

Laws of Inheritance

Mendel's Laws of Heredity

Mendel formed the Laws of Heredity (the Law of Segregation and the Law of Independent Assortment) from his pea plant experiments.

KEY TAKEAWAYS

Key Points

- By crossing purple and white pea plants, Mendel found the offspring were purple rather than mixed, indicating one color was dominant over the other.
- Mendel's Law of Segregation states individuals possess two alleles and a parent passes only one allele to his/her offspring.
- Mendel's Law of Independent Assortment states the inheritance of one pair of factors (genes) is independent of the inheritance of the other pair.
- If the two alleles are identical, the individual is called homozygous for the trait; if the two alleles are different, the individual is called heterozygous.
- Mendel cross-bred dihybrids and found that traits were inherited independently of each other.

Key Terms

- **homozygous**: of an organism in which both copies of a given gene have the same allele
- **heterozygous**: of an organism which has two different alleles of a given gene
- **allele**: one of a number of alternative forms of the same gene occupying a given position on a chromosome

Introduction

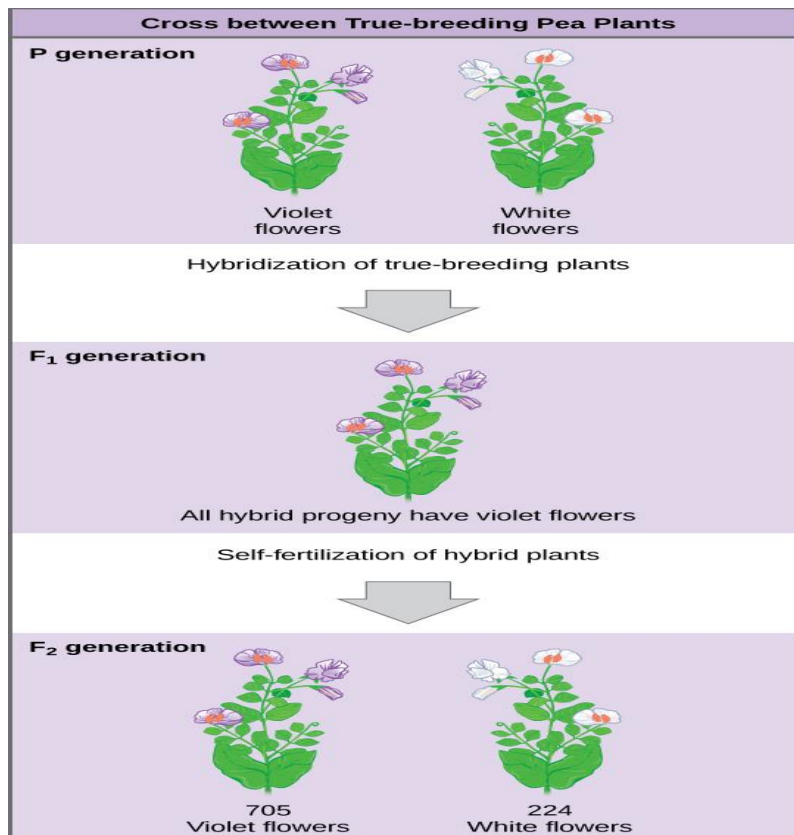
Mendelian inheritance (or Mendelian genetics or Mendelism) is a set of primary tenets relating to the transmission of hereditary characteristics from parent organisms to their children; it underlies much of genetics. The tenets were initially derived from the work of Gregor Mendel published in 1865 and 1866, which was "re-discovered" in 1900; they were initially very controversial, but they soon became the core of classical genetics.

The laws of inheritance were derived by Gregor Mendel, a 19th century monk conducting hybridization experiments in garden peas (*Pisum sativum*). Between 1856 and 1863, he cultivated and tested some 28,000 pea plants. From these experiments, he deduced two

generalizations that later became known as Mendel's Laws of Heredity or Mendelian inheritance. He described these laws in a two part paper, "Experiments on Plant Hybridization", which was published in 1866.

Mendel's Laws

Mendel discovered that by crossing true-breeding white flower and true-breeding purple flower plants, the result was a hybrid offspring. Rather than being a mix of the two colors, the offspring was purple flowered. He then conceived the idea of heredity units, which he called "factors", one of which is a recessive characteristic and the other dominant. Mendel said that factors, later called genes, normally occur in pairs in ordinary body cells, yet segregate during the formation of sex cells. Each member of the pair becomes part of the separate sex cell. The dominant gene, such as the purple flower in Mendel's plants, will hide the recessive gene, the white flower. After Mendel self-fertilized the F₁ generation and obtained an F₂ generation with a 3:1 ratio, he correctly theorized that genes can be paired in three different ways for each trait: AA, aa, and Aa. The capital A represents the dominant factor while the lowercase a represents the recessive.



