Cycle 5: Genetics and Inheritance

Introduction to Mendelian Inheritance

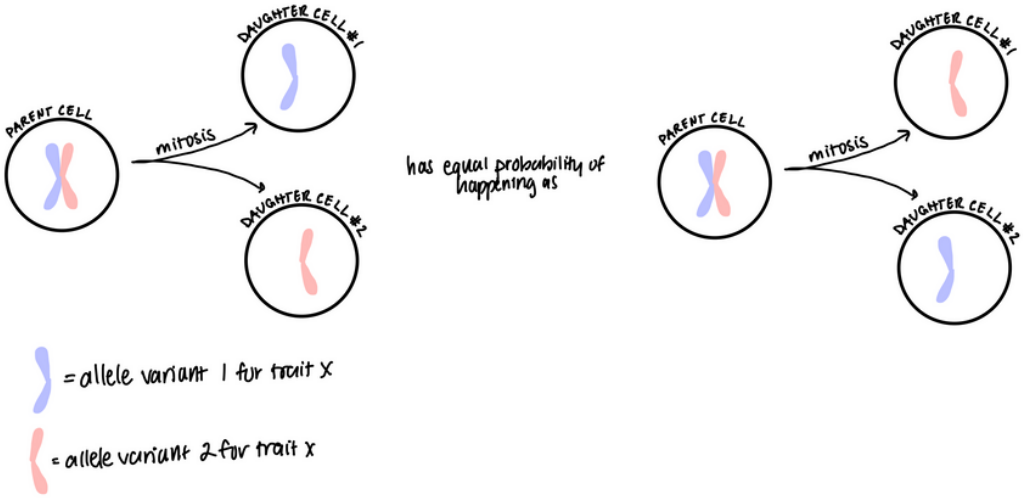
Arguably the most prominent genetics researcher of the 1800s was Gregor Mendel, to whom we credit the concept of **Mendelian inheritance**, which makes up one of the most basic but fundamental pillars of genetics as we know it today. Before Mendel, the reigning theory of how traits were passed down from parent to offspring was the **blending theory of inheritance**: *because offspring were observed to have characteristics of both parents, then offspring must be a genetic blend of the parent generation.* This means if the father had dark brown hair and the mother had blond hair, the child must then have light brown hair.

The problem with this theory is that if it were true, it would mean that as generations pass, the population would become *homogenized* and consist of only one singular intermediate phenotype/genotype. This would mean that eventually, every organism in the population would have the same shade of light brown hair. This theory would therefore not hold as it implies that genetic variation cannot persist over time, which we know is not true.

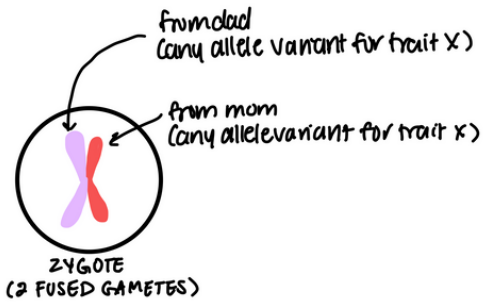
Mendel's Experiments

Mendel started running his own experiment using the scientific method, outlined in the following steps:

