Non-Mendelian Genetics

Mendel's Laws

1. Principle of Segregation

Two alleles segregate randomly during formation of gametes

2. Independent Assortment

Two genes will assort independently and randomly from each other

Mendel's Laws are Not Perfect:

- Shortly after people began to notice that not all traits are "Mendelian"
  - This means, they do NOT follow Mendel's laws
  - Was he just lucky?
- his laws were correct and did explain how genetics works
  - Real life is just more complicated than peas!

There are some exceptions altering Mendel's ratios…

Exceptions of mendelian rules.

1. Multiple alleles
2. Lethal genotypes
3. Incomplete dominance
4. Codominance
5. Penetrance
6. Expressivity
7. Pleiotropy
8. Epistasis
9. Inheritance of Organelles
10. Sex-linked inheritance

MULTIPLE ALLELES

- Mendel studied just two alleles of his pea genes, but real populations often have multiple alleles of a given gene. Genes may have more than two alleles at a single genetic locus
- About 30% of the genes in humans are **di-allelic**, that is they exist in two forms, (they have two alleles)
- About 70% are **mono-allelic**, they only exist in one form and they show no variation
- A very few are **poly-allelic** having more than two forms

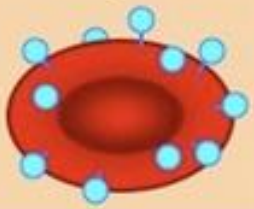
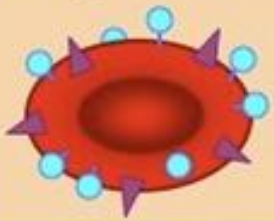
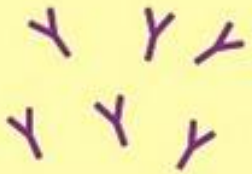
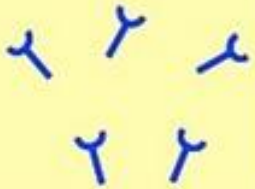
The ABO blood system

- This is a controlled by a **tri-allelic gene**
- It can generate **6 genotypes**

- The alleles control the production of **antigens** on the surface of the red blood cells
- Two of the alleles are **codominant** to one another and both are dominant over the third

- Allele I^A produces antigen **A**
- Allele I^B produces antigen **B**
- Allele **i** produces **no** antigen

ABO Blood Groups

	Antigen A	Antigen B	Antigens A + B	Neither A or B
Antigen (on RBC)				
Antibody (in plasma)	Anti-B Antibody 	Anti-A Antibody 	Neither Antibody	Both Antibodies 
Blood Type	**Type A** Cannot have B or AB blood Can have A or O blood	**Type B** Cannot have A or AB blood Can have B or O blood	**Type AB** Can have any type of blood Is the universal recipient	**Type O** Can only have O blood Is the universal donor

https://knowledgeclass.blogspot.com/2015/11/blood-group-abo-system.html

The ABO blood system

Genotypes	Phenotypes (Blood types)
$I^A I^A$	A
$I^A I^B$	AB
$I^A i$	A
$I^B I^B$	B
$I^B i$	B
ii	O

Note:

- Blood types A and B have two possible genotypes – homozygous and heterozygous.
- Blood types AB and O only have one genotype each.

Blood types and transfusions

- People who are Type A blood produce antibodies to agglutinate cells which carry Type B antigens
  They recognise them as **non-self**
- The opposite is true for people who are Type B
- Neither of these people will agglutinate blood cells which are Type O
  Type O cells do not carry any antigens for the ABO system

Donor-recipient compatibility

Recipient

Donor: Type	A	B	AB	O
A				
B				
AB				
O				

= Agglutination

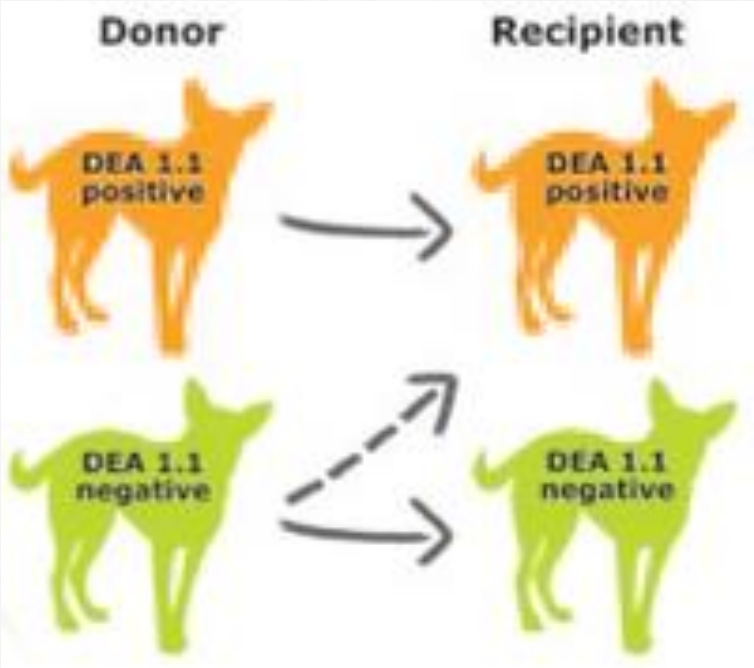
= Safe transfusion

Note:

- **Type O blood** may be transfused into all the other types = the **universal donor**.
- **Type AB blood** can receive blood from all the other blood types = the **universal recipient**.

