 1:2:1
Phenotype- 1:2:1

Codominance

Dominance & Phenotype

- We have seen a range of dominance from complete to incomplete to codominance.
- Understand that alleles are not dominant because they somehow subdue the other gene.
- A dominant gene is simply the gene that is shows up in the phenotype
- Remember alleles are variations in nucleotide sequences, so when a dominant and recessive alleles coexist they do not even actually interact.
- Thus it is the pathway from genotype to phenotype that dominance comes into play

Dominance & Phenotype

Unbranched Starch

r= ↓ **Defective Enzyme**

Unbranched Starch

↓

Excessive Water Enters

↘

seed dries

Having one dominant allele results in 50% of the "enzymes" being effective. As we can see having at least 50% of the enzymes effective converts enough unbranched starch that we see the smooth phenotype.

Unbranched Starch

R= ↓ **Effective Enzyme**

Branched Starch

↓

Normal Amount Water Enters Seed

↙

seed dries

Dominance & Phenotype

- In fact this relationship is even more intriguing.
- For any character, the observed dominant/recessive relationship of alleles depends on the level at which we examine the phenotype.
- Consider **Tay-Sachs Disease**, an inherited disorder in humans that results in seizures, blindness, degeneration of motor and mental skills all followed by death because a faulty enzyme in brain cells allows lipids to accumulate to dangerous levels.

Carrier Statistics

1 in 27 Ashkenazi Jews, French Canadians, or Louisiana Cajuns...

1 in 50 Irish-Americans...

1 in 250 from the general population...

Carries the Tay-Sachs gene!

Tay-Sachs Genetics

Consider a carrier for the disease: **Aa**

- Organismal Level: The genotype of **Aa** is free of disease,
  - *thus the **A** to **a** relationship is simple and complete dominance.*

Tay-Sachs Genetics

Consider a carrier for the disease: **Aa**

- Biochemical Level: The **AA** shows no lipid accumulation, the **aa** shows deadly levels of lipid accumulation and the **Aa** shows lipid accumulation but not to deadly levels,
  - *thus the **A** to **a** relationship is incomplete dominance.*

Tay-Sachs Genetics

Consider a carrier for the disease: **Aa**

- Molecular Level: The **AA** shows 100% effective enzymes, the **aa** shows 0% effective enzymes and the **Aa** shows 50% effective enzymes,
- *thus the **A** to **a** relationship is codominance.*

Frequency of Dominant Alleles

- **Dominant alleles are NOT necessarily more common in population.**

- Consider polydactyly, a condition where humans are born with extra toes or fingers.

- Some cases of polydactyly are caused by a dominant allele.

- Only 1 in 400 babies are born with this condition, thus most people are homozygous recessive.

- Same is true of blood group alleles, the recessive gene "i" is more common globally than either of the dominant forms.

    - *About 63% of all people worldwide carry the recessive "i" allele.*

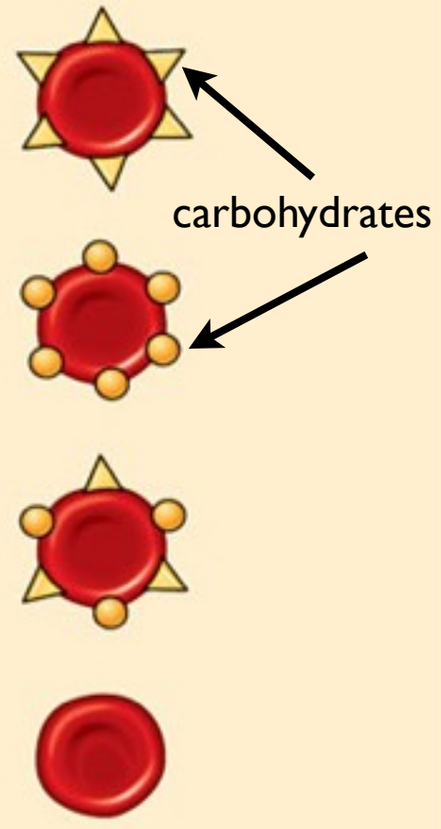
Multiple Alleles

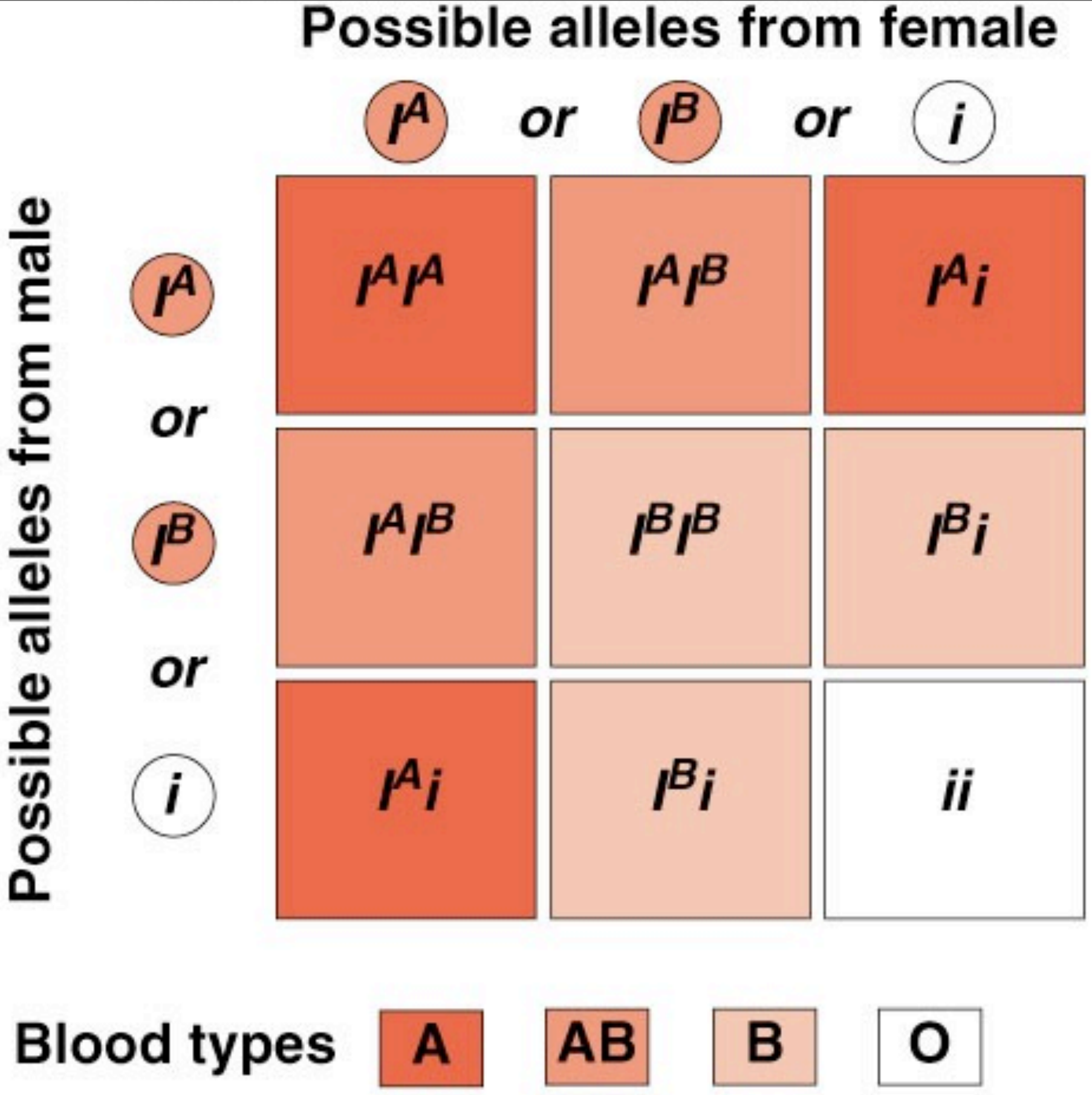
- Some traits are controlled by more than two alleles.
- Some traits are controlled by more than two alleles for instance the ABO blood groups.
- The ABO blood groups are controlled by two codominant alleles and one recessive allele.

Type "O" used to be called "C" but was later changed to reflect the german word "ohne" meaning without.

Determination of ABO Blood Group by Multiple Alleles

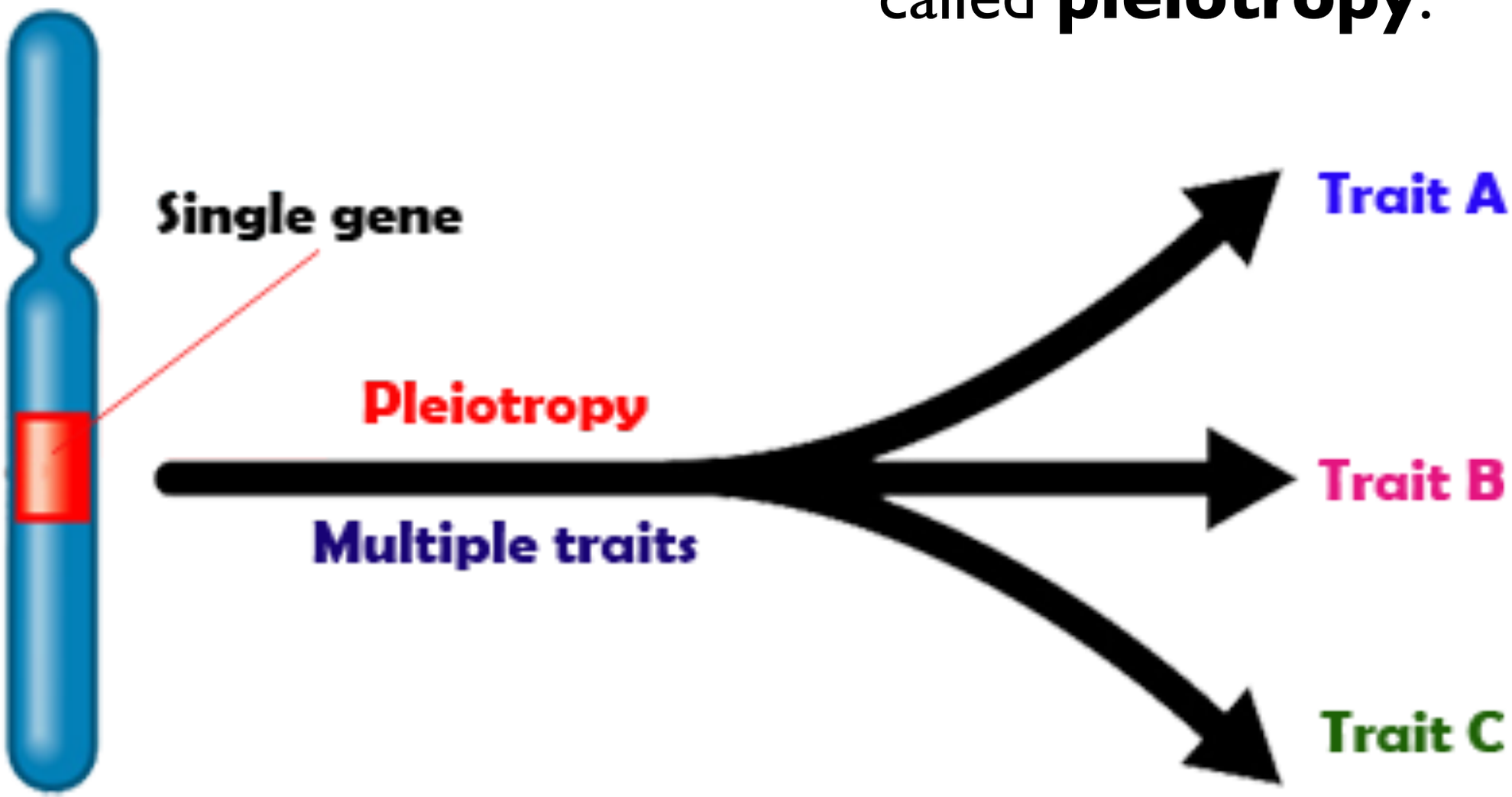
Genotype	Phenotype (Blood Group)	Red Blood Cells
$I^A I^A$ or $I^A i$	A	
$I^B I^B$ or $I^B i$	B	
$I^A I^B$	AB	
ii	O	




Possible alleles from female
I^A or I^B or i
Possible alleles from male
I^A or I^B or i
$I^A I^A$
$I^A I^B$
$I^A i$
$I^A I^B$
$I^B I^B$
$I^B i$
$I^A i$
$I^B i$
ii
Blood types
A
AB
B
O

Pleiotropy

- Most genes have multiple phenotypic effects, a property called **pleiotropy**.