Mendel's Pea Plants: In one of his experiments on inheritance patterns, Mendel crossed plants that were true-breeding for violet flower color with plants true-breeding for white flower color (the P generation). The resulting hybrids in the F₁ generation all had violet flowers. In the F₂ generation, approximately three-quarters of the plants had violet flowers, and one-quarter had white flowers.

Mendel stated that each individual has two alleles for each trait, one from each parent. Thus, he formed the “first rule”, the Law of Segregation, which states individuals possess two alleles and a parent passes only one allele to his/her offspring. One allele is given by the female parent and the other is given by the male parent. The two factors may or may not contain the same information. If the two alleles are identical, the individual is called homozygous for the trait. If the two alleles are different, the individual is called heterozygous. The presence of an allele does not promise that the trait will be expressed in the individual that possesses it. In heterozygous individuals, the only allele that is expressed is the dominant. The recessive allele is present, but its expression is hidden. The genotype of an individual is made up of the many alleles it possesses. An individual’s physical appearance, or phenotype, is determined by its alleles as well as by its environment.

Mendel also analyzed the pattern of inheritance of seven pairs of contrasting traits in the domestic pea plant. He did this by cross-breeding dihybrids; that is, plants that were heterozygous for the alleles controlling two different traits. Mendel then crossed these dihybrids. If it is inevitable that round seeds must always be yellow and wrinkled seeds must be green, then he would have expected that this would produce a typical monohybrid cross: 75 percent round-yellow; 25 percent wrinkled-green. But, in fact, his mating generated seeds that showed all possible combinations of the color and texture traits. He found 9/16 of the offspring were round-yellow, 3/16 were round-green, 3/16 were wrinkled-yellow, and 1/16 were wrinkled-green. Finding in every case that each of his seven traits was inherited independently of the others, he formed his “second rule”, the Law of Independent Assortment, which states the inheritance of one pair of factors (genes) is independent of the inheritance of the other pair. Today we know that this rule holds only if the genes are on separate chromosomes

Mendel’s Law of Dominance

In a heterozygote, the allele which masks the other is referred to as dominant, while the allele that is masked is referred to as recessive.

KEY TAKEAWAYS

Key Points

- Dominant alleles are expressed exclusively in a heterozygote, while recessive traits are expressed only if the organism is homozygous for the recessive allele.
- A single allele may be dominant over one allele, but recessive to another.
- Not all traits are controlled by simple dominance as a form of inheritance; more complex forms of inheritance have been found to exist.

Key Terms

- **dominant:** a relationship between alleles of a gene, in which one allele masks the expression (phenotype) of another allele at the same locus
- **recessive:** able to be covered up by a dominant trait

Alleles Can Be Dominant or Recessive

Most familiar animals and some plants have paired chromosomes and are described as diploid. They have two versions of each chromosome: one contributed by the female parent in her ovum and one by the male parent in his sperm. These are joined at fertilization. The ovum and sperm cells (the gametes) have only one copy of each chromosome and are described as haploid.



Recessive traits are only visible if an individual inherits two copies of the recessive allele: The child in the photo expresses albinism, a recessive trait.

Mendel's law of dominance states that in a heterozygote, one trait will conceal the presence of another trait for the same characteristic. Rather than both alleles contributing to a phenotype, the dominant allele will be expressed exclusively. The recessive allele will remain "latent," but will be transmitted to offspring by the same manner in which the dominant allele is transmitted. The recessive trait will only be expressed by offspring that have two copies of this allele; these offspring will breed true when self-crossed.

By definition, the terms dominant and recessive refer to the genotypic interaction of alleles in producing the phenotype of the heterozygote. The key concept is genetic: which of the two alleles present in the heterozygote is expressed, such that the organism is phenotypically identical to one of the two homozygotes. It is sometimes convenient to talk about the trait corresponding to the dominant allele as the dominant trait and the trait corresponding to the hidden allele as the recessive trait. However, this can easily lead to confusion in understanding the concept as phenotypic. For example, to say that “green peas” dominate “yellow peas” confuses inherited genotypes and expressed phenotypes. This will subsequently confuse discussion of the molecular basis of the phenotypic difference. Dominance is not inherent. One allele can be dominant to a second allele, recessive to a third allele, and codominant to a fourth. If a genetic trait is recessive, a person needs to inherit two copies of the gene for the trait to be expressed. Thus, both parents have to be carriers of a recessive trait in order for a child to express that trait.