Blood types in animals

Animals	Blood types
Dogs	DEA 1.1, 1.2, 3, 4, 7, and *Dal*. (DEA system=Dog Erythrocyte antigen system) DEA 1.1 negative= Universal Donor DEA 1.1 positive=Universal Recipient (Wardrop, 2007)



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Cats	The main blood group system in cats is the A-B grouping. Cats can be either type A, type B or type AB. (http://www.catblooddonors.com/for-cat-owners/about-cat-blood-transfusions.php)
Cattle	The polymorphic systems in cattle include the A, B, C, F, J, L, M, S, and Z polymorphisms. (http://en.wikipedia.org/wiki/Blood_type_non-human)
Horses	There are eight major recognized blood groups in horses *Viz*., A, C, D, K, P, Q, U and T. (http://en.wikipedia.org/wiki/Blood_type_non-human)

Blood Types in Various Breeds of Cats

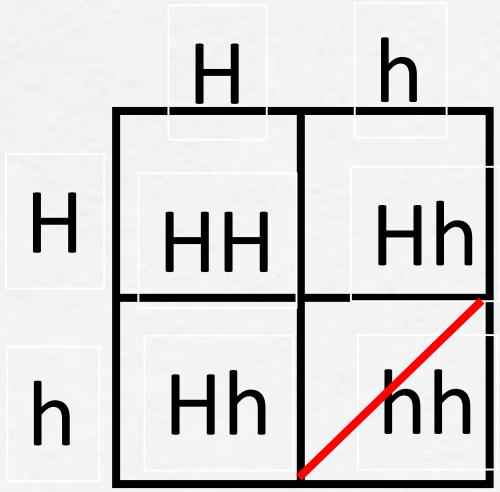
*Numbers in parenthesis indicate the percentage of type B cats in a specific study of over 10,000 cats. Where a range has been given, this indicates important higher limits in other studies. Percentages may vary with different statistical studies.

Blood Type A Only No Risk Breeds	1-10% Blood Type B Low Risk Breeds	10-25% Blood Type B Medium Risk Breeds	25% or Higher Blood Type B HIGH Risk Breeds
• Siamese • Burmese • Tonkinese • American Shorthair • Oriental Shorthair	• Maine Coon (2%) • Manx (no data) • Norwegian Forest Cat (7%)	• Abyssinian (20%) • Birman (16%) • **Exotic** (no data) • **Himalayan** (7-20%) • Japanese Bobtail (16%) • **Persian** (14-24%) • Scottish Fold (15-18%) • Somali (17-22%) • Sphynx (19%)	• British Shorthair (40-59%) • Devon Rex (41%) • Cornish Rex (34%)

The frequency of blood Type B in other breeds of cats has not been determined

Lethal Genotypes

- If a certain genotype (combination of alleles) causes death …
- Usually stillbirth or miscarriage
  - Don't ever see the phenotype



Two alleles; one dominant and one recessive
Producing the 1:2:1 genotypic ratio
Only the phenotypic ratio that is changed

Expect to see 3:1 ratio

Instead see 100% dominant

- An example of a recessive lethal allele occurs in the Manx cat. Manx cats possess a heterozygous mutation resulting in a shortened or missing tail. Crosses of two heterozygous Manx cats result in 2 offspring displaying the heterozygous shortened tail phenotype, and 1 offspring of normal tail length that is homozygous for a normal allele. Homozygous offspring for the mutant allele cannot survive birth and are therefore not seen in these crosses.

Tail-lessness in Manx cats is due to a locus (T) that affects development of the post-axial skeleton. Cats with standard tails are tt. There is a series of dominant T alleles that lead to reduction of the tail. The TT homozygote combination is lethal.

https://www.mun.ca/biology/scarr/Manx_cat_genetics.html

Incomplete Dominance

- One allele is not completely dominant over the other
  - Causing the heterozygote to have a third, different phenotype