Pleiotropy

The gene that affects pigmentation in cats also affects hearing.

Approximately 40% of white fur, blue eyed cats are deaf.

The gene that causes Frizzle feathered trait also effects the chickens: metabolic rate, body temp, digestive capacity, blood flow and the number of eggs they lay.

Epistasis

- In **epistasis**, the phenotypic expression of a gene at one locus alters that of a gene at a second locus.

B- E-

bb E-

B- ee

bb ee

B- black pigment
b- brown pigment

E- controls/allows pigment deposition
e- controls/ does not allow pigment deposition

Epistasis

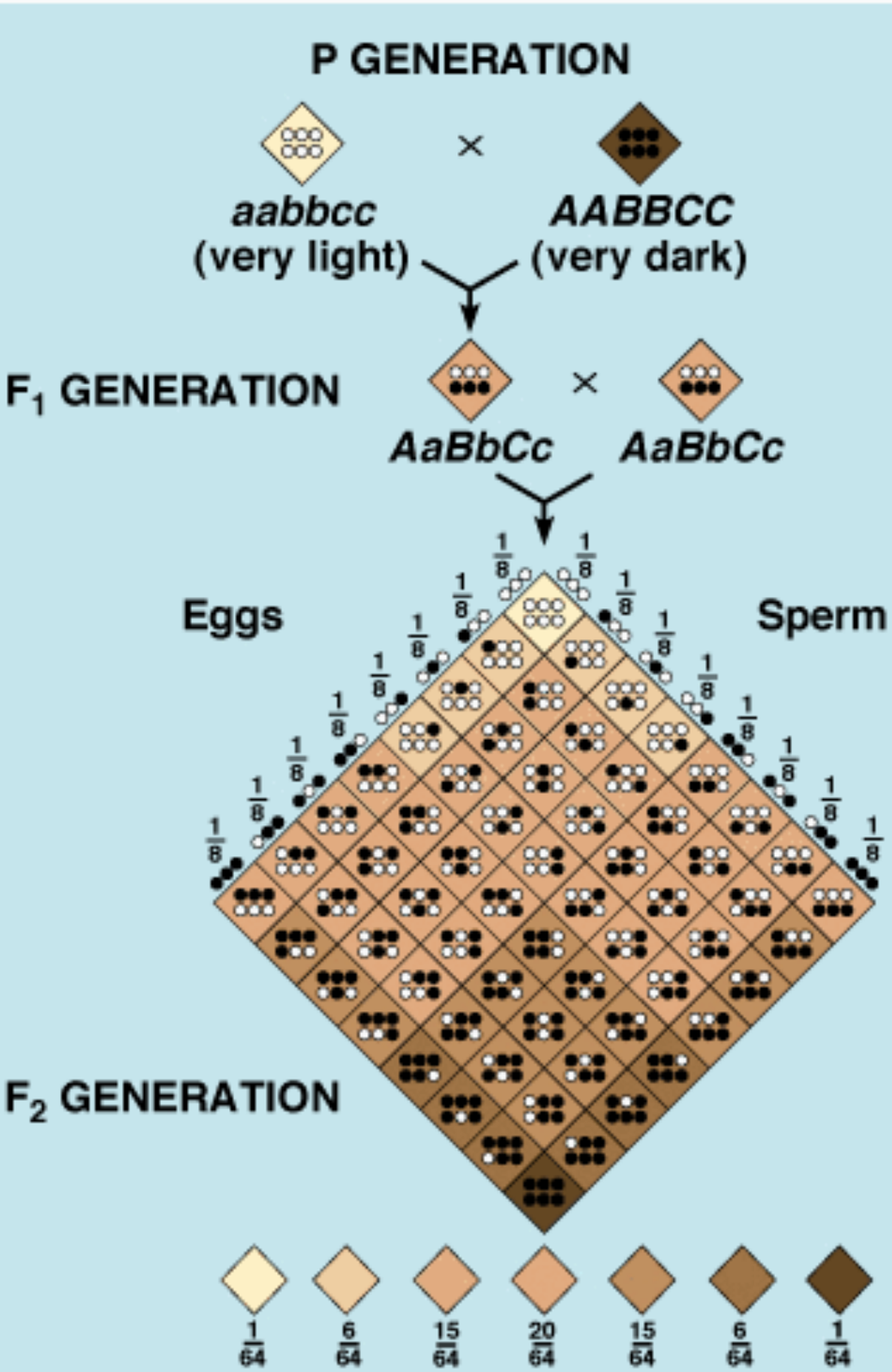
	AB	Ab	aB	ab
AB	 AABB Walnut	 AABb Walnut	 AaBB Walnut	 AaBb Walnut
Ab	 AABb Walnut	 AAbb Rose	 AaBb Walnut	 Aabb Rose
aB	 AaBB Walnut	 AaBb Walnut	 aaBB Pea	 aaBb Pea
ab	 AaBb Walnut	 Aabb Rose	 aaBb Pea	 aabb Single

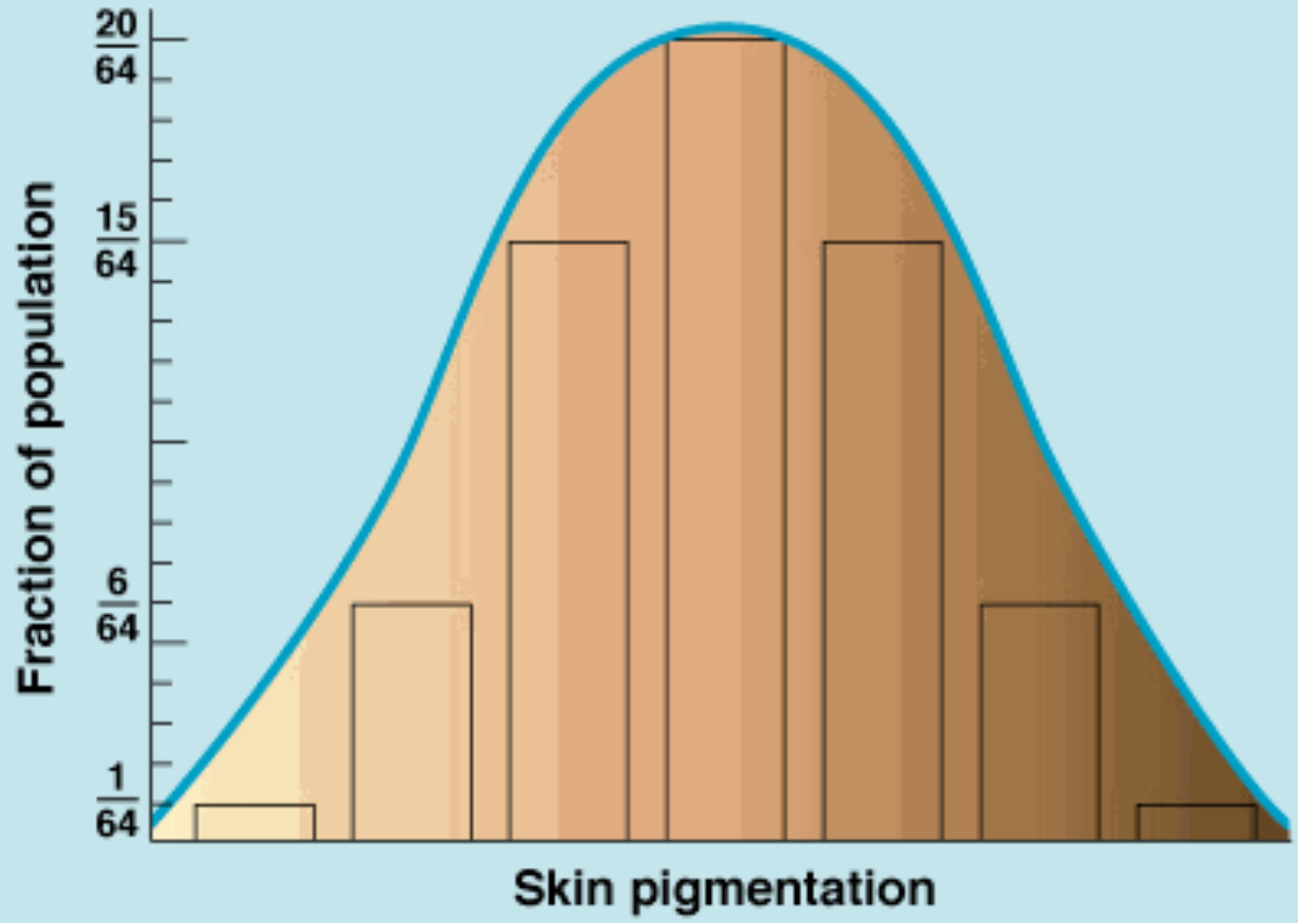
Polygenic Inheritance

- Mendel studied traits that could be described as "either-or traits".
  - *smooth OR wrinkled seeds, purple OR white flowers*
- Many characters can not be described in this manner because they display themselves in a continuum or gradation, they are called **quantitative characters**.

- Quantitative characters usually indicates **polygenic inheritance**, an additive effect of two or more genes on a single phenotypic character.

Skin Color is Polygenic





Note: The environment can also play a role skin color.

Polygenic Inheritance

Environmental Impact on Phenotypes

- Another departure from simple Mendelian inheritance occurs when the environment and the genotype work together to produce the phenotype..
- A TREE, is born with certain and specific genes but its overall shape, branch characteristics and leaf characteristics vary depending on environmental conditions.
  - For example, the number, shape and greenness of its leaves depend on wind, sun, water and nutrient availability.