Since Mendel’s experiments with pea plants, other researchers have found that the law of dominance does not always hold true. Instead, several different patterns of inheritance have been found to exist.

Mendel’s Law of Segregation

Mendel’s Law of Segregation states that a diploid organism passes a randomly selected allele for a trait to its offspring, such that the offspring receives one allele from each parent.

KEY TAKEAWAYS

Key Points

- Each gamete acquires one of the two alleles as chromosomes separate into different gametes during meiosis.
- Heterozygotes, which possess one dominant and one recessive allele, can receive each allele from either parent and will look identical to homozygous dominant individuals; the Law of Segregation supports Mendel’s observed 3:1 phenotypic ratio.
- Mendel proposed the Law of Segregation after observing that pea plants with two different traits produced offspring that all expressed the dominant trait, but the following generation expressed the dominant and recessive traits in a 3:1 ratio.

Key Terms

- **law of segregation:** a diploid individual possesses a pair of alleles for any particular trait and each parent passes one of these randomly to its offspring

Equal Segregation of Alleles

Observing that true-breeding pea plants with contrasting traits gave rise to F_1 generations that all expressed the dominant trait and F_2 generations that expressed the dominant and recessive traits in a 3:1 ratio, Mendel proposed the law of segregation. The law of segregation states that

each individual that is a diploid has a pair of alleles (copy) for a particular trait. Each parent passes an allele at random to their offspring resulting in a diploid organism. The allele that contains the dominant trait determines the phenotype of the offspring. In essence, the law states that copies of genes separate or segregate so that each gamete receives only one allele.

The Law of Segregation states that alleles segregate randomly into gametes: When gametes are formed, each allele of one parent segregates randomly into the gametes, such that half of the parent's gametes carry each allele.

For the F₂ generation of a monohybrid cross, the following three possible combinations of genotypes could result: homozygous dominant, heterozygous, or homozygous recessive. Because heterozygotes could arise from two different pathways (receiving one dominant and one recessive allele from either parent), and because heterozygotes and homozygous dominant individuals are phenotypically identical, the law supports Mendel's observed 3:1 phenotypic ratio. The equal segregation of alleles is the reason we can apply the Punnett square to accurately predict the offspring of parents with known genotypes.

The physical basis of Mendel's law of segregation is the first division of meiosis in which the homologous chromosomes with their different versions of each gene are segregated into daughter nuclei. The behavior of homologous chromosomes during meiosis can account for the segregation of the alleles at each genetic locus to different gametes. As chromosomes separate into different gametes during meiosis, the two different alleles for a particular gene also segregate so that each gamete acquires one of the two alleles. In Mendel's experiments, the segregation and the independent assortment during meiosis in the F₁ generation give rise to the F₂ phenotypic ratios observed by Mendel. The role of the meiotic segregation of chromosomes in sexual reproduction was not understood by the scientific community during Mendel's lifetime.

Mendel's Law of Independent Assortment

Independent assortment allows the calculation of genotypic and phenotypic ratios based on the probability of individual gene combinations.

KEY TAKEAWAYS

Key Points

- Mendel's law of independent assortment states that genes do not influence each other with regard to the sorting of alleles into gametes; every possible combination of alleles for every gene is equally likely to occur.
- The calculation of any particular genotypic combination of more than one gene is, therefore, the probability of the desired genotype at the first locus multiplied by the probability of the desired genotype at the other loci.
- The forked line method can be used to calculate the chances of all possible genotypic combinations from a cross, while the probability method can be used to calculate the chance of any one particular genotype that might result from that cross.