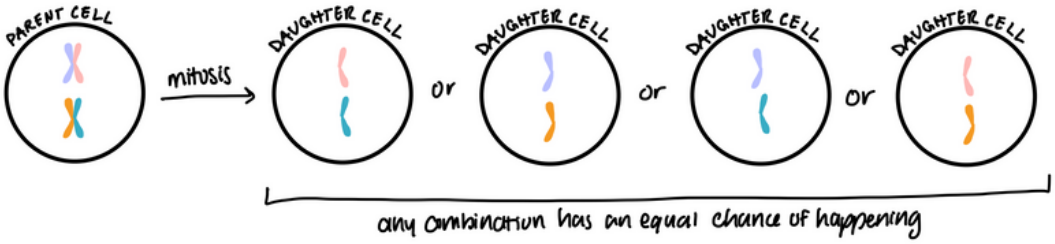
1. **Controlled crosses**: he made the plants he worked on unable to self-pollinate and then he physically cross-pollinated plants of various genotypes together
2. He analyzed the offspring of those crosses to determine which traits were dominant and which were recessive
    a. Note that the classifications he used were:
        i. *P for parental generation (usually one parent homozygous for the recessive allele and one parent homozygous for the dominant allele)*
        ii. *F1 for the offspring produced by crossing the parental generation*
        iii. *F2 for the offspring produced by crossing the F1 generation*
        iv. *etc.*
3. Mendel came to five related conclusions:
    a. Variation in traits (such as hair colour) is due to variation in **alleles**, which are *differences in genetic sequence*
    b. Alleles segregate *randomly* into gametes–this is called the *law of segregation*: inside a cell undergoing meiosis, the pair of alleles of the same gene will segregate. One allele will go into each gamete, and the allocation of which allele goes into which gamete is completely random



c.Organisms inherit two alleles for each trait (one from each parent)

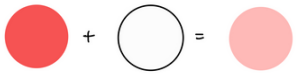


d.During the segregation of alleles into gametes, alleles of different pairs (i.e. different genes) get allocated independently of each other–this is called the *law of independent assortment*: just because a gamete inherits the b allele from the Bb pair doesn't necessarily mean that it will also inherit the a allele from the Aa pair, and vice versa. Basically, the inheritance of an allele for any gene has no correlation with the inheritance of a specific allele for another gene

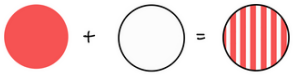


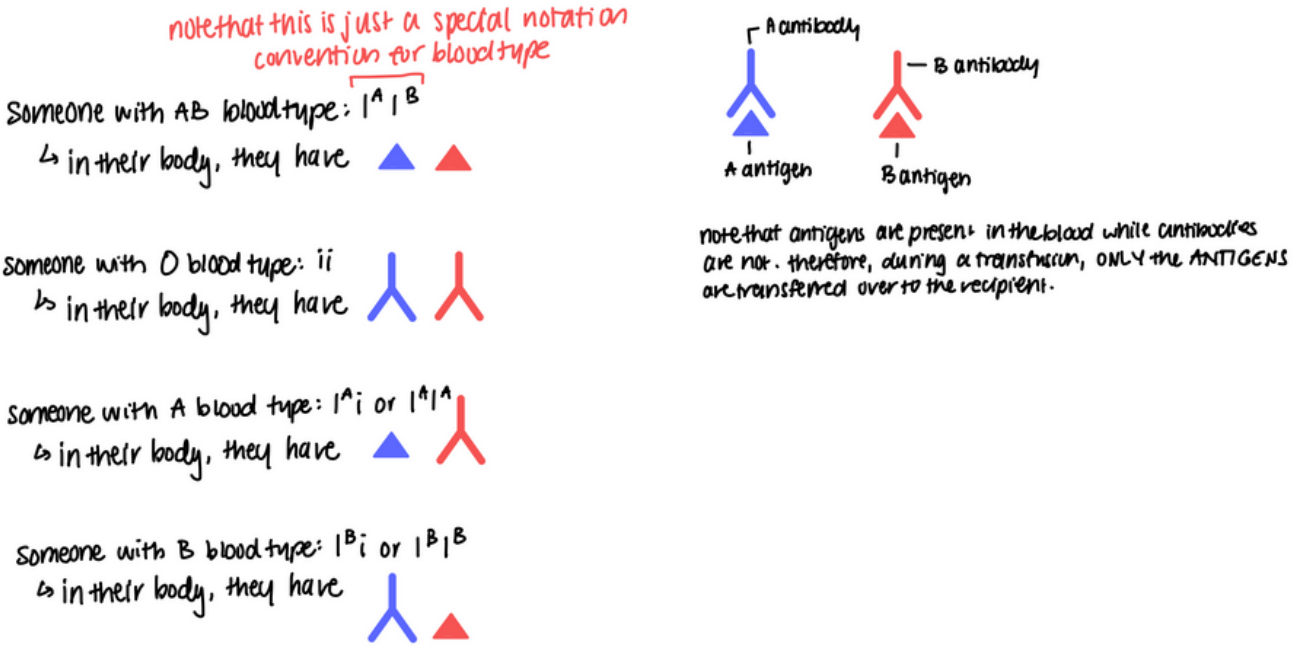
e.The phenotype of heterozygous organisms is determined by the dominant allele