Nature vs. Nurture

- A HUMAN Being is born with certain and specific genes but many characteristics from skin color to intelligence to height to athletic ability vary depending on environmental conditions.
    - Identical twins although genetically the same develop phenotypic differences through their life.
- The question of whether "WE" are more a product of our genes or our environment is very old and hotly contested.
- Biology can say that genotypes are generally not associated rigidly with a phenotype.
- Rather a "phenotypic range" for a genotype exists due to environmental conditions called the **norm of reaction.**

Norm of Reaction

- Some traits have a very narrow norm of reaction like ABO blood groups.
  - If your genotype is "ii" then you will have O blood.
- Other traits have a broad norm of reaction like blood cell count.
  - The number of blood cells varies widely due to altitude, physical fitness and infections.
- Generally norm of reaction is broadest in polygenic traits and are consequently termed **multifactorial characters** by many geneticists.

Essential knowledge 3.A.4: The inheritance pattern of many traits cannot be explained by simple Mendelian genetics.

b. Some traits are determined by genes on sex chromosomes.

To foster student understanding of this concept, instructors can choose an illustrative example such as:

- Sex-linked genes reside on sex chromosomes (X in humans).
- In mammals and flies, the Y chromosome is very small and carries few genes.
- In mammals and flies, females are XX and males are XY; as such, X-linked recessive traits are always expressed in males.
- Some traits are sex limited, and expression depends on the sex of the individual, such as milk production in female mammals and pattern baldness in males.

Sex Linked Inheritance

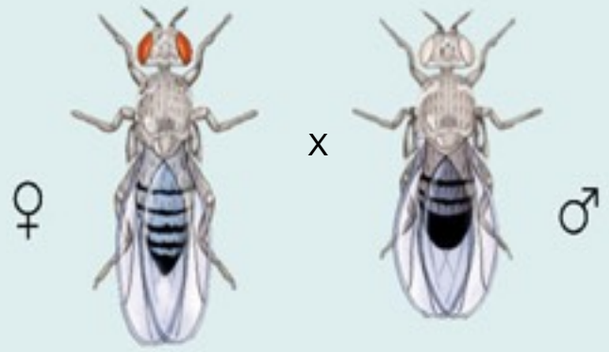
- Thomas Hunt Morgan, an embryologist from Columbia University, provided the first solid evidence that genes were in fact located on chromosomes.
    - *Like Mendel his discovery was both insightful and a little lucky.*
- After years of tedious work with fruit flies, Morgan provided the first support for the **chromosome theory of inheritance**, that specific genes are carried on specific chromosomes.
    - *fruit flies breed quickly and have only 4 chromosomes*
- In addition, he showed that genes located on the sex chromosomes exhibit a unique pattern of inheritance.

Morgan's Experiment

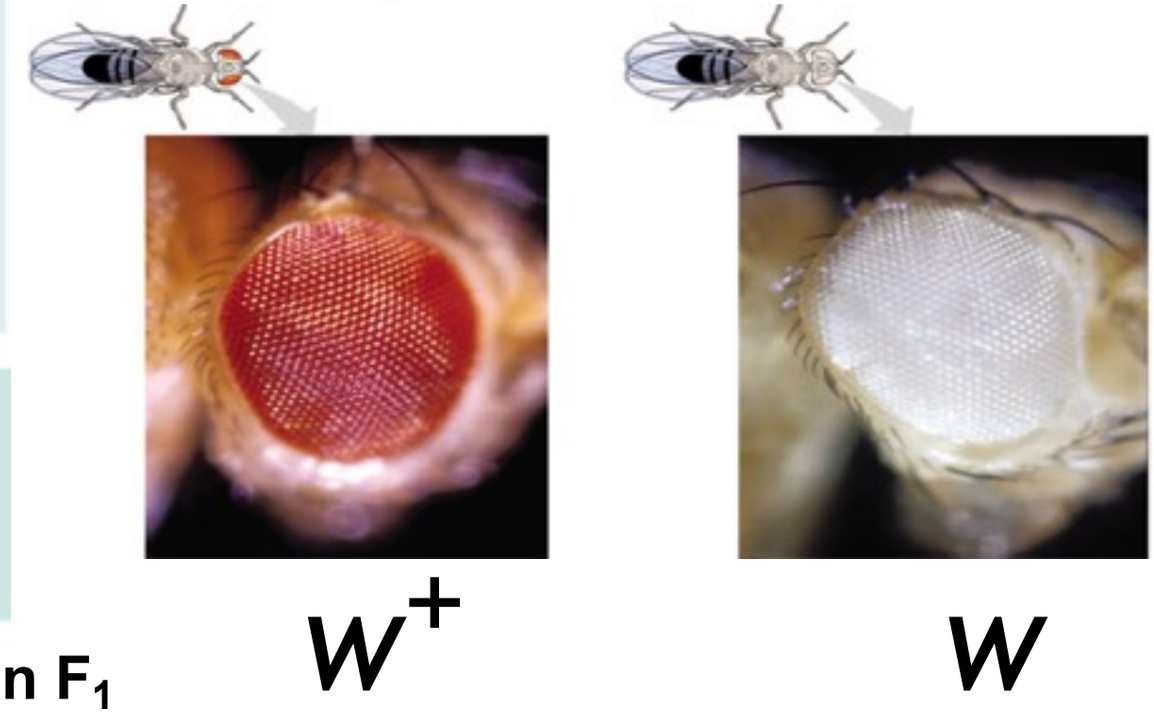
Morgan mated a wild-type (red-eyed) female with a mutant white-eyed male. The F_1 offspring all had red eyes.

EXPERIMENT

P Generation



F_1 Generation



Morgan then bred an F_1 red-eyed female to an F_1 red-eyed male to produce the F_2 generation.

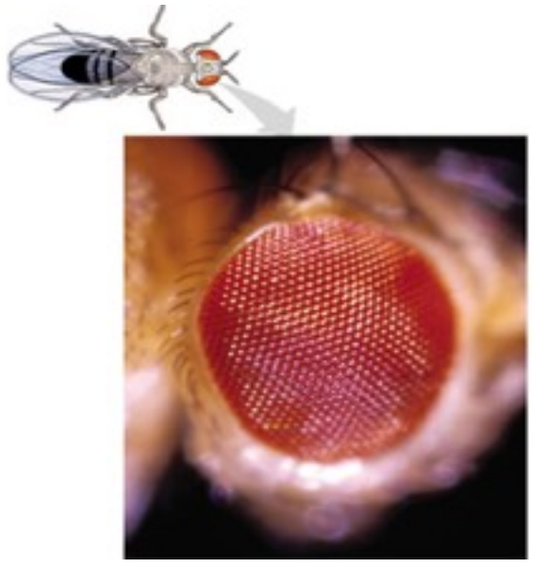
RESULTS

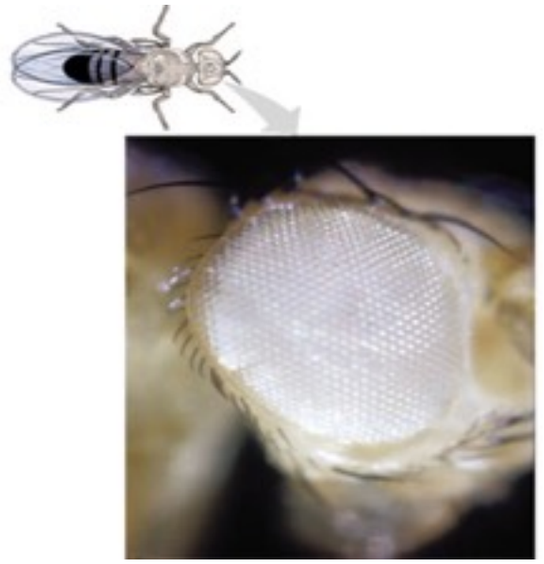
F_2 Generation

The F_2 generation showed a typical Mendelian 3:1 ratio of red eyes to white eyes. However, no females displayed the white-eye trait; they all had red eyes. Half the males had white eyes, and half had red eyes.

Fruit Fly Genetic Symbols

Now called "wild type" instead of dominant





Now called "mutant" instead of recessive

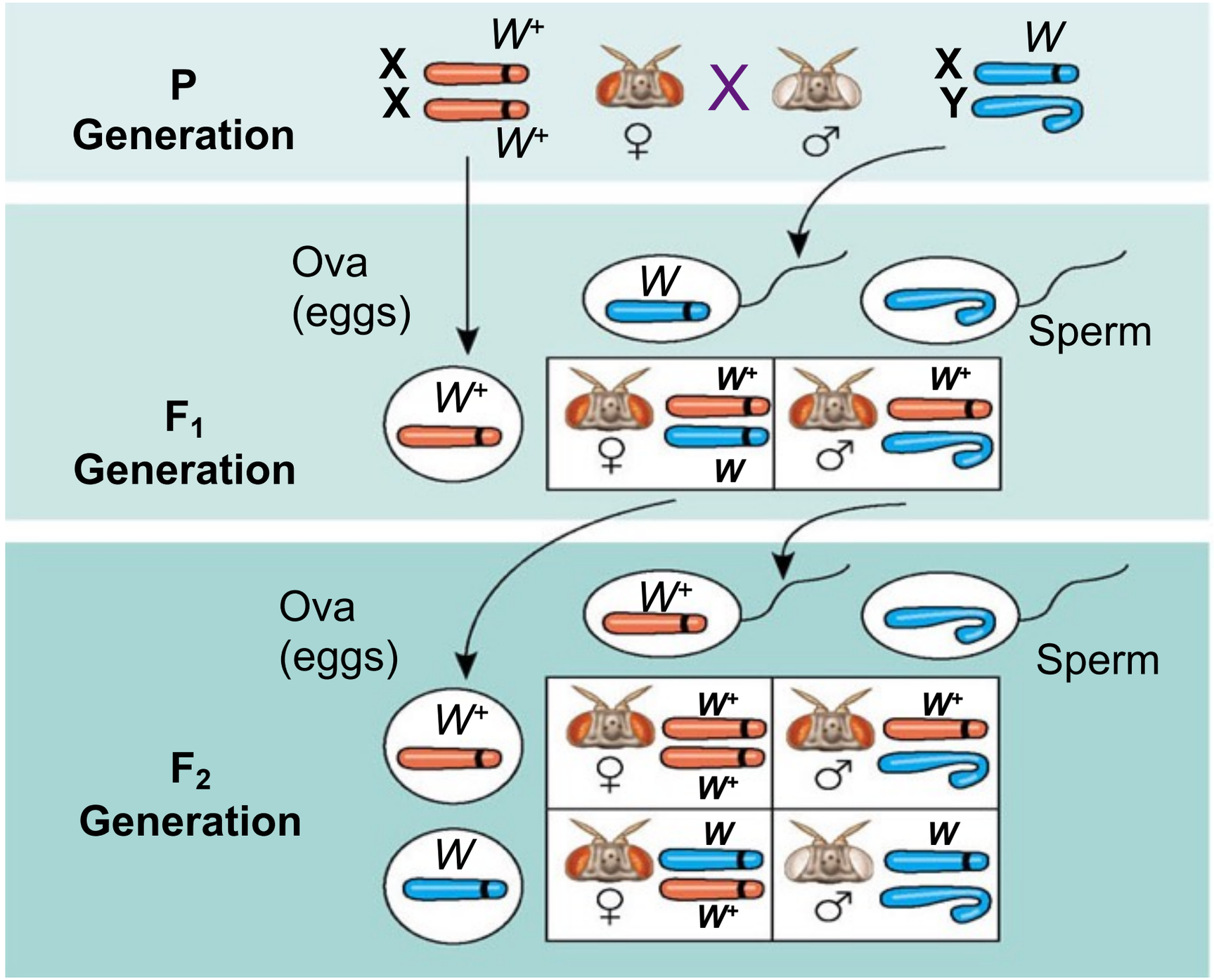
(+) superscript now used instead of capital letter