Key Terms

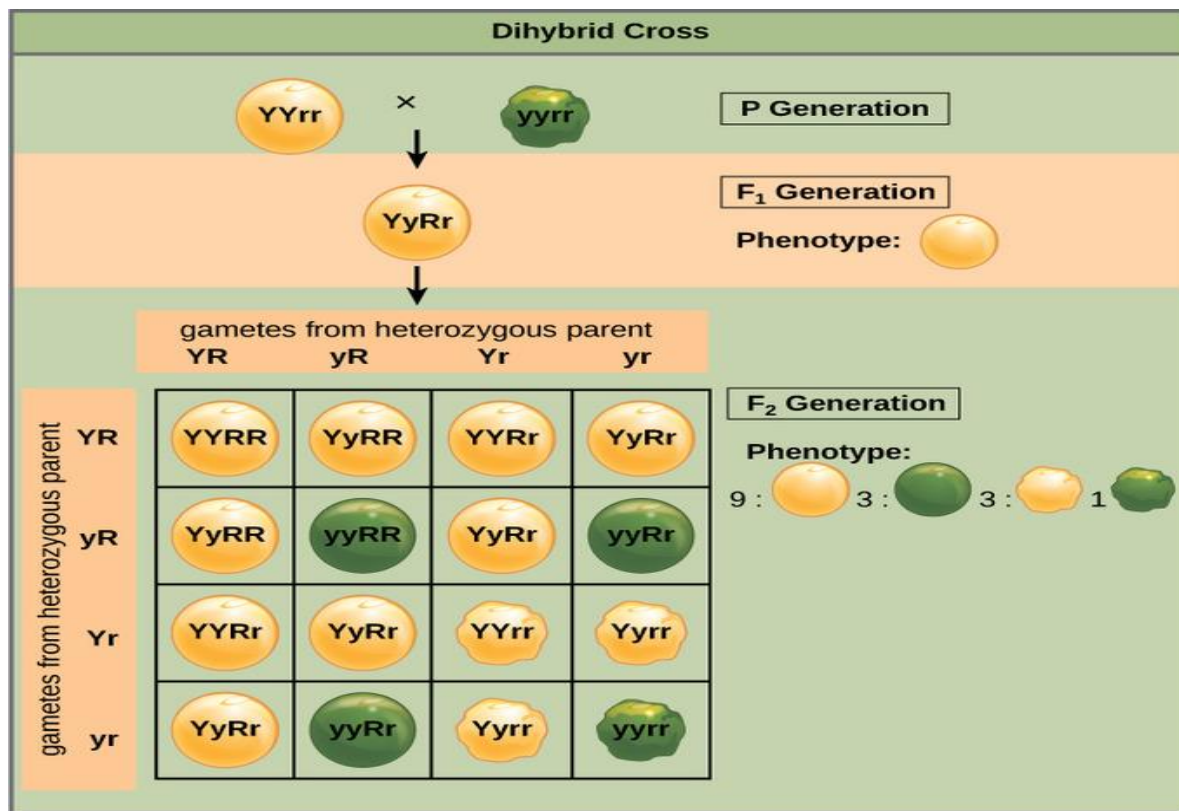
- **independent assortment:** separate genes for separate traits are passed independently of one another from parents to offspring

Independent Assortment

Mendel's law of independent assortment states that genes do not influence each other with regard to the sorting of alleles into gametes: every possible combination of alleles for every

gene is equally likely to occur. The independent assortment of genes can be illustrated by the dihybrid cross: a cross between two true-breeding parents that express different traits for two characteristics. Consider the characteristics of seed color and seed texture for two pea plants: one that has green, wrinkled seeds ($yyrr$) and another that has yellow, round seeds ($YYRR$). Because each parent is homozygous, the law of segregation indicates that the gametes for the green/wrinkled plant all are yr , while the gametes for the yellow/round plant are all YR . Therefore, the F_1 generation of offspring all are $YyRr$.

For the F_2 generation, the law of segregation requires that each gamete receive either an R allele or an r allele along with either a Y allele or a y allele. The law of independent assortment states that a gamete into which an r allele sorted would be equally likely to contain either a Y allele or a y allele. Thus, there are four equally likely gametes that can be formed when the $YyRr$ heterozygote is self-crossed as follows: YR , Yr , yR , and yr . Arranging these gametes along the top and left of a 4×4 Punnett square gives us 16 equally likely genotypic combinations. From these genotypes, we infer a phenotypic ratio of 9 round/yellow:3 round/green:3 wrinkled/yellow:1 wrinkled/green. These are the offspring ratios we would expect, assuming we performed the crosses with a large enough sample size.



Independent assortment of 2 genes: This dihybrid cross of pea plants involves the genes for seed color and texture.