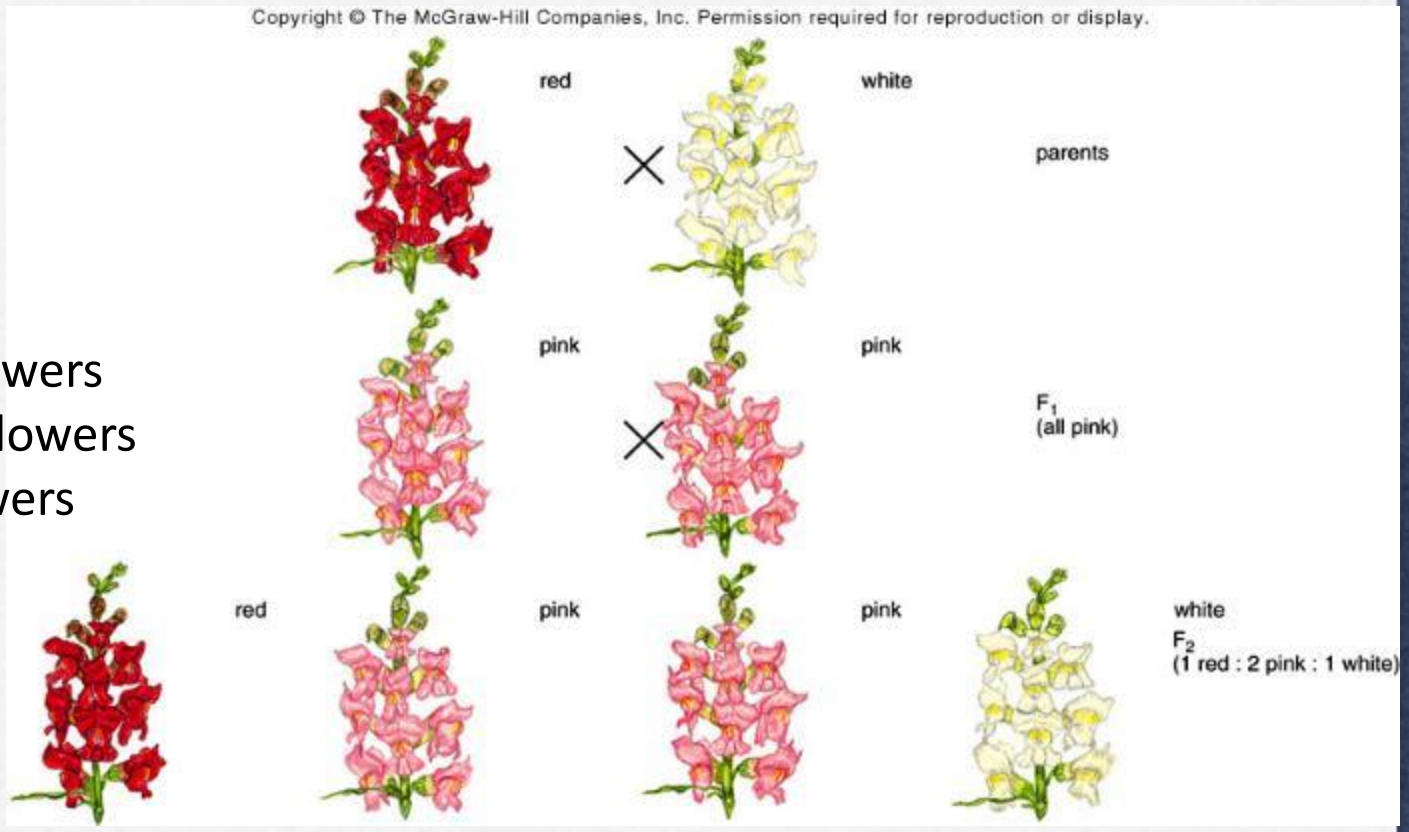
- Snapdragon Flower Color is controlled by **Incomplete Dominance**

Blending in flowers

Homo Dominant = red flowers

Homo recessive = white flowers

Heterozygotes = pink flowers



Horses

(Chestnut x Cremello → Palomino)

Codominance

A cross between 2 tabbies (the heterozygotes) results in 1 black : 2 tabbies : 1 tan cat

Two alleles may be simultaneously expressed when both are present, rather than one fully determining the phenotype.

The same ratios as Incomplete Dominance occur:

A ratio of 1:2:1 for both genotype and phenotypes of a monohybrid cross

→

Different Phenotype:

The two original phenotypes are combined to give a SPOTTED or MULTICOLORED phenotype.

X

	B^W	B^W
B^B	B^B B^W	B^B B^W
B^B	B^B B^W	B^B B^W

	B^B	B^W
B^B	$B^B B^B$ 	$B^B B^W$ 
B^W	$B^B B^W$ 	$B^W B^W$ 

Fenotype: 1:2:1
Genotype: 1:2:1

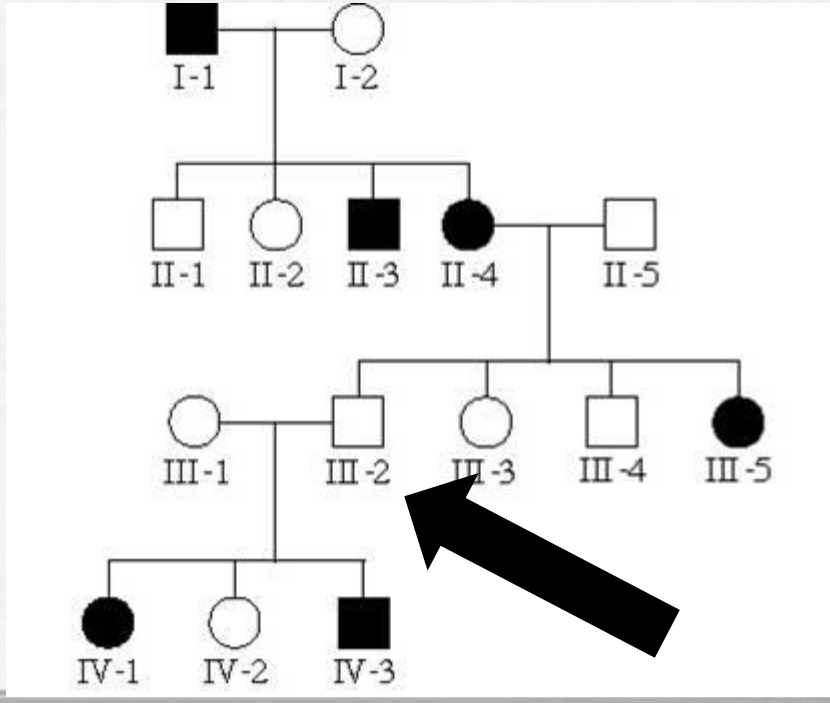
Penetrance

- Sometimes the same genotype will not produce the phenotype in all individuals. an organism may have a particular genotype but may not express the corresponding phenotype, because of modifiers, epistatic genes, or suppressors in the rest of the genome or because of a modifying effect of the environment.
- Penetrance = the percent of individuals who have a certain genotype and show the expected phenotype
  - Mendel traits penetrance = 100 %
  - Some traits penetrance is less than 100%