Complete dominance: dominant allele + recessive allele → dominant phenotype
Incomplete dominance: dominant allele + dominant allele → intermediate phenotype

- Neither allele is fully expressed
- Example: mild Tay Sachs disease is not as severe as full Tay Sachs but not as benign as no Tay Sachs
- Example: a red rose + a white rose produces a pink rose 

Codominance: dominant allele + dominant allele → both phenotypes

- Both alleles are equally expressed
- Example: AB blood types have both the A antigen and B antigen
  - How this translates to blood transfusions: someone with AB blood type has both antigens (the thing that antibodies recognize and attack) and so therefore does not have either the A or the B antibody (if they did, the antibodies would attack the antigens in their own blood and it would be considered an autoimmune disease). This means that when they get a blood transfusion, they can receive blood from all types (A, B, and O): BLOOD TYPE AB IS CONSIDERED A **UNIVERSAL RECIPIENT.** However, since they have both antigens, they cannot donate to any other type than their own (if they donate to type A, the B antibodies in the recipient will attack the B antigens in the donated blood, and etc.).
  - On the other hand, people with blood type O have neither A nor B antigens but have both A and B antibodies. This means that if they were to get a blood transfusion with blood containing either the A or B antigen (i.e. type A/B/AB), their antibodies will attack the new blood and cause issues. For this reason, type O can only receive blood from type O. However, since type O doesn't contain any antigens, it is safe to be donated to any blood type since there's nothing for the recipient's antibodies to attack: BLOOD TYPE O IS CONSIDERED A **UNIVERSAL DONOR.**
- Example: a red rose + a white rose produces a rose with red and white stripes 



The process of transfusion involves mixing blood from 2 people — the donor and the recipient. Any combination of donor-recipient that results in the presence of both an antigen and its corresponding antibody in the recipient is dangerous (antibody attacks antigen = inflammation). Therefore, the following example scenarios can happen:

DONOR	RECIPIENT	MOLECULES IN RECIPIENT	REACTION?
$I^A I^B$	$I^A I^A$		yes → unsafe
$I^A I^B$	$I^A I^B$		no → safe
ii	$I^A I^B$		no → safe
$I^A I^B$	ii		yes → unsafe

Monohybrid and dihybrid crosses

We can study Mendelian inheritance using **monohybrid** (which follows the inheritance of one gene) and **dihybrid** (which follows the inheritance of two genes that get assorted independently) crosses. From these crosses we can determine the ratio of different phenotypes that theoretically occur in the offspring. Note that these crosses and their ratios show the PROBABILITY of obtaining offspring of these phenotypes; it doesn't necessarily mean that the offspring will follow the ratio exactly.