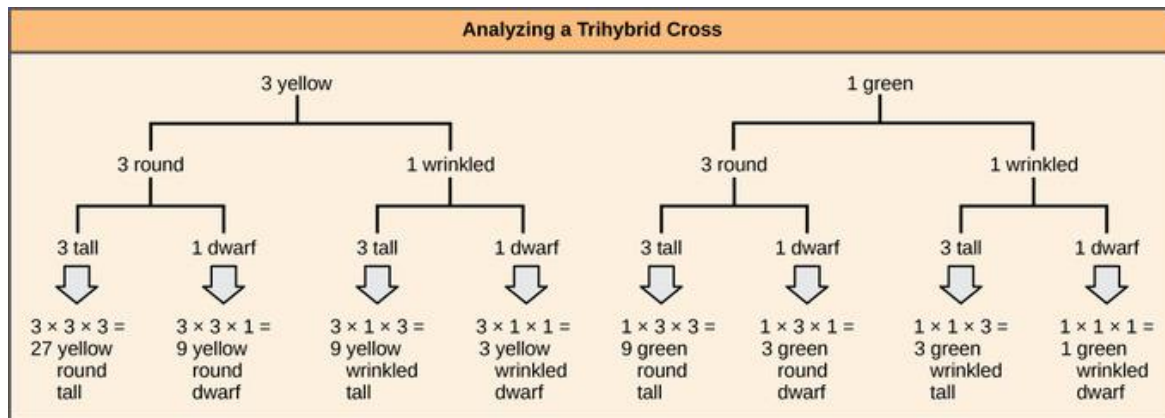
Because of independent assortment and dominance, the 9:3:3:1 dihybrid phenotypic ratio can be collapsed into two 3:1 ratios, characteristic of any monohybrid cross that follows a dominant and recessive pattern. Ignoring seed color and considering only seed texture in the above dihybrid cross, we would expect that three-quarters of the F_2 generation offspring would be round and one-quarter would be wrinkled. Similarly, isolating only seed color, we would assume that three-quarters of the F_2 offspring would be yellow and one-quarter would be green. The

sorting of alleles for texture and color are independent events, so we can apply the product rule. Therefore, the proportion of round and yellow F₂ offspring is expected to be $(3/4) \times (3/4) = 9/16$, and the proportion of wrinkled and green offspring is expected to be $(1/4) \times (1/4) = 1/16$. These proportions are identical to those obtained using a Punnett square. Round/green and wrinkled/yellow offspring can also be calculated using the product rule as each of these genotypes includes one dominant and one recessive phenotype. Therefore, the proportion of each is calculated as $(3/4) \times (1/4) = 3/16$.

Forked-Line Method

When more than two genes are being considered, the Punnett-square method becomes unwieldy. For instance, examining a cross involving four genes would require a 16×16 grid containing 256 boxes. It would be extremely cumbersome to manually enter each genotype. For more complex crosses, the forked-line and probability methods are preferred.

To prepare a forked-line diagram for a cross between F₁ heterozygotes resulting from a cross between AABBCC and aabbcc parents, we first create rows equal to the number of genes being considered and then segregate the alleles in each row on forked lines according to the probabilities for individual monohybrid crosses. We then multiply the values along each forked path to obtain the F₂ offspring probabilities. Note that this process is a diagrammatic version of the product rule. The values along each forked pathway can be multiplied because each gene assort independently. For a trihybrid cross, the F₂ phenotypic ratio is 27:9:9:9:3:3:3:1.



Independent assortment of 3 genes: The forked-line method can be used to analyze a trihybrid cross. Here, the probability for color in the F₂ generation occupies the top row (3 yellow:1 green). The probability for shape occupies the second row (3 round:1 wrinkled), and the probability for height occupies the third row (3 tall:1 dwarf). The probability for each possible combination of traits is calculated by multiplying the probability for each individual trait. Thus, the probability of F₂ offspring having yellow, round, and tall traits is $3 \times 3 \times 3$, or 27.

Probability Method

While the forked-line method is a diagrammatic approach to keeping track of probabilities in a cross, the probability method gives the proportions of offspring expected to exhibit each phenotype (or genotype) without the added visual assistance.

To fully demonstrate the power of the probability method, however, we can consider specific genetic calculations. For instance, for a tetrahybrid cross between individuals that are heterozygotes for all four genes, and in which all four genes are sorting independently in a dominant and recessive pattern, what proportion of the offspring will be expected to be homozygous recessive for all four alleles? Rather than writing out every possible genotype, we can use the probability method. We know that for each gene the fraction of homozygous recessive offspring will be $1/4$. Therefore, multiplying this fraction for each of the four genes, $(1/4) \times (1/4) \times (1/4) \times (1/4)$, we determine that $1/256$ of the offspring will be quadruply homozygous recessive.

Genetic Linkage and Violation of the Law of Independent Assortment

Genes that are on the same chromosome, or “linked”, do not assort independently, but can be separated by recombination.