- Penetrance is calculated as=

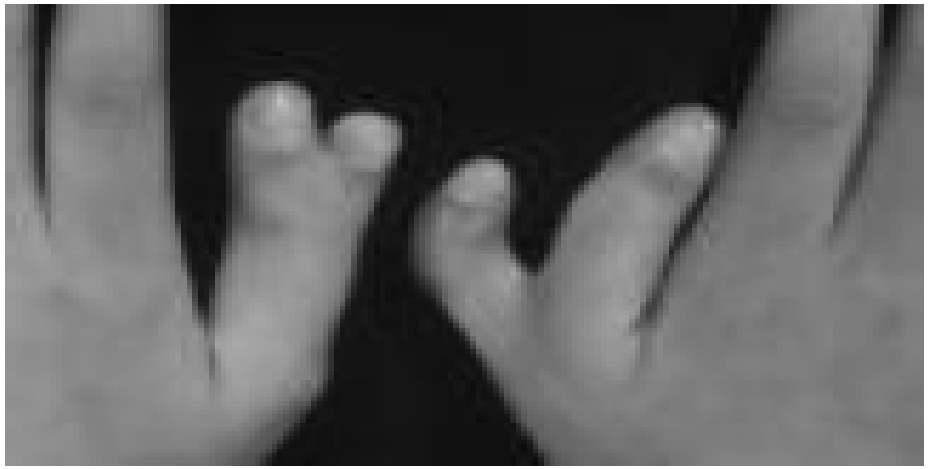
$$\frac{\text{Number of individuals who have genotype and expected phenotype}}{\text{Total number of individuals who have genotype (any phenotype)}}$$

- Usually decrease caused by interaction of additional genes or environment



Example: Polydactyly (P) extra digits

pp	Pp	PP
normal	10 % normal	polydactyly
	90 % polydactyly	



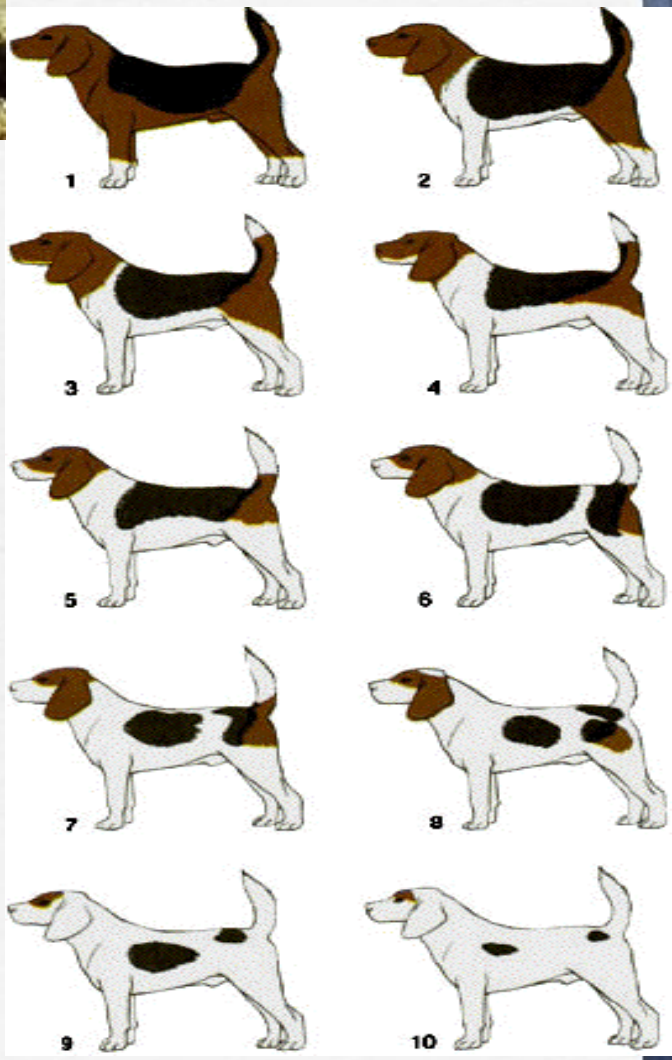
Expressivity

Sometimes the same genotype will produce different "degrees" of phenotype in individuals

- Expressivity = the severity or extent of the phenotype an individual shows

  Hypercholesterolemia

  - Some individuals have extremely high cholesterol from birth, others can control with diet and exercise and lead normal lives


1
2
3
4
5
6
7
8
9
10

Pleiotropy

One gene causes more than one phenotype

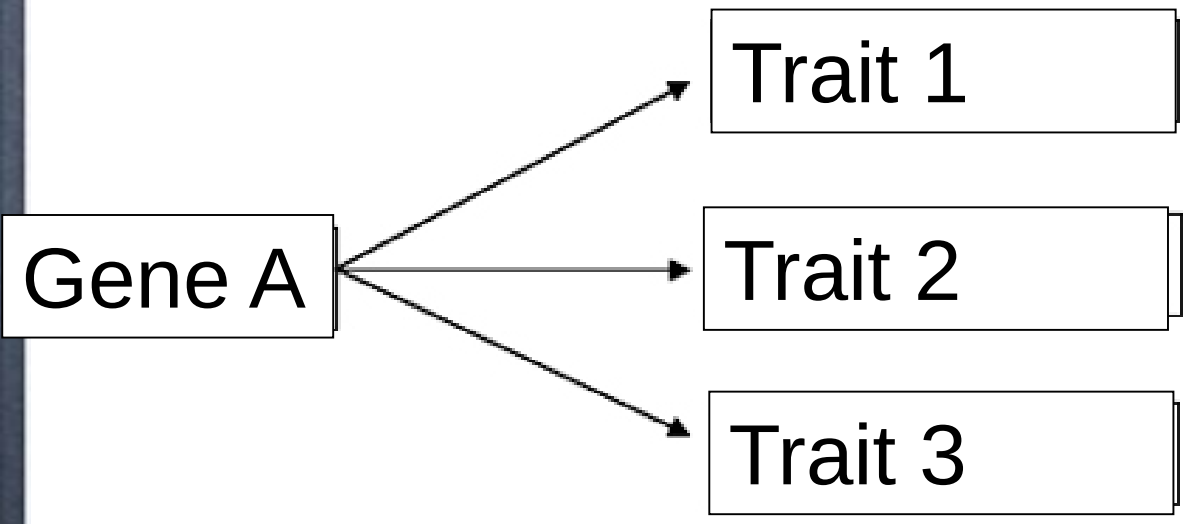
- Pleiotropy occurs when one gene controls more than one pathway or is expressed in more than one body part