W^+

W lower case letters still used for recessive allele

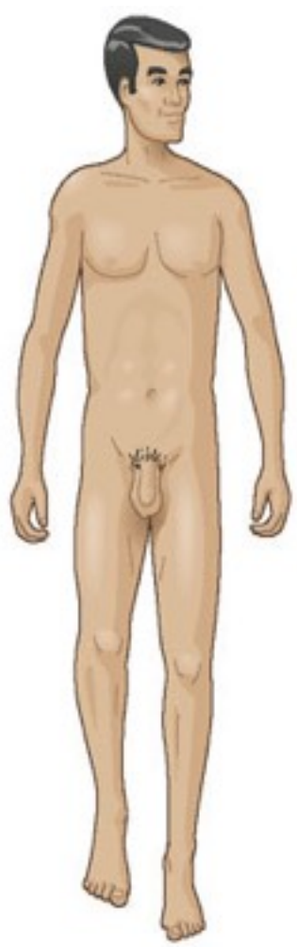
CONCLUSION

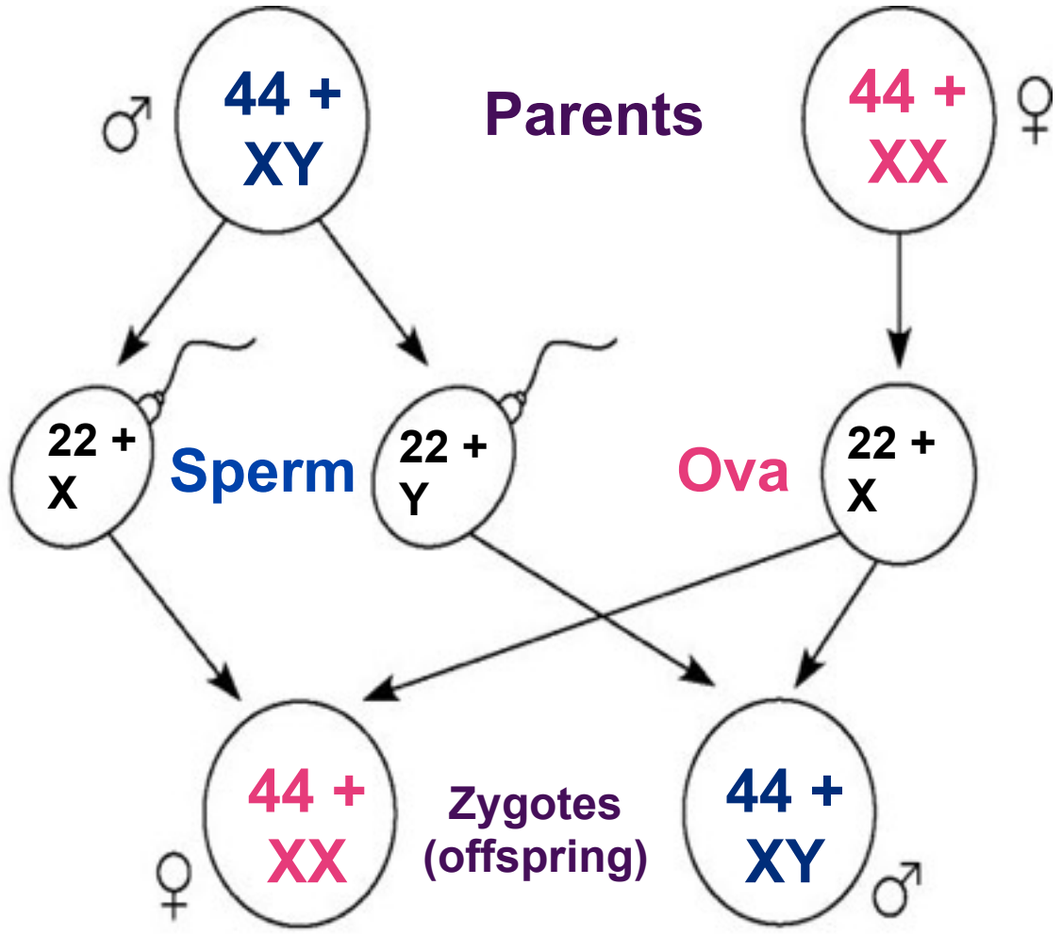
Since all F_1 offspring had red eyes, the mutant white-eye trait (*w*) must be recessive to the wild-type red-eye trait (w^+). Since the recessive trait—white eyes—was expressed only in males in the F_2 generation, Morgan hypothesized that the eye-color gene is located on the X chromosome and that there is no corresponding locus on the Y chromosome, as diagrammed here.



Chromosomal Basis of Sex

- There are two varieties of sex chromosomes X and Y.
- An organisms sex is determined by the presence or absence of certain sex chromosomes.

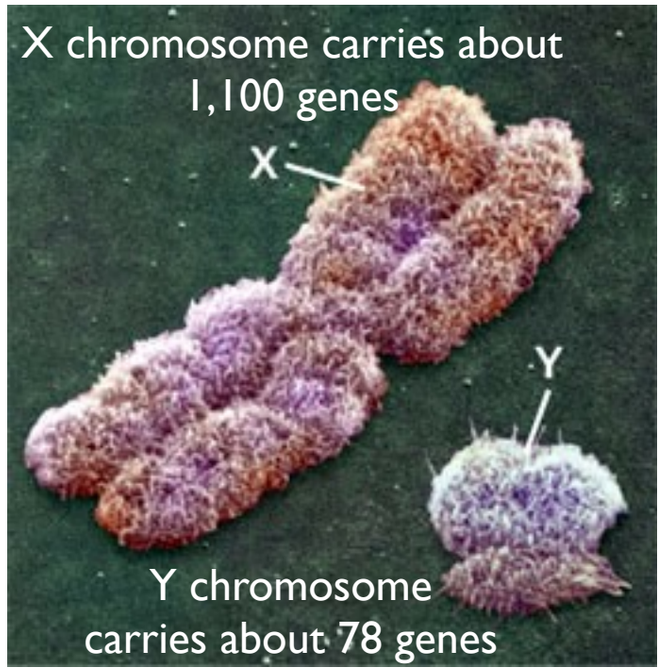




The X-Y system

XX= Girl

XY= Boy



Other Systems of Sex Determination

22 + XX

♀

22 + X

♂

The X–0 system

76 + ZW

♀

76 + ZZ

♂

The Z–W system

16 (Diploid)

♀

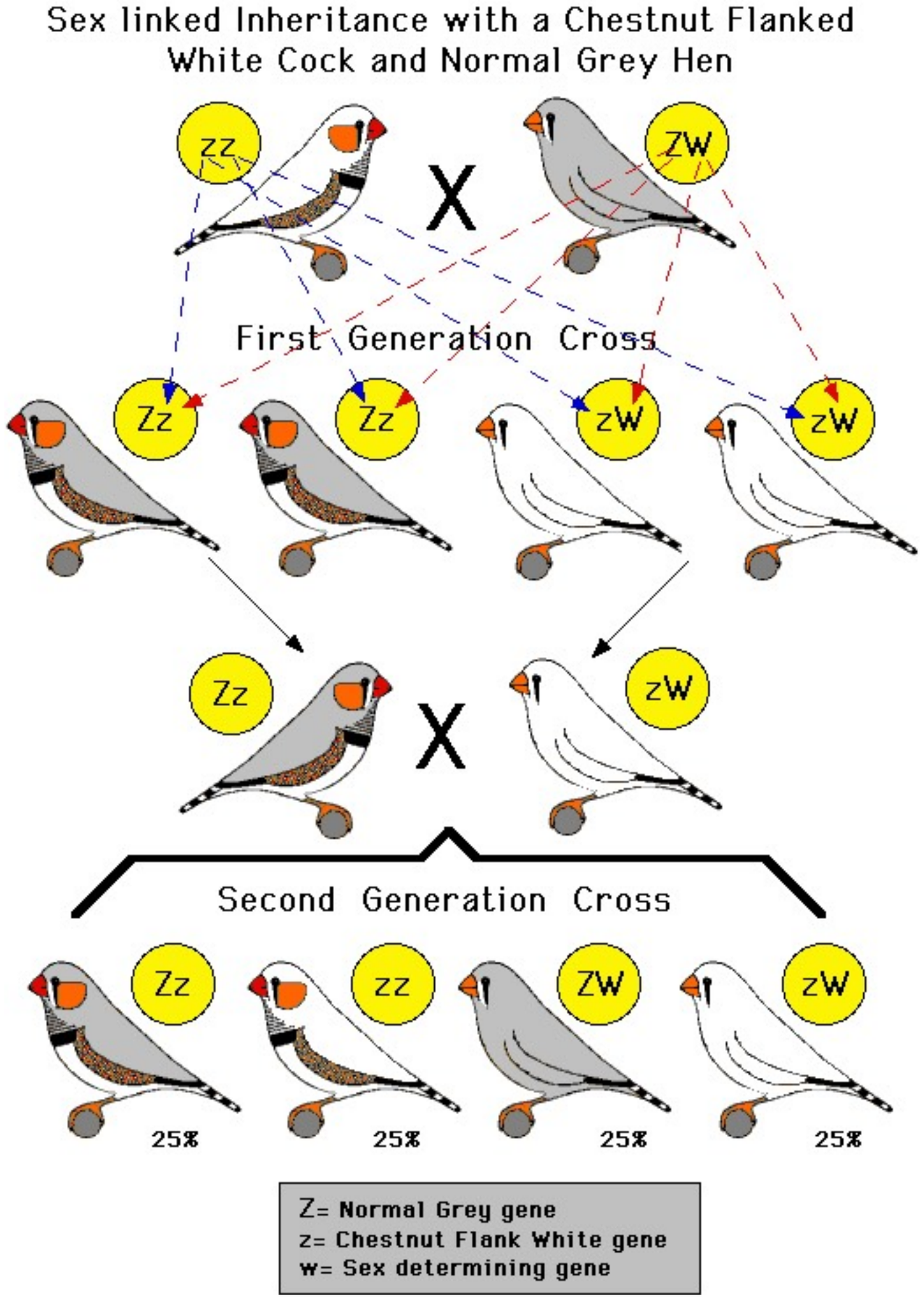
16 (Haploid)

