Autosomal Dominant and Recessive Inheritance

Mendel's Laws

* The simple genetic characters are those which presences or absence depends on the **genotype** at a single **locus**.
* Expression of any human character is required a large number of genes and environmental factors. **Mendel stated that each individual has two alleles for each trait, one from each parent**.
* The two alleles may or may not contain the same genetic information.
- If the two alleles are identical, the individual is called **homozygous** for the trait.
- If the two alleles have different information, the individual is called **heterozygous**.

* In **heterozygous** individuals the only allele that is expressed is the **dominant.** The **recessive** allele is present but its expression is hidden.
* **Note** that dominance and recessiveness are properties of characters not genes.
* **Most human dominant syndromes are known only in heterozygous.**

The central principles of Mendel's work are two laws:

1. Law of Segregation (The "First Law")

It states that sexually reproducing organisms posses genes that occur in pairs **(diploid)**

* for any particular trait each parent passes **a randomly selected copy (allele)** of only one of these to its offspring (segregates).
- More precisely the law states that when any individual produces **gametes,** the copies of a **gene** separate so that each gamete receives only one copy (allele). A gamete will receive one **allele** .
- The principle of segregation state is that genes are not blended in the offspring, in contrast genes remain intact and distinct. (e.g. the color of a person's eyes).
- An allele can be transmitted to an offspring in the next generation. So it would be impossible to trace genetic inheritance from one generation to the next.

2. Law of Independent Assortment (The "Second Law")

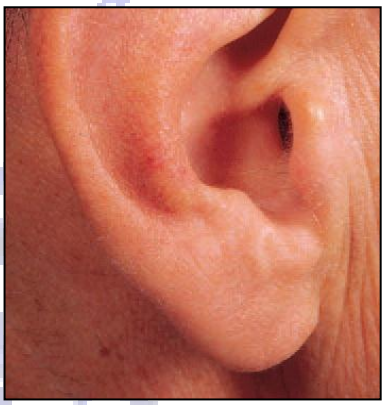
* Genes at different loci are transmitted independently of one another during gamete formation from parents to offspring.
* The principle of independent assortment is that the allele transmitted at one locus to the offspring has no effect on the selection of other allele at the other locus.
* Mendel concluded that different traits are inherited independently of each other, so that there is no relation, for example, between a cat's color and tail length. This is actually true only for genes that are **not linked** to each other.

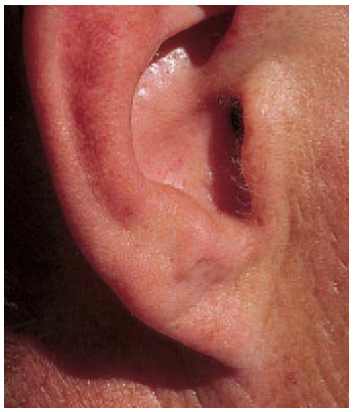
* In independent assortment the chromosomes that result are randomly sorted from all possible combinations of maternal and paternal chromosomes, and the gametes end up with a random mix instead of a pre-defined "set" from either parent

Punnet square illustrating a cross between *HH* and *hh* homozygote parents

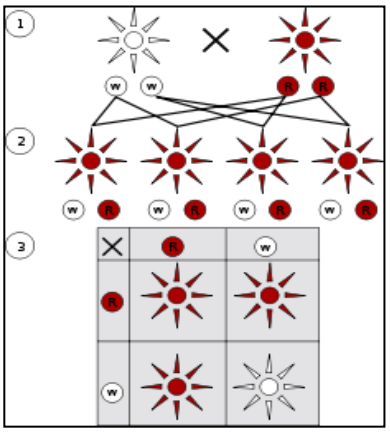
* Mendel's experiment also showed that **the effects of one allele may mask those of another.** He performed crosses (mating) between plants homozygous for the red tall gene (two identical copies of an allele label *H*), and plants homozygous for the short gene (having two copies of an allele *h*). This cross can only reproduce heterozygous (*Hh*) offspring. This reflect the fact that ***H* allele is dominant**, while ***h* alelle is recessive.**
* **For example,** unattached (free) earlobes (picture on the left) are dominant over attached earlobes (picture on the right), so a suitable key would be *EE or Ee for unattached earlobes and ee for attached earlobe*

		Parent	
		h	h
Parent	H	Hh	Hh
	H	Hh	Hh





Mendel's experiments with mixing one trait always resulted in a 3:1 ratio between dominant and recessive phenotypes in the second generation.



This figure show the Dominant and recessive phenotypes.
(1) Parental generation.
(2) F_1 generation.
(3) F_2 generation.