Marfan syndrome

One gene makes connective tissue

- Needed for lens of eye
- Heart Muscle
- Limbs, skin and muscles

Therefore a mutation in this one gene will cause defects in eye sight, heart attacks, and weakness in muscles and limbs



1. Deafness
2. Hair color
3. Eye color

The dominant white gene is associated with developmental defects where melanocytes fail to migrate to the skin during embryologic development. This can result in one or both blue eyes, in degenerative changes of the ear resulting in partial or total deafness and uniform white hair color.

GENE INTERACTIONS

Other variations on Mendel's rules involve interactions between pairs of genes. Many characteristics are controlled by more than one gene, and when two genes affect the same process, they can interact with each other in a variety of different ways.

For example:

Epistasis: The alleles of one gene may mask or conceal the alleles of another gene.

- In addition, some gene pairs lie near one another on a chromosome and are genetically linked, meaning that they don't assort independently.
- The term epistasis describes a certain relationship between genes, where an allele of one gene (e.g., 'spread') hides or masks the visible output, or phenotype, of another gene.

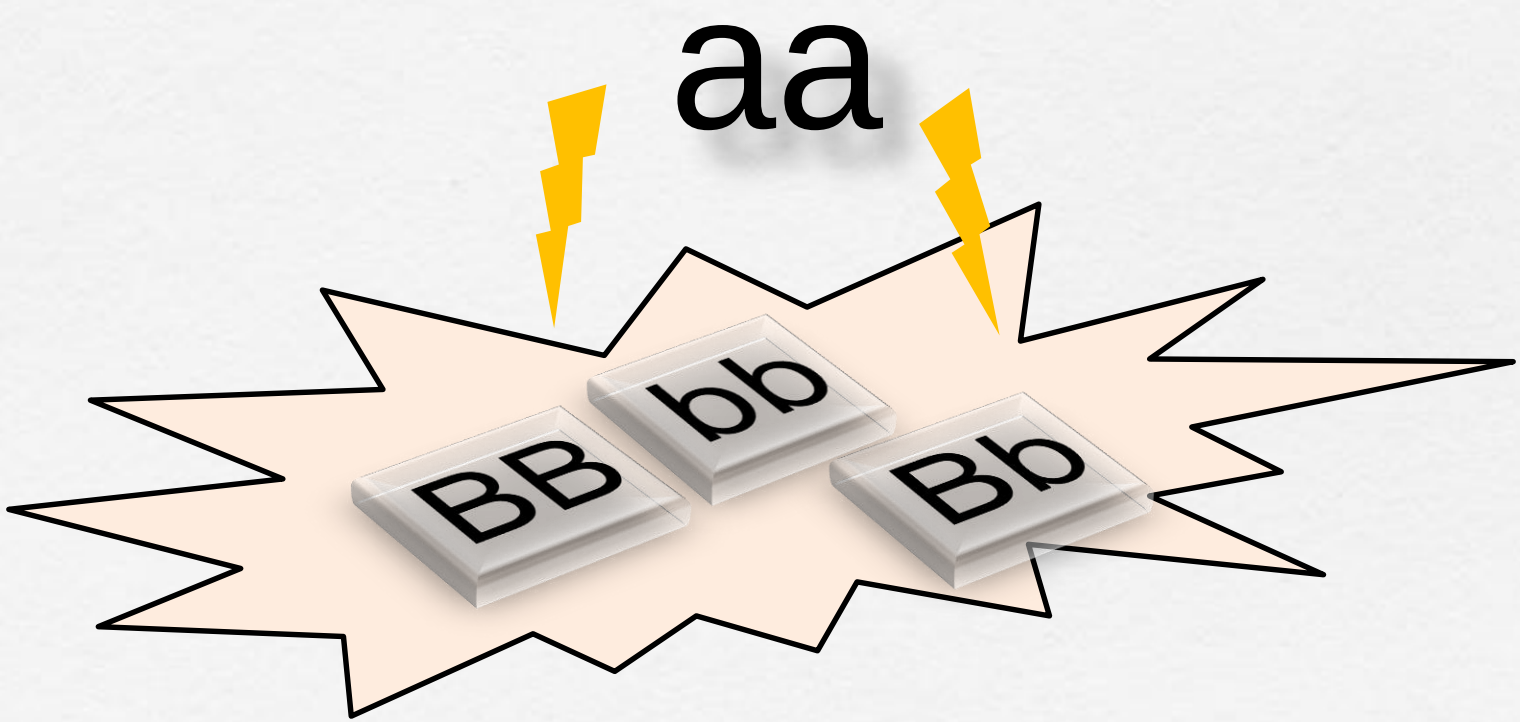
- Epistasis occurs when genes at **two different loci interact to affect the expression of a single trait**. A gene can either mask or modify the phenotype controlled by the other gene.