KEY TAKEAWAYS

Key Points

- Two genes close together on the same chromosome tend to be inherited together and are said to be linked.
- Linked genes can be separated by recombination in which homologous chromosomes exchange genetic information during meiosis; this results in parental, or nonrecombinant genotypes, as well as a smaller proportion of recombinant genotypes.
- Geneticists can use the amount of recombination between genes to estimate the distance between them on a chromosome.

Key Terms

- **linkage**: the property of genes of being inherited together
- **recombination**: the formation of genetic combinations in offspring that are not present in the parents

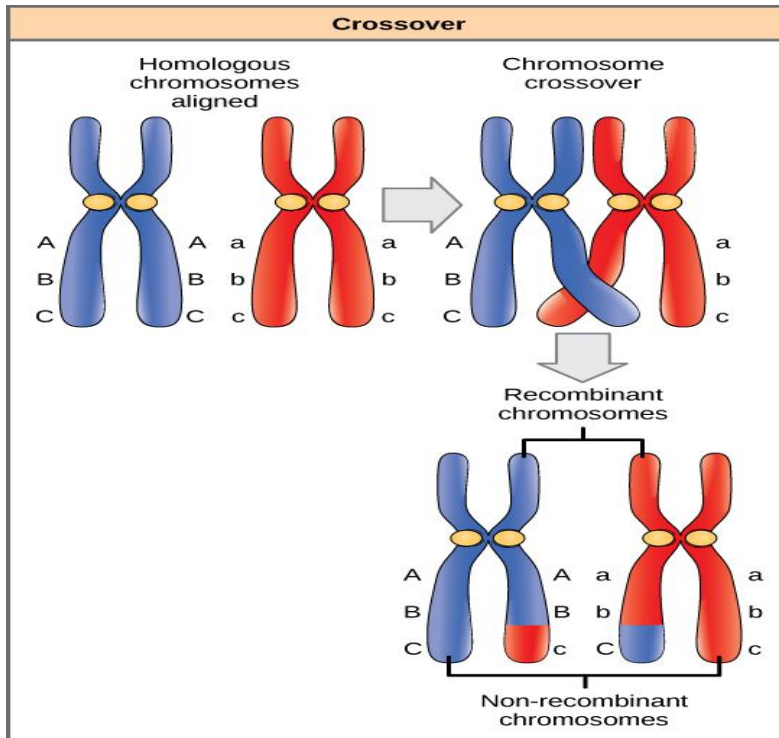
Linked Genes Violate the Law of Independent Assortment

Although all of Mendel’s pea characteristics behaved according to the law of independent assortment, we now know that some allele combinations are not inherited independently of each other. Genes that are located on separate non-homologous chromosomes will always sort independently. However, each chromosome contains hundreds or thousands of genes organized linearly on chromosomes like beads on a string. The segregation of alleles into gametes can be influenced by linkage, in which genes that are located physically close to each other on the same chromosome are more likely to be inherited as a pair. However, because of the process of recombination, or “crossover,” it is possible for two genes on the same chromosome to behave independently, or as if they are not linked. To understand this, let’s consider the biological basis of gene linkage and recombination.

		<i>TtIi</i>			
		<i>TI</i>	<i>Ti</i>	<i>tI</i>	<i>ti</i>
<i>TtIi</i>	<i>TI</i>	<i>TTII</i>	<i>TTIi</i>	<i>TtII</i>	<i>TtIi</i>
	<i>Ti</i>	<i>TTIi</i>	<i>TTii</i>	<i>TtIi</i>	<i>Ttii</i>
	<i>tI</i>	<i>TtII</i>	<i>TtIi</i>	<i>ttII</i>	<i>ttIi</i>
	<i>ti</i>	<i>TtIi</i>	<i>Ttii</i>	<i>ttIi</i>	<i>ttii</i>

Unlinked genes assort independently: This figure shows all possible combinations of offspring resulting from a dihybrid cross of pea plants that are heterozygous for the tall/dwarf and inflated/constricted alleles.

Homologous chromosomes possess the same genes in the same linear order. The alleles may differ on homologous chromosome pairs, but the genes to which they correspond do not. In preparation for the first division of meiosis, homologous chromosomes replicate and synapse. Like genes on the homologs align with each other. At this stage, segments of homologous chromosomes exchange linear segments of genetic material. This process is called recombination, or crossover, and it is a common genetic process. Because the genes are aligned during recombination, the gene order is not altered. Instead, the result of recombination is that maternal and paternal alleles are combined onto the same chromosome. Across a given chromosome, several recombination events may occur, causing extensive shuffling of alleles.