♂

The haplo-diploid system

A gene located on any sex chromosome is said to be sex linked

Sex Linked Example on the ZW System

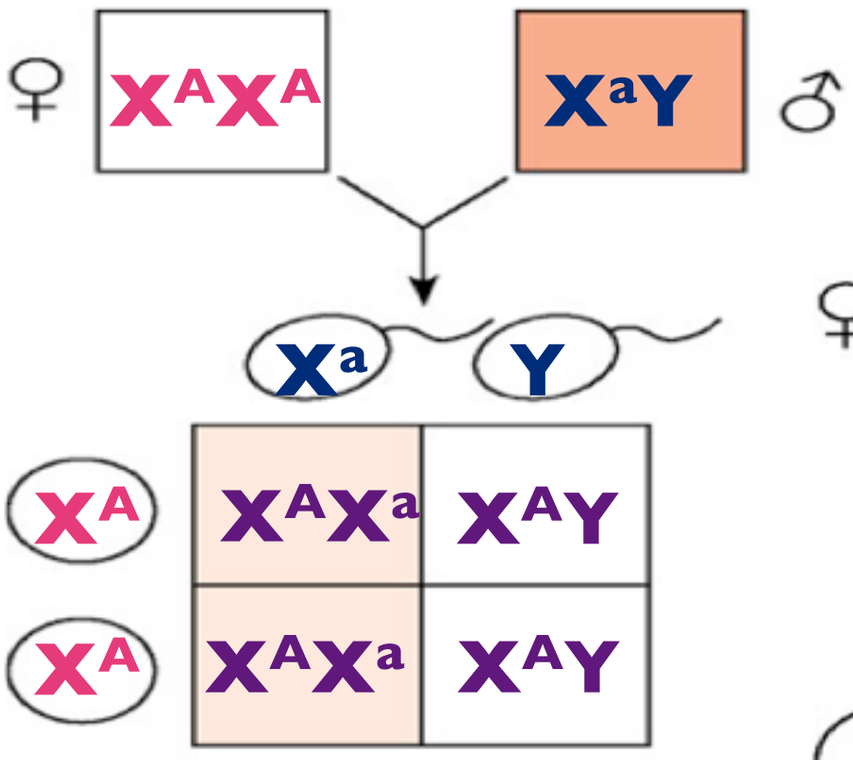


A gene located on any sex chromosome is said to be sex linked

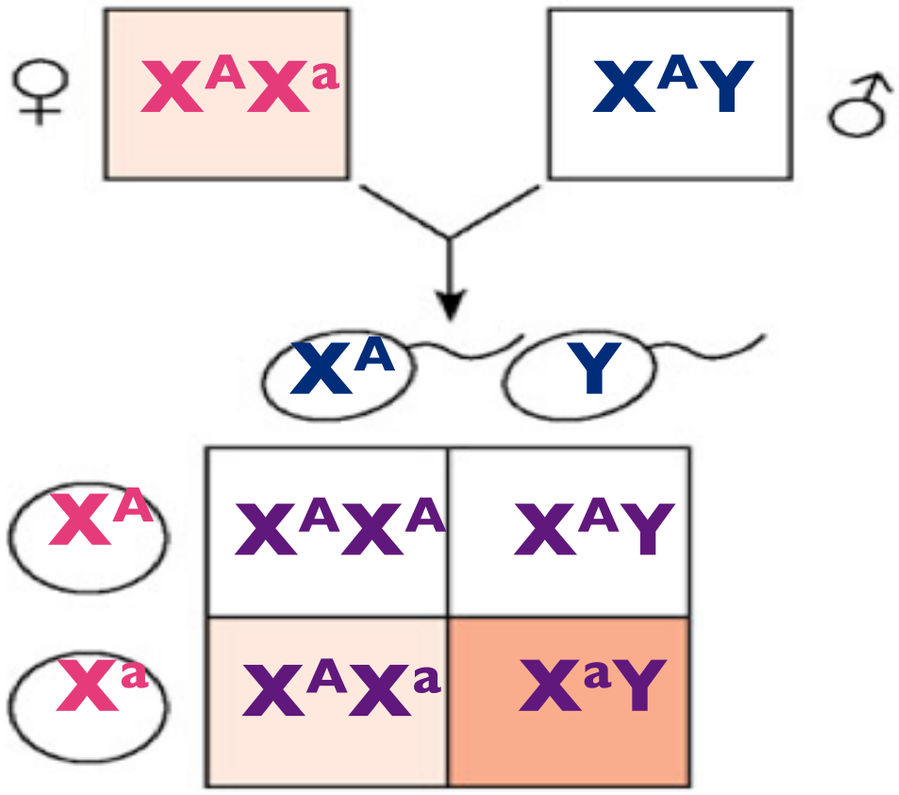
Inheritance of Sex Linked Traits

- Although a sex linked trait can be found on the X or Y chromosome, **most** genetic problems you will encounter will be "X-linked" traits.
  - *Y linked traits are few and mainly sex determinate*
- X-linked traits are far more numerous and some diseases are carried on this chromosome consequently most genetic problems are X-linked.
  - *Duchenne Muscular Dystrophy, Hemophilia & Color Blindness*
- **Most importantly X-linked traits follow a unique pattern of inheritance, the same pattern seen in Morgan's fruit flies.**

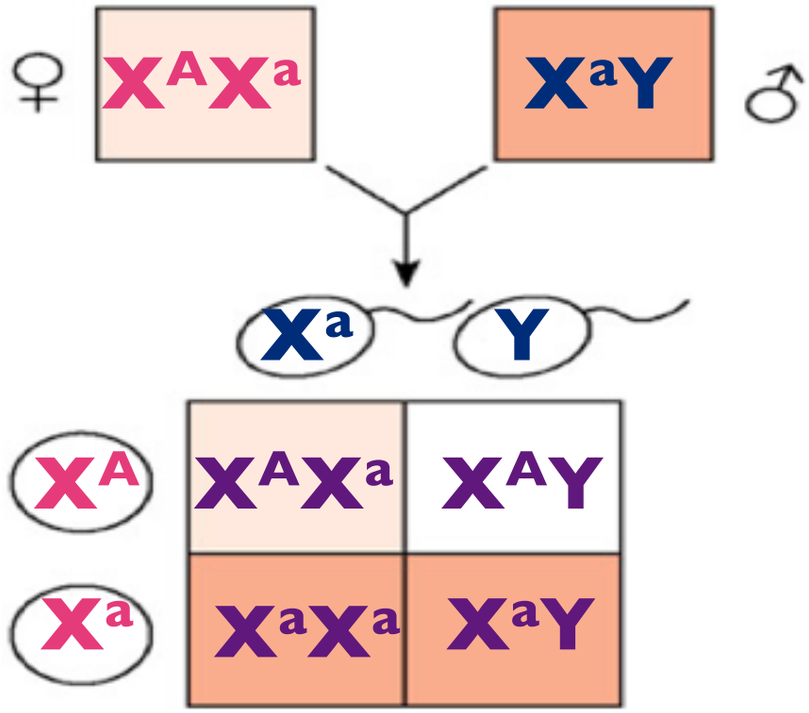
Inheritance of Sex Linked Traits



A father with the disorder will transmit the mutant allele to all daughters but to no sons. When the mother is a dominant homozygote, the daughters will have the normal phenotype but will be carriers of the mutation.



If a carrier mates with a male of normal phenotype, there is a 50% chance that each daughter will be a carrier like her mother, and a 50% chance that each son will have the disorder.



If a carrier mates with a male who has the disorder, there is a 50% chance that each child born to them will have the disorder, regardless of sex. Daughters who do not have the disorder will be carriers, where as males without the disorder will be completely free of the recessive allele.

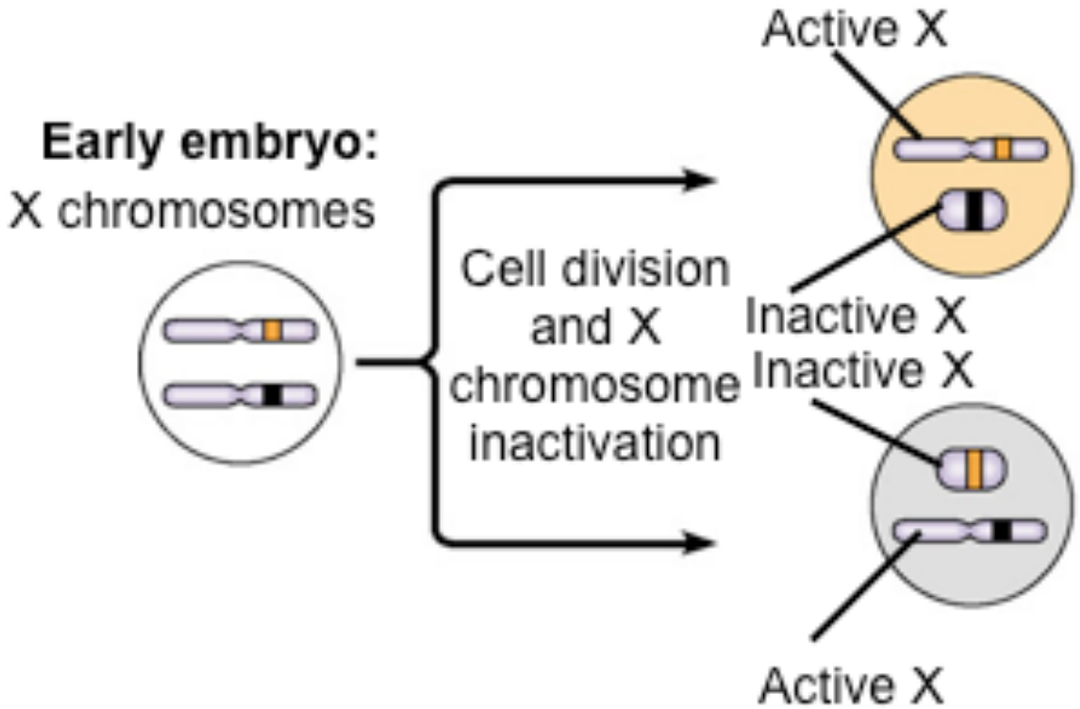
X Inactivation in Female Mammals

- Females receive 2 "X" chromosomes compared to males who only get 1.
    - *If females used both chromosomes then their effective gene dose would be double that of males!*
- When a gene on the X chromosome makes its protein product females would have 2X the normal amount or if that amount was normal then males would only ever get 1/2X the normal amount.
    - *To make the gene dose equal females only use 1 of their X chromosomes.*

X Inactivation in Female Mammals

- **Every cell in a female mammal will randomly select and inactivate one of the two X chromosomes there by making the gene dose equal to that in males.**

- The inactivate X chromosome is called the **Barr Body** and lies just inside the edge of the nuclear envelope.



What one and only cell type reactivates the Barr Body?