(think about the differences between pleitropy and epistasis)

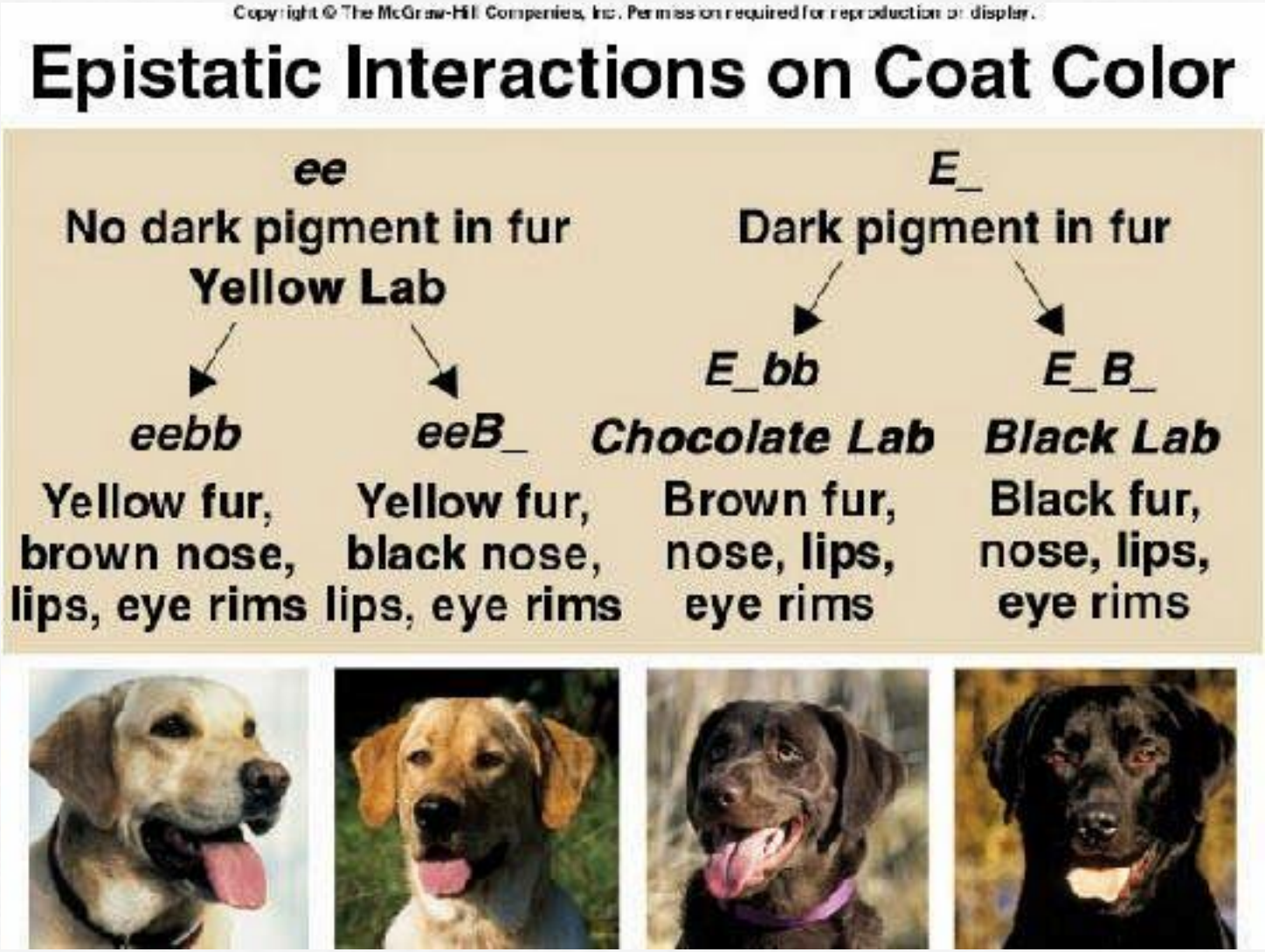
- The gene that does the masking/modifying is referred to as **epistatic**, while the gene that is masked/modified is referred to as **hypostatic**.

Recessive epistasis

the recessive allele of the gene "A" masks the phenotypic expression of the allele of the gene ”B".