* **Dominant (red)** and **recessive (white)** phenotype look alike in the F_1 (first) generation and show a 3:1 ratio in the F_2 (second) generation. (ww) homozygous recessive

* Any of the possible combinations of gametes formed from maternal and paternal chromosomes will occur with equal frequency. For human gametes, with **23 pairs of chromosomes**, the number of possibilities is $\mathbf{2^{23}}$ **or 8,388,608** possible combinations.

* The gametes will normally end up with 23 chromosomes, but the origin of any particular one will be randomly selected from paternal or maternal chromosomes. This contributes to the genetic variability of progeny.

Dominance and recessiveness are properties of character, not genes:

A character is **dominant** if it is manifest in the heterozygote and **recessive** if not. Thus **sickle cell anemia is recessive** because only HbS homozygous manifest it. Heterozygous for the same gene show sickling trait, which is therefore a dominant character. Most human dominant syndromes are known only in heterozygotes. Sometimes homozygotes are born from mating two heterozygous affected people, and much more severely affected.

There are five basic mendelian pedigree patterns:

* Mendilian characters may be determined by loci on an autosome or on the X or Y sex chromosomes.
* Autosomal character in both sexes and X- linked character in females can be dominant or recessive.
* Nobody has two genetically different Y chromosome (in the rare XYY males, the two Y chromosomes are duplicated).

Thus there are five mendelian pedigree patterns.

1. Autosomal Dominant inheritance:

* An affected offspring usually has at least one affected parent.
* Affects either sex
* Transmitted by either sex
* A child of an affected X unaffected mating has 50% chance of being affected (this assumes the affected parent is heterozygous). So half of the children will be heterozygotes and will express the disease, while half will be normal homozygotes.

Example: **Postaxial polydactyly,** the presence of an extra digit next to the fifth digit.

* There is no skipping of generations: if an individual has polydactyly, one parent must also have it.
* This leads to **a vertical transmission** pattern, in which the disease phenotype is usually seen in one generation after another.
* If neither parent has the trait, none of the children will have it.
* Roughly equal numbers of affected males and females. **Recurrence Risk:** Each birth is an independent event, thus even the parent have already had a child with disease, their recurrence risk remain and the probability that their next child will have the disease is still ½ (50%).

The Punnett square illustrates that the affected parent can pass either a disease gene or a normal gene to his or her children, each event has the probability of 0.5%.

	Unaffected parent		
		a	a
Affected parent	A	Aa	Aa
	a	aa	aa

2. Autosomal recessive inheritance:

* Affected people are usually born to unaffected parents (heterozygous).
* Parents of affected people are usually asymptomatic carriers.
* There is an increased incidence of parental consanguinity (Latin, with blood) refers to the mating of related individuals.
* Affect either sex
* **Example: Albinism** that results from mutation in the gene that encodes tryrosinase, a tyrosine- metabolizing enzyme. The resulting tyrosinase deficiency creates a block in the metabolic pathway that normally leads to the synthesis of melanin pigment. The affected individual has very little pigment in the skin, hair and eyes.
* Because melanin is also required for the normal development of the optic fibers, albinos may also display nystagmus (rapid uncontrolled eye movement) and reduced visual acuity.
* Unlike autosomal dominant disease, autosomal recessive disease are horizontaly transmitted usually observed multiple siblings but not in earlier generation.
* **Recurrence Risk**: After the birth of an affected child, each subsequent child has a 25% chance of being affected

The Punnett square demonstrate one fourth (1/4)of the offspring of two heterozygotes will be normal homozygotes, half (1/2)will be phenotypically normal heterozygous carriers, and one fourth (1/4)will be homozygotes affected with the disease

		Carrier Parent	
		A	**a**
Carrier Parent	**A**	**AA**	**Aa**
	a	**Aa**	**aa**

3. X- linked recessive inheritance:

* Affect mainly males
* Affected males are usually born to unaffected parents, the mother is normally an asymptomatic carrier and may have affected male relatives
* Females may be affected if the father is affected and the mother is a carrier, or occasionally as a result of non- random X- inactivation
* There is no male- to- male transmission in the pedigree **(but mating of an affected male and carrier female can give the appearance of male transmission)**

4. X- linked dominant inheritance:

* Affects either sex, but more females than males
* Females are often more mildly and more variably affected than males
* **The child of an affected female, regardless of its sex, has 50% chance of being affected**
* **For an affected male, all his daughters but none of his sons are affected**

5. Y- linked inheritance:

* Affect only males
* Affected males always have an affected father (unless there is a new mutation)
* All sons of affected man are affected