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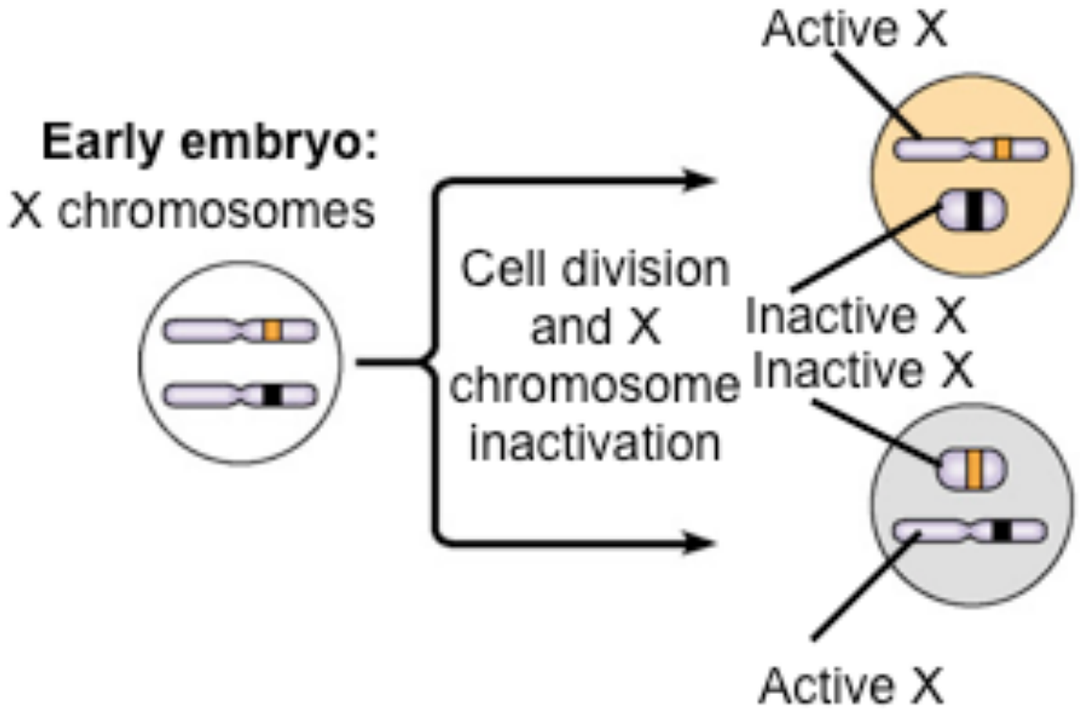
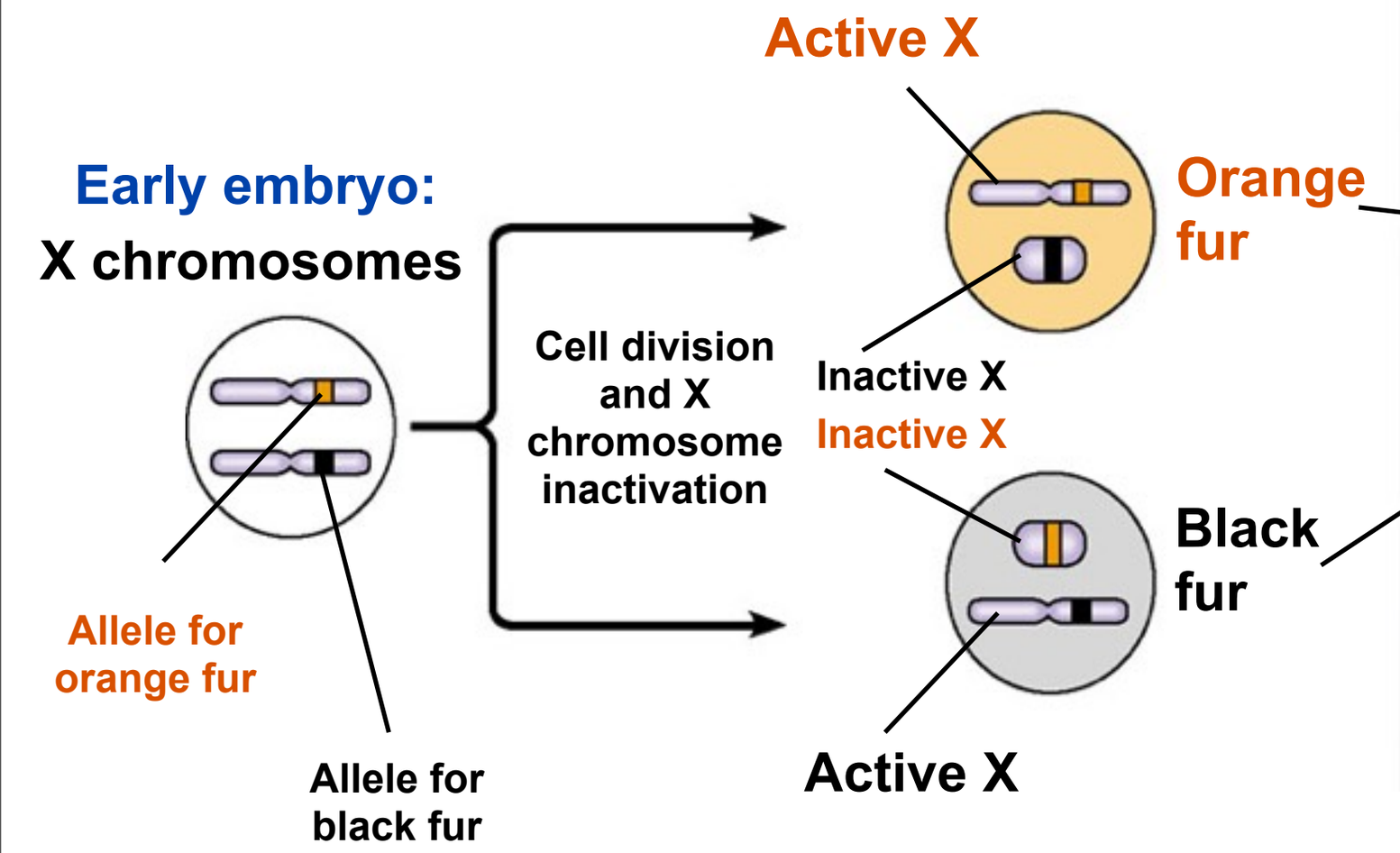


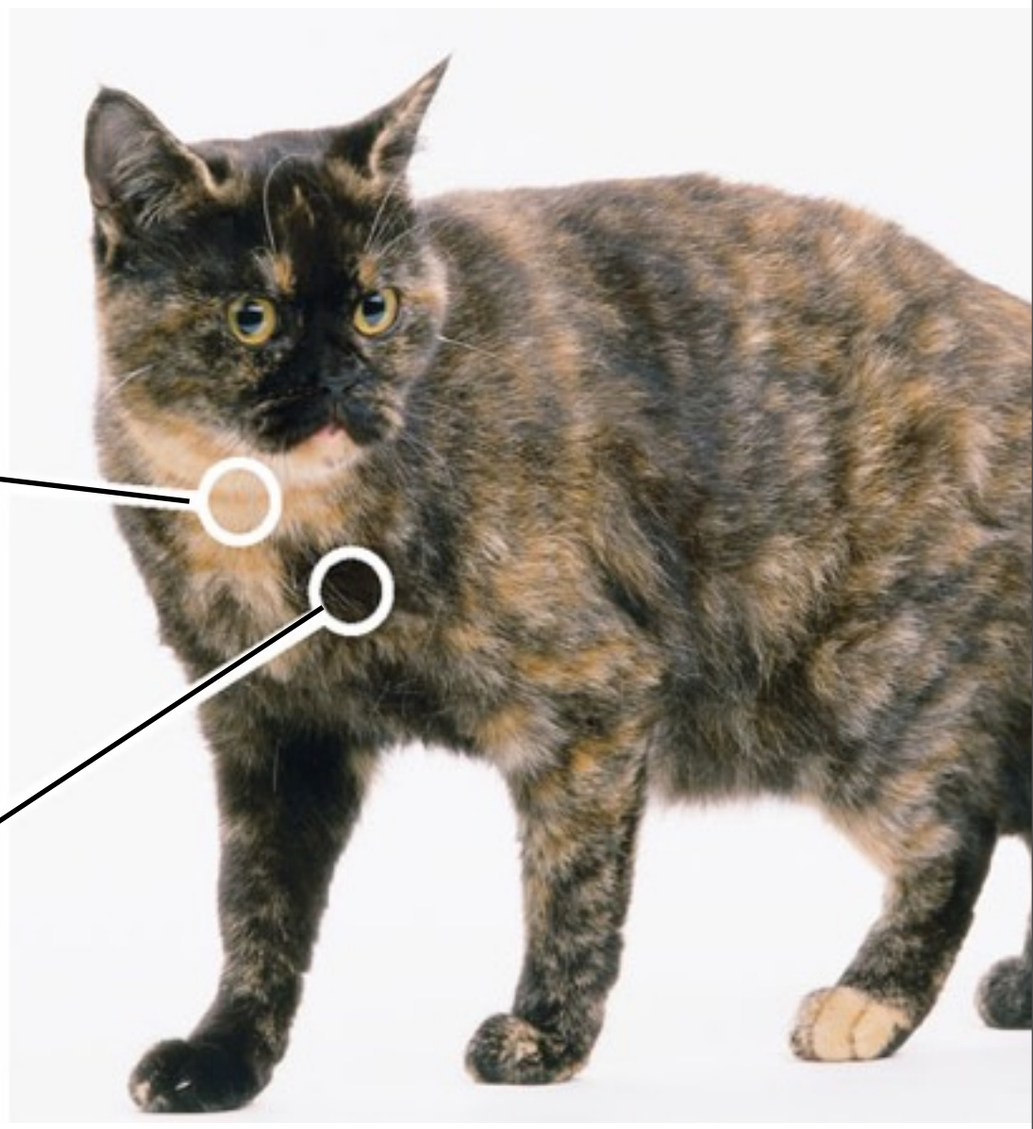
What one and only cell type reactivates the Barr Body?

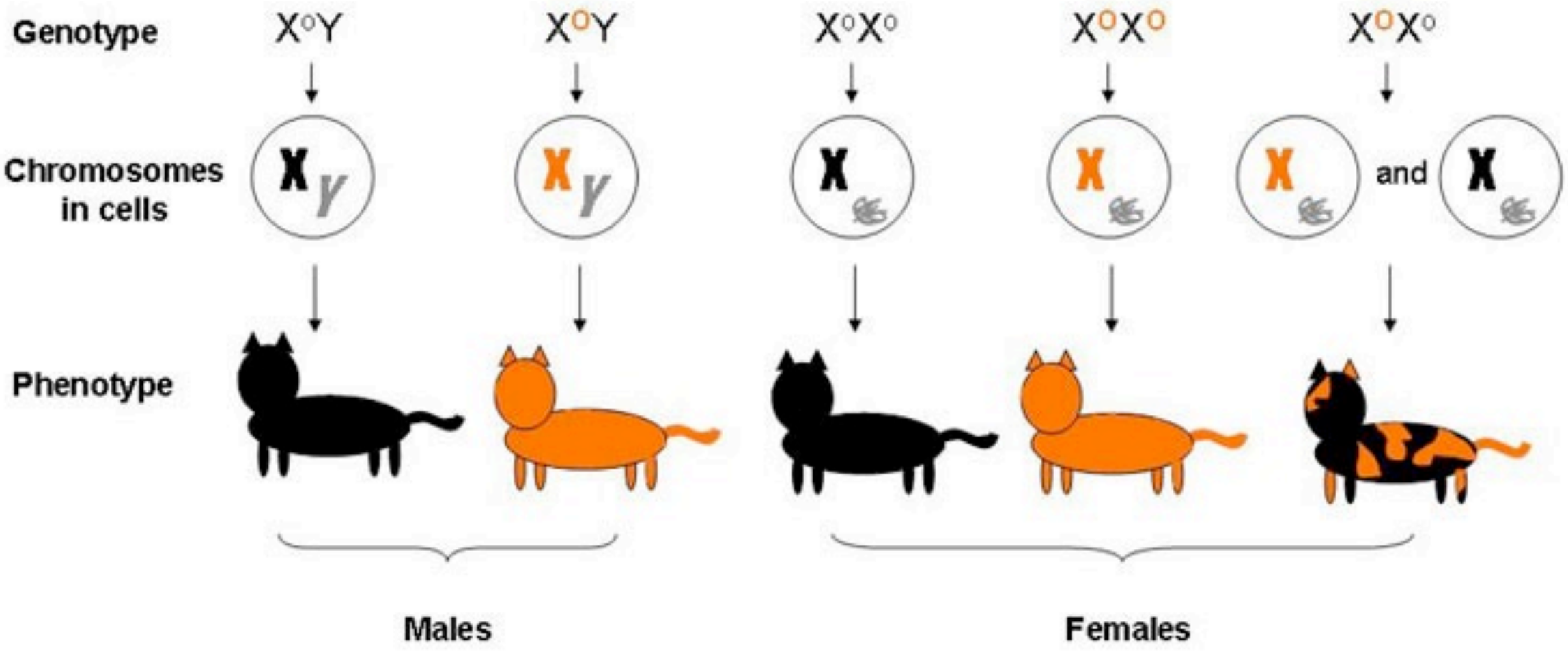
...germ cells, that give rise to ova

Mosaic Female Phenotypes

Two cell populations in adult cat:







Can a male calico cat exist?