Linked genes can be separated by recombination: The process of crossover, or recombination, occurs when two homologous chromosomes align during meiosis and exchange a segment of genetic material. Here, the alleles for gene C were exchanged. The result is two recombinant and two non-recombinant chromosomes.

When two genes are located in close proximity on the same chromosome, they are considered linked, and their alleles tend to be transmitted through meiosis together. To exemplify this, imagine a dihybrid cross involving flower color and plant height in which the genes are next to each other on the chromosome. If one homologous chromosome has alleles for tall plants and red flowers, and the other chromosome has genes for short plants and yellow flowers, then when the gametes are formed, the tall and red alleles will go together into a gamete and the short and yellow alleles will go into other gametes. These are called the parental genotypes because they have been inherited intact from the parents of the individual producing gametes. But unlike if the genes were on different chromosomes, there will be no gametes with tall and yellow alleles and no gametes with short and red alleles. If you create the Punnett square with these gametes, you will see that the classical Mendelian prediction of a 9:3:3:1 outcome of a dihybrid cross would not apply. As the distance between two genes increases, the probability of one or more crossovers between them increases, and the genes behave more like they are on separate chromosomes. Geneticists have used the proportion of recombinant gametes (the ones not like the parents) as a measure of how far apart genes are on a chromosome. Using this information, they have constructed elaborate maps of genes on chromosomes for well-studied organisms, including humans.

Mendel's seminal publication makes no mention of linkage, and many researchers have questioned whether he encountered linkage, but chose not to publish those crosses out of concern that they would invalidate his independent assortment postulate. The garden pea has seven chromosomes and some have suggested that his choice of seven characteristics was not a coincidence. However, even if the genes he examined were not located on separate

chromosomes, it is possible that he simply did not observe linkage because of the extensive shuffling effects of recombination.

Epistasis

Epistasis occurs when one gene masks or interferes with the expression of another.

LEARNING OBJECTIVES

Key Points

- In many cases, several genes may contribute to a particular phenotype; when the actions of one gene masks the effects of another, this gene is said to be epistatic to the second.
- Epistasis can occur when a recessive genotype masks the actions of another gene, or when a dominant allele masks the effects of another gene.
- Epistasis can be reciprocal: either gene, when present in the dominant (or recessive) form, expresses the same phenotype.
- Any single characteristic that results in a phenotypic ratio that totals 16 (such as 12:3:1, 9:3:4, or others) is typical of a two-gene interaction.

Key Terms

- **epistasis:** the modification of the expression of a gene by another unrelated one