Sex-linked traits

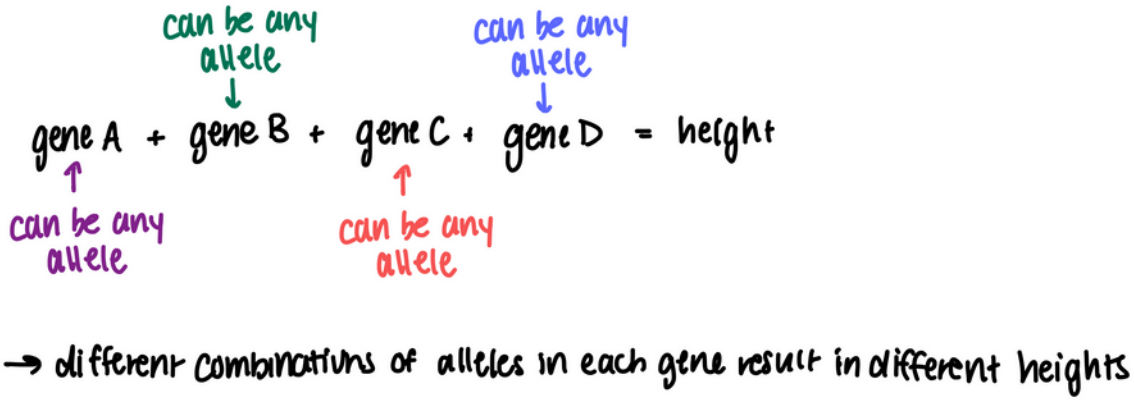
Sex-linked characteristics are those encoded by alleles found on the sex chromosomes (i.e. X and Y chromosomes). Since males and females have different sets of sex chromosomes, it follows that sex-linked characteristics/diseases follow different inheritance patterns between the two sexes.

Females have two X chromosomes: this means that if the female is heterozygous for a gene with a dominant and a recessive allele, the dominant allele (usually the functional/non-pathological one) is expressed and the female is NOT affected by the disease. However, she is still a **carrier** and can pass down the recessive allele to her offspring.

In contrast, for the male who has only one X chromosome, whatever the allele he inherits on that X chromosome is the one that is expressed. This means he only has one copy of the gene and if it's the recessive allele, he will be affected. Due to this, we can see that *X-linked recessive disorders can have high probabilities of affecting offspring* when compared to autosomal recessive disorders.

Introduction to Epistasis

Epistasis is an example of non-Mendelian genetics: the genotypic and phenotypic ratios that occur from epistasis can differ from the classic Mendelian ratio of 9:3:3:1. It is considered non-Mendelian because it explains how multiple genes can work together to determine one specific trait, whereas Mendel predicted that each trait was only determined by one specific gene. In fact, with epistasis, we can even observe a continuous distribution of variation of phenotypes in a population–for example, with Mendelian genetics, we might predict either a brown hair phenotype or a blond hair phenotype and no in-between. With epistasis, however, we might be able to observe brown hair and blond hair and also the different shades of brown that exist in between. This is because certain traits that participate in epistasis are **polygenic**, meaning that they're encoded by more than one gene. For example, human height is a polygenic trait: our height is influenced by multiple genes working together, not just one. These genes can combine together to form distinct genotypes which then produce distinct phenotypes.



Polygenic Inheritance

Epistasis is the process in which **polygenic inheritance** happens: epistasis is defined as an inheritance where *one gene can interfere with the expression of another gene*, somewhat similar to what happens during Mendelian incomplete dominance. For example, we can look at two genes that could code for the colour of a dog's fur. Gene B's dominant allele might code for the production of pigment while gene E's dominant allele might code for the deposition of pigment (and of course, the recessive allele for both genes would mean no production/deposition). Therefore, for full hair colour, you'd need both production and deposition of pigment. We can follow the polygenic inheritance of these genes in a dihybrid cross.

Note the notation of alleles that lead to a specific phenotype. For example, if a fully black furred dog requires the expression of a dominant allele for both genes B and E, the notation would be B_E_. This means that both a B and an E allele are required for this black phenotype, and the alleles that go into the blank spots could be B or b (for the first blank) and E or e (for the second blank).

gene B has 2 alleles: B → production of pigment
b → no production of pigment

gene E has 2 alleles: E → deposition of pigment
e → no deposition of pigment