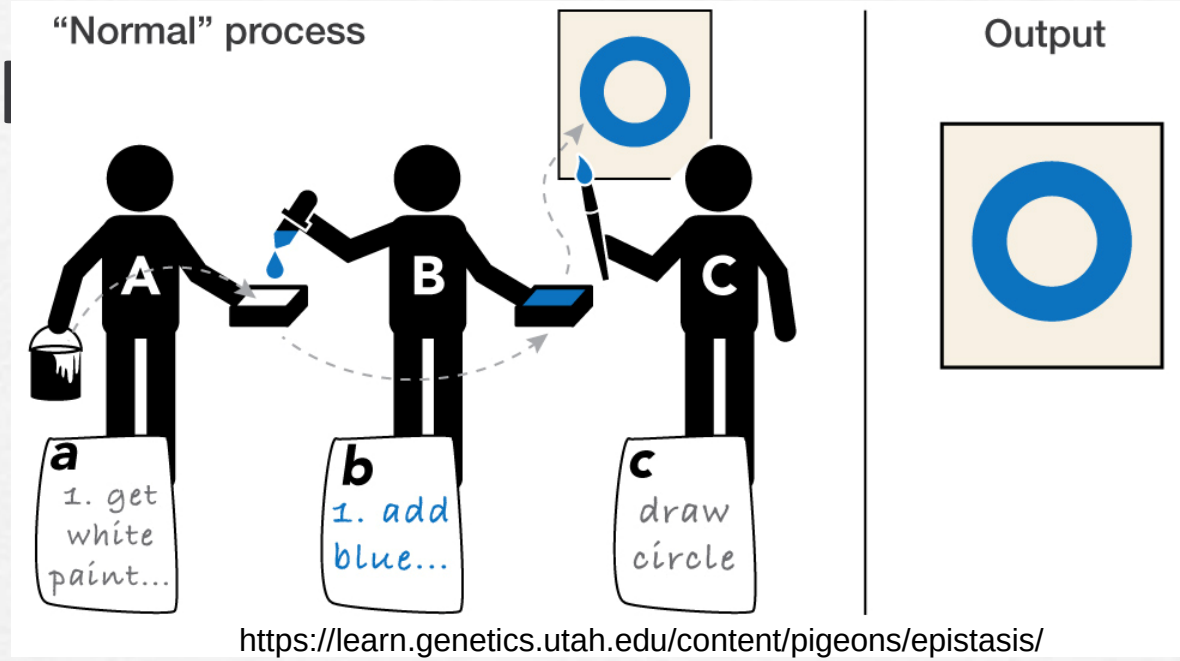


- Black is dominant to chocolate; represented by letters B (black) or b (chocolate). Yellow is recessive epistatic (when present, it blocks the expression of the black and chocolate alleles) E or e.



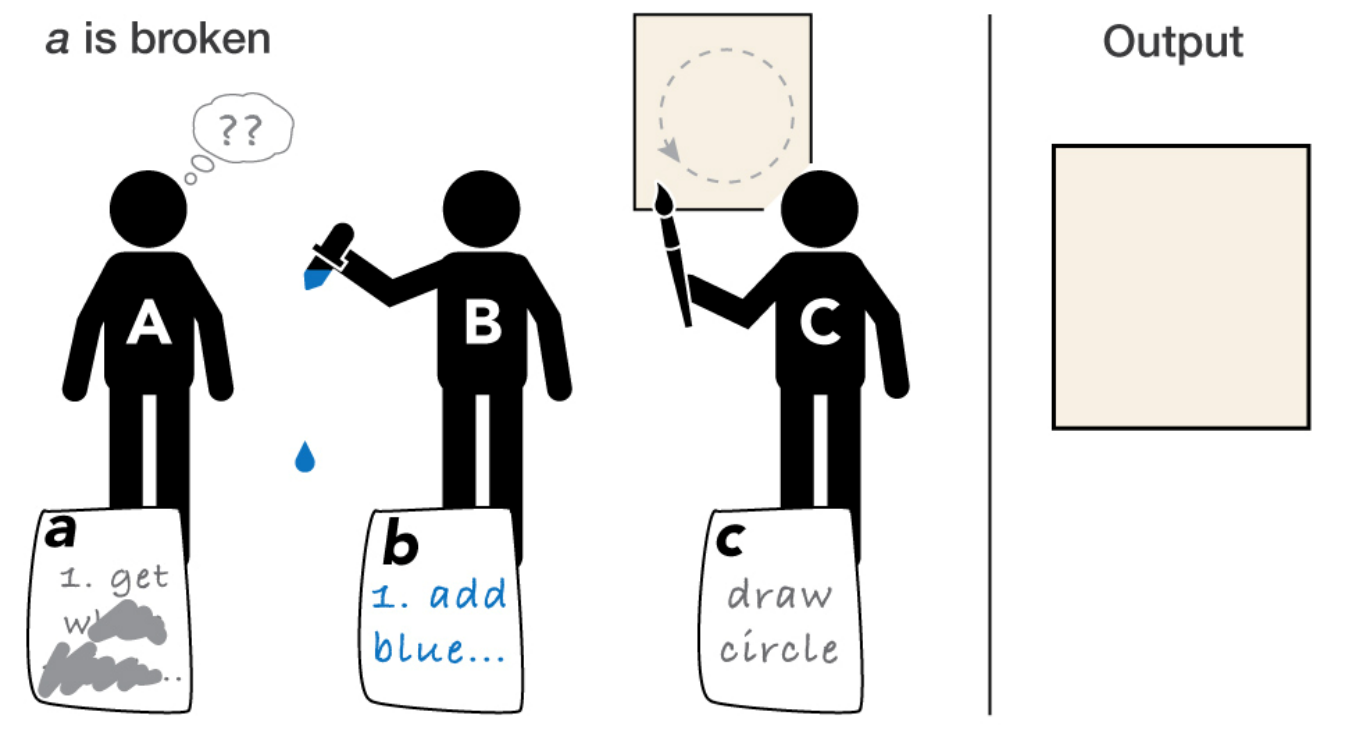
	EE	Ee	ee
BB			
Bb			
bb			

An analogy might be easier to u



https://learn.genetics.utah.edu/content/pigeons/epistasis/

- Let's say workers A, B, and C carry out the steps for painting a design on a poster. Like genes, a, b, and c are the instructions.
- Worker A puts paint into the tray; a tells it how.
- Worker B adds dye to the paint; b tells it what color.
- Worker C paints a design on the poster; c tells it what design.