= inactivated X chromosome, also called a Barr body

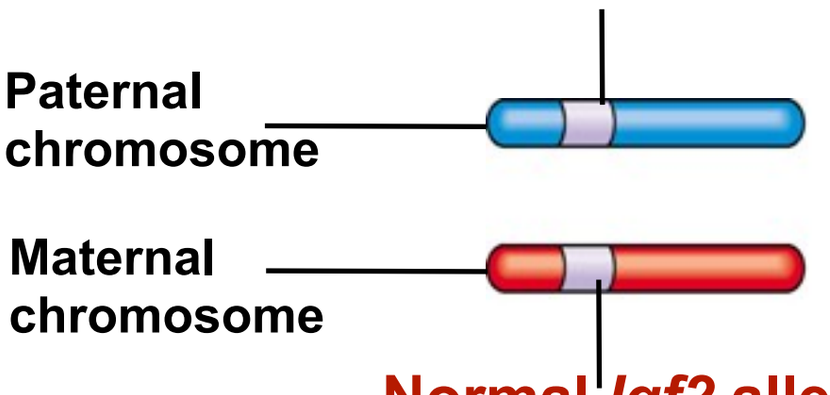
No & Yes, Under normal circumstances No but if nondisjunction occurs in meiosis then a male could get 2 "X" chromosomes along with his Y, if this occurs then... Yes

Genomic Imprinting

- Genomic Imprinting occurs during gamete formation and results in the silencing of certain alleles.
    - *roughly similar to X inactivation where a chromosome is silenced, here a single allele is silenced.*
- Since sperm and eggs imprint differently the zygote only ever expresses one of the two alleles.
- As the zygote divides each daughter cell carries the same imprint, only when that sexually mature organism makes its own gametes will the old imprints be erased new imprints be made.
    - *All members of the same species the same genes are imprinted in the same way.*

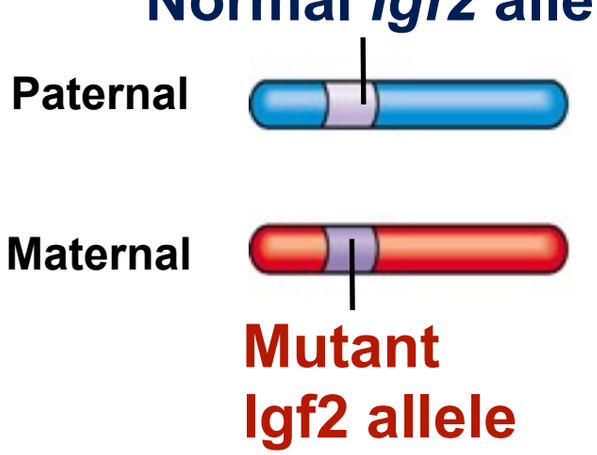
Genomic Imprinting (mammals)

- For most inherited traits the given allele would will have the same effect whether it comes from the mother or the father.
- In recent years, geneticists have uncovered 2 to 3 dozen traits where the phenotype not only depends on the alleles but also which parent donated them.
- **Genomic Imprinting-** describes inheritance where the phenotype varies depending on which parent donated which allele.
- *most imprinting occurs in autosomes*



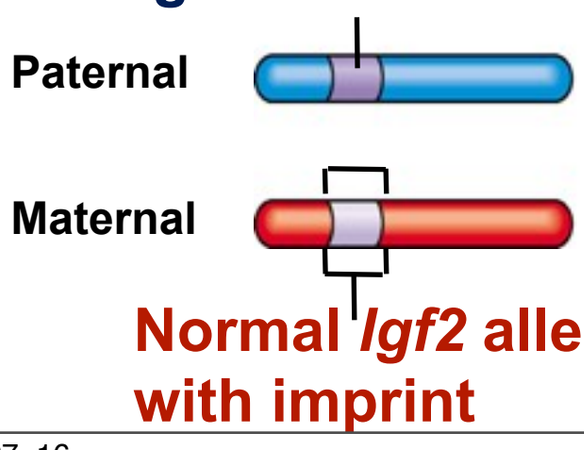
A wild-type mouse is homozygous for the normal *Igf2* allele.

Wild-type mouse(normal



Normal size mouse

When a normal Igf2 allele is inherited from the father, heterozygous mice grow to normal size.



Dwarf mouse

But when a mutant allele is inherited from the father, heterozygous mice have the dwarf phenotype.

Genomic Imprinting

- Genomic Imprinting accomplished through DNA methylation, a process we will learn about later.
  - *in most cases DNA methylation turns off genes but here it actually turns on the genes (another story all together).*
- Although genomic imprinting occurs in few genes, it plays critical roles in embryological development.
  - *Apparently a single gene dose is key in these cases.*

Essential knowledge 3.A.4: The inheritance pattern of many traits cannot be explained by simple Mendelian genetics.

c. Some traits result from nonnuclear inheritance.

Evidence of student learning is a demonstrated understanding of each of the following:

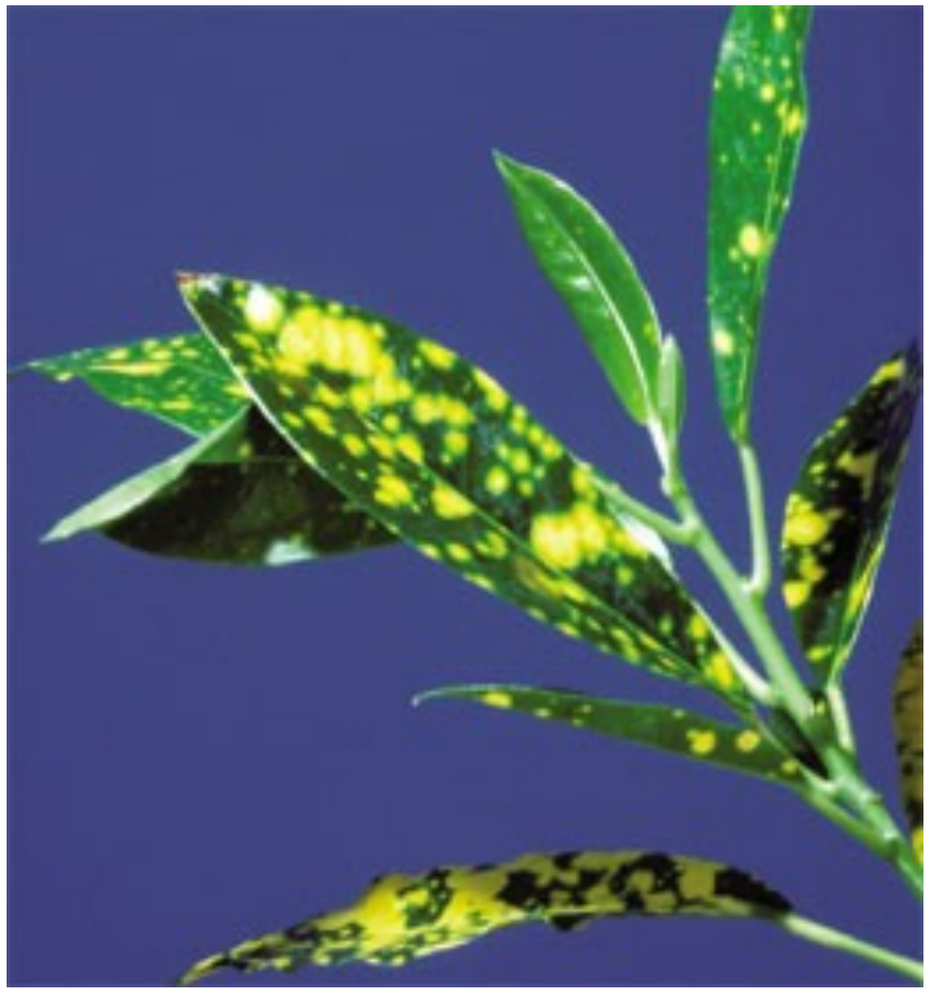
1. Chloroplasts and mitochondria are randomly assorted to gametes and daughter cells; thus, traits determined by chloroplast and mitochondrial DNA do not follow simple Mendelian rules.

2. In animals, mitochondrial DNA is transmitted by the egg and not by sperm; as such, mitochondrial-determined traits are maternally inherited.

✘✘ Epistasis and pleiotropy are beyond the scope of the course and the AP Exam.