https://learn.genetics.utah.edu/content/pigeons/epistasis/

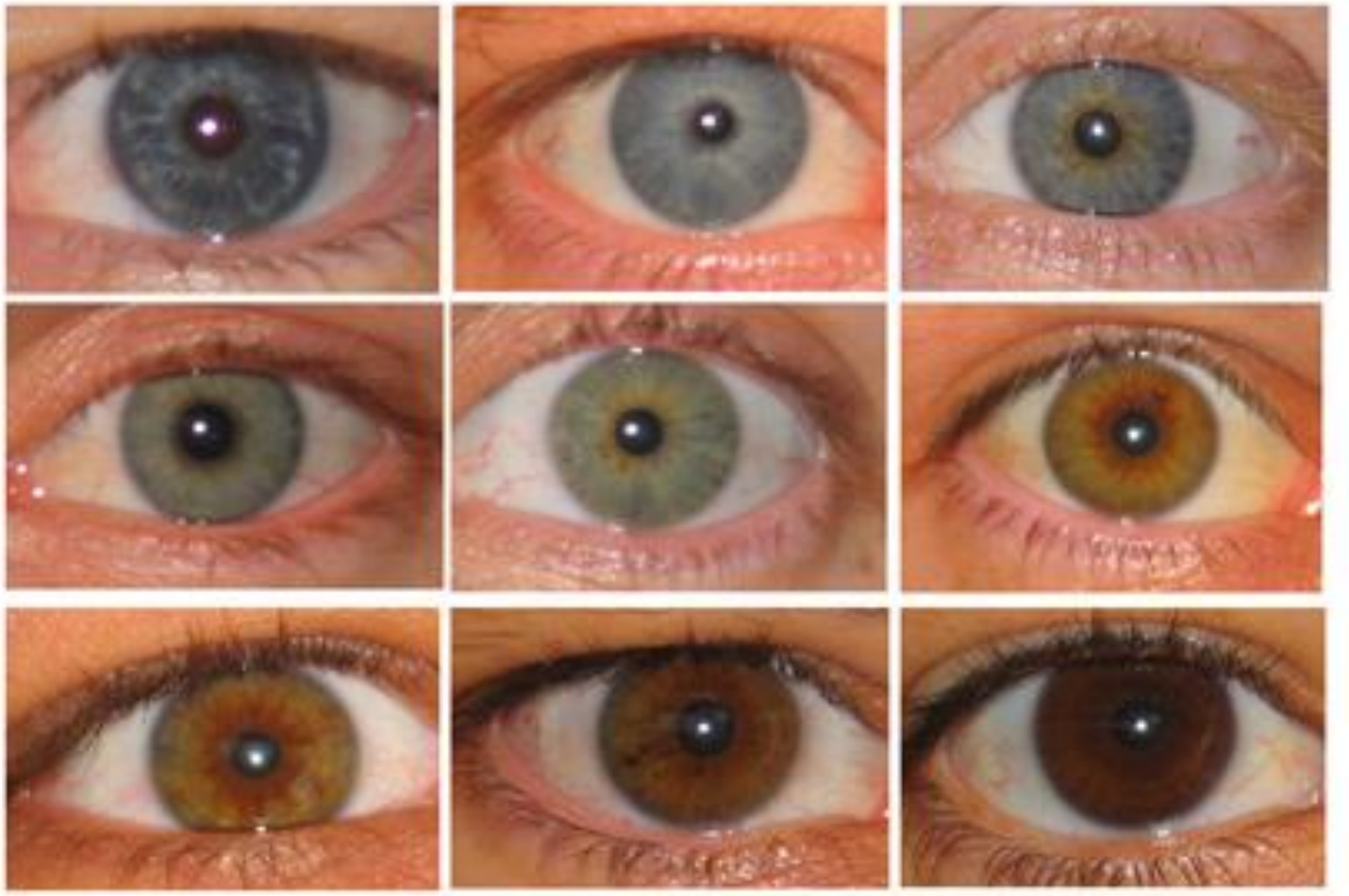
This broken version of a is epistatic to b and c: the final product (a blank poster) shows no evidence of what B and C have been told to do. We can't tell if B's instructions said to add red or blue, or if C's said to draw a circle or a square.

The important aspect of epistasis is that it doesn't just influence the phenotype, it hides the output of another gene or genes.

MULTIPLE GENES

- Height and other similar features are controlled not just by one gene, but rather, by multiple (often many) genes that each make a small contribution to the overall outcome. This inheritance pattern is sometimes called polygenic inheritance (poly- = many). For instance, a recent study found over 400 genes linked to variation in height.
- When there are large numbers of genes involved, it becomes hard to distinguish the effect of each individual gene, and even harder to see that gene variants (alleles) are inherited according to Mendelian rules. In an additional complication, height doesn’t just depend on genetics: it also depends on environmental factors, such as a child’s overall health and the type of nutrition he or she gets while growing up.

- Under different environmental conditions, polygenic inheritance leads to a continuous, or quantitative, variation of the character in a biological population.
- Most characters are quantitative, for example, **an organism's size, weight, color, and sometimes, resistance to disease, as well as many economically important properties possessed by agricultural animals, for example, the yield and fat content of milk in cows, the clip and color of wool in sheep, and the egg-laying capacity and egg size in chickens.**



Sex-linked inheritance

- The rules of inheritance considered so far, with the use of Mendel's analysis as an example, are the rules of autosomes. Most of the chromosomes in a genome are autosomes. The sex chromosomes are fewer in number, and, generally in diploidorganisms, there is just one pair.

- In females, there is a pair of identical sex chromosomes called the **X chromosomes.** The **Y chromosome** is considerably shorter than the X. At meiosis in females, the two X chromosomes pair and segregate like autosomes so that each egg receives one X chromosome. Hence the female is said to be the **homogametic** sex. At meiosis in males, the X and the Y pair over a short region, which ensures that the X and Y separate so that half the sperm cells receive X and the other half receive Y. Therefore the male is called the **heterogametic** sex.

Inheritance of Organelle Genes

- Extranuclear genes (or cytoplasmic genes) are found in organelles in the cytoplasm
- Mitochondria, chloroplasts, and other plant plastids carry small circular DNA molecules
- Extranuclear genes are inherited maternally because the zygote's cytoplasm comes from the egg