Inheritance of Organelle Genes

- Not all genes are located in the nuclear chromosomes, or even the nucleus they are located in organelles.
  - *these genes are often called extranuclear or cytoplasmic genes.*
  - *specifically these genes are located in the mitochondria and chloroplasts.*
- These genes do not follow Mendelian Laws of Inheritance.
  - *The first of this came in 1909, when a German scientist, Karl Correns noticed yellow/white spots on otherwise green leaves.*
  - *He later determined that the inheritance of the spots was strictly due the eggs/mother.*

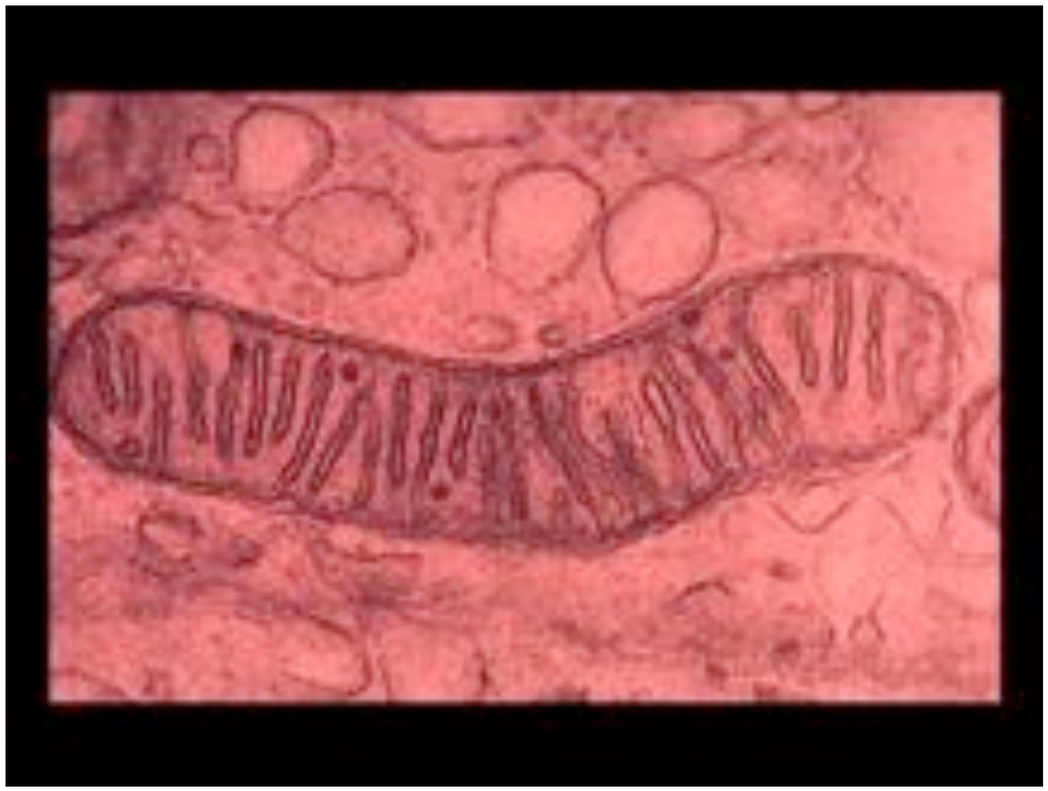


Turns out the spots are due to a mutations in plastid genes that control pigment.

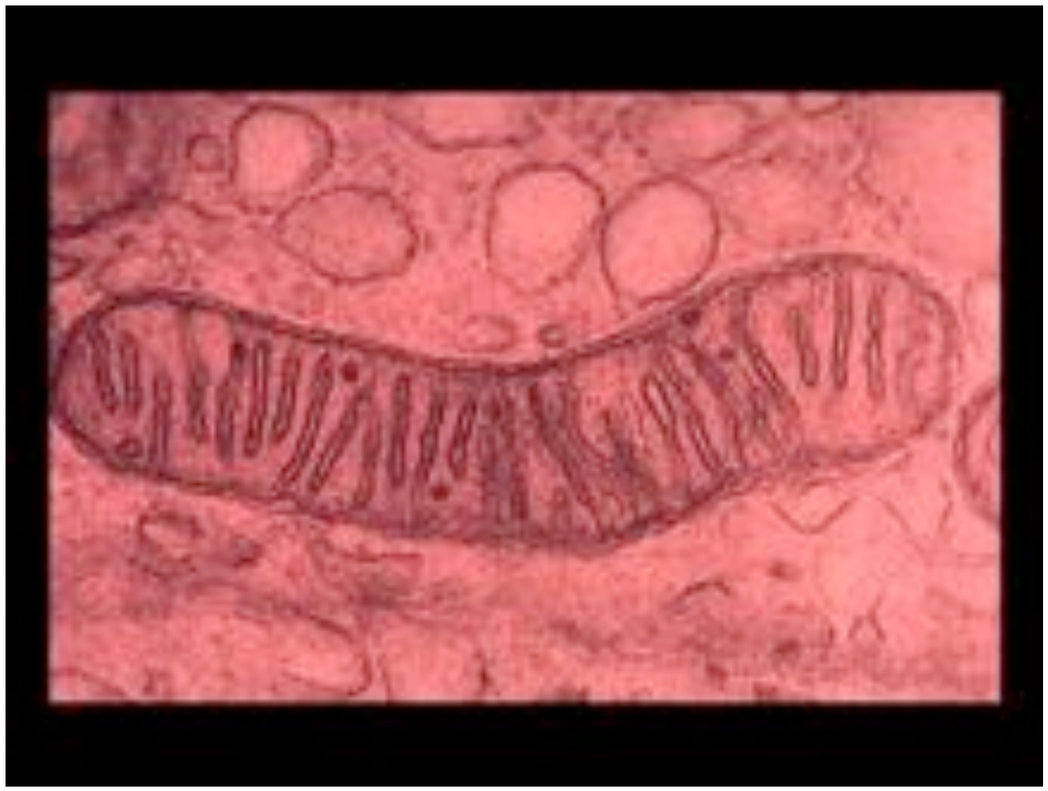
Plastid genes are located in the chloroplast's genes

Since sperm only contribute the haploid set of chromosomes, the egg supplies all organelles including the chloroplasts

The egg may contain plastids with different alleles, these plastids are randomly distributed to daughter cells, the color variation is due to the ratio of wild-type & mutant plastids in various tissue



Maternal inheritance is also the rule for the mitochondria, the egg supplies the mitochondria for the zygote.



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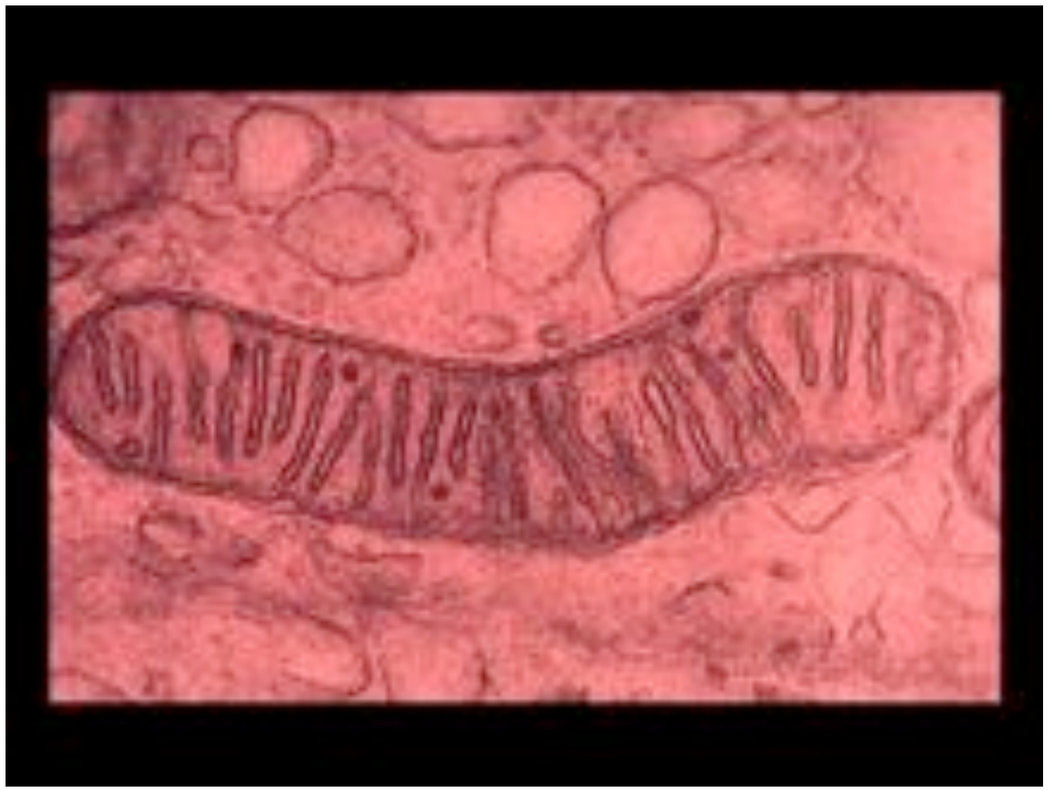
What do you think most mitochondrial genes code for?



Maternal inheritance is also the rule for the mitochondria, the egg supplies the mitochondria for the zygote.

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proteins that make up the electron transport chain and the ATP synthase, components of oxidation phosphorylation

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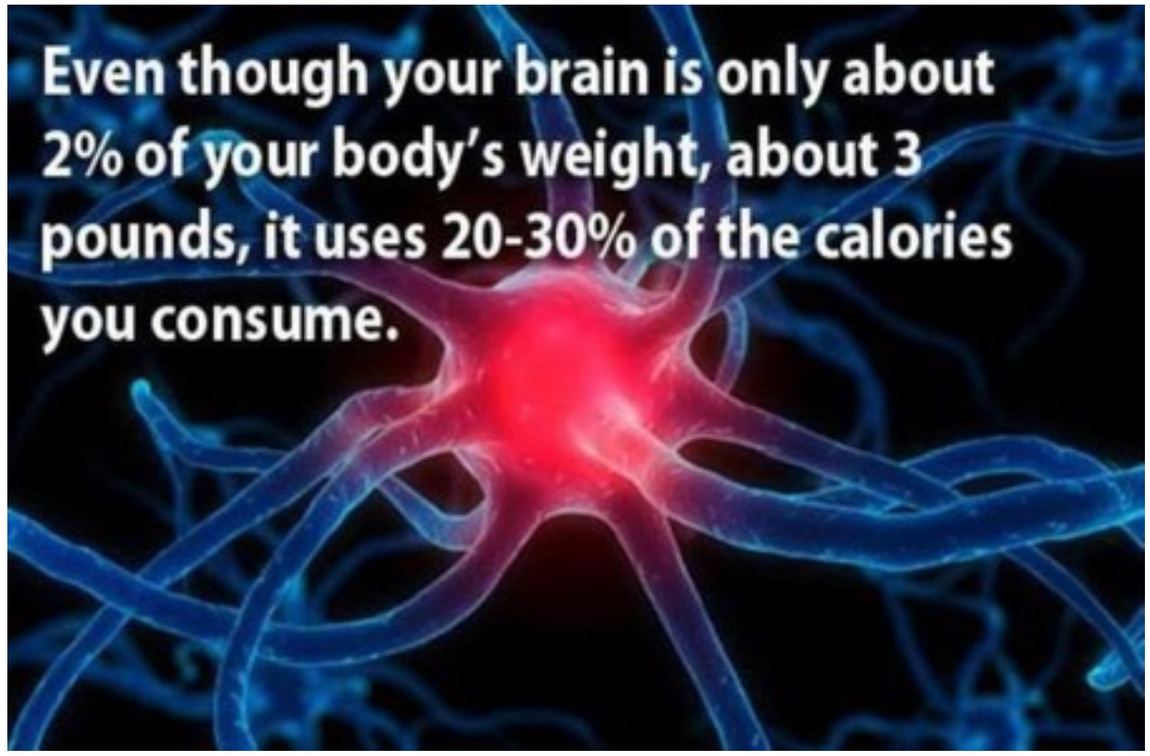

Learning Objectives:

LO 3.15 The student is able to explain deviations from Mendel's model of the inheritance of traits. [See SP 6.2, 6.5]

LO 3.16 The student is able to explain how the inheritance patterns of many traits cannot be accounted for by Mendelian genetics. [See SP 6.3]

LO 3.17 The student is able to describe representations of an appropriate example of inheritance patterns that cannot be explained by Mendel's model of the inheritance of traits. [See SP 1.2]