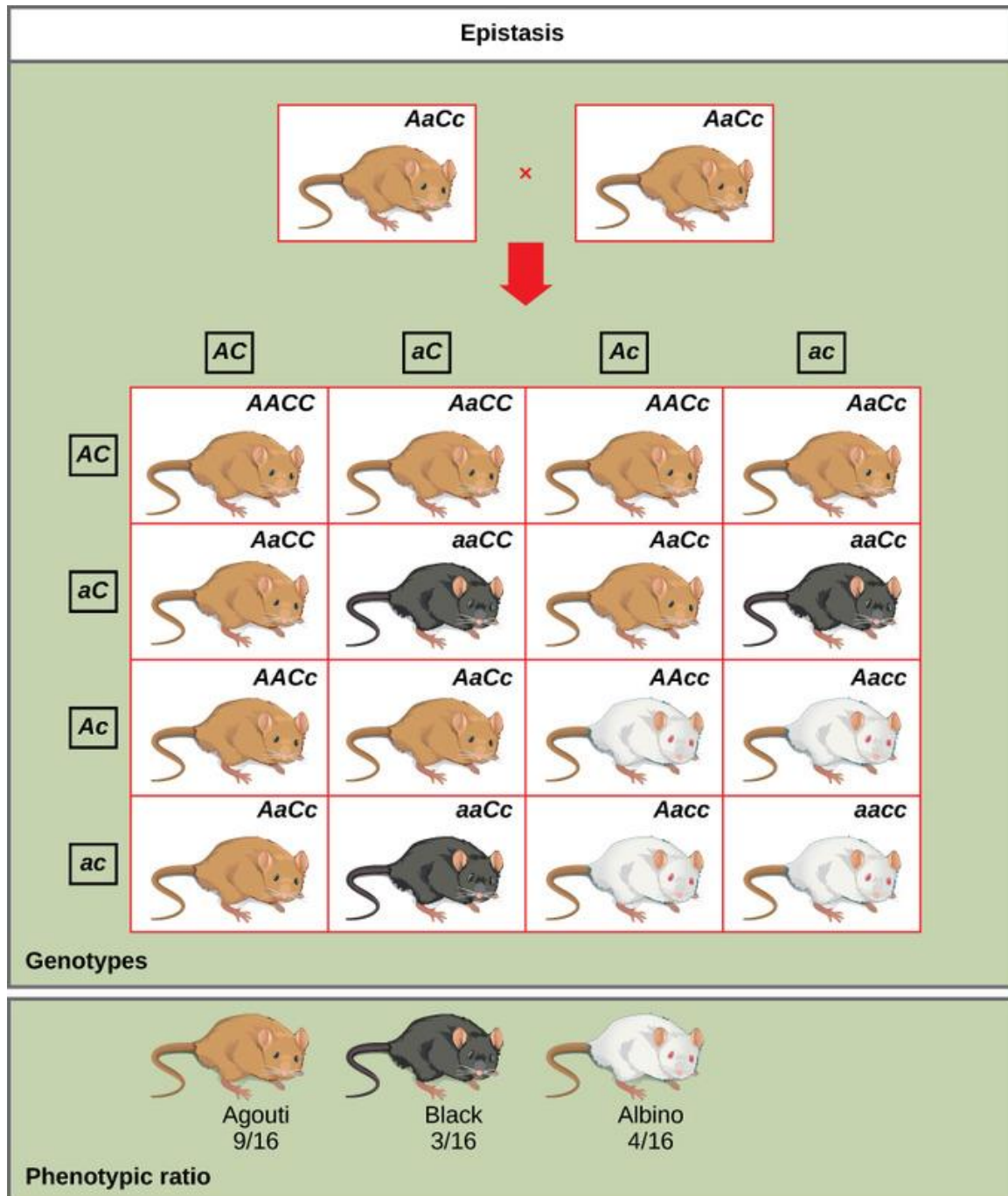
Epistasis

Mendel's studies in pea plants implied that the sum of an individual's phenotype was controlled by genes (or as he called them, unit factors): every characteristic was distinctly and completely controlled by a single gene. In fact, single observable characteristics are almost always under the influence of multiple genes (each with two or more alleles) acting in unison. For example, at least eight genes contribute to eye color in humans.

In some cases, several genes can contribute to aspects of a common phenotype without their gene products ever directly interacting. In the case of organ development, for instance, genes may be expressed sequentially, with each gene adding to the complexity and specificity of the organ. Genes may function in complementary or synergistic fashions: two or more genes need to be expressed simultaneously to affect a phenotype. Genes may also oppose each other with one gene modifying the expression of another.

In epistasis, the interaction between genes is antagonistic: one gene masks or interferes with the expression of another. "Epistasis" is a word composed of Greek roots that mean "standing upon." The alleles that are being masked or silenced are said to be hypostatic to the epistatic alleles that are doing the masking. Often the biochemical basis of epistasis is a gene pathway in which the expression of one gene is dependent on the function of a gene that precedes or follows it in the pathway.

An example of epistasis is pigmentation in mice. The wild-type coat color, agouti (AA), is dominant to solid-colored fur (aa). However, a separate gene (C) is necessary for pigment production. A mouse with a recessive c allele at this locus is unable to produce pigment and is albino regardless of the allele present at locus A. Therefore, the genotypes AAcc, Aacc, and aacc all produce the same albino phenotype. A cross between heterozygotes for both genes (AaCc x AaCc) would generate offspring with a phenotypic ratio of 9 agouti:3 solid color:4 albino. In this case, the C gene is epistatic to the A gene.



Epistasis in mouse coat color: In mice, the mottled agouti coat color (A) is dominant to a solid coloration, such as black or gray. A gene at a separate locus (C) is responsible for pigment production. The recessive c allele does not produce pigment and a mouse with the homozygous recessive cc genotype is albino regardless of the allele present at the A locus. Thus, the C gene is epistatic to the A gene.

Epistasis can also occur when a dominant allele masks expression at a separate gene. Fruit color in summer squash is expressed in this way. Homozygous recessive expression of the W gene (ww) coupled with homozygous dominant or heterozygous expression of the Y gene (YY or Yy) generates yellow fruit, while the wwyy genotype produces green fruit. However, if a dominant copy of the W gene is present in the homozygous or heterozygous form, the summer squash will produce white fruit regardless of the Y alleles. A cross between white heterozygotes for both genes (WwYy × WwYy) would produce offspring with a phenotypic ratio of 12 white:3 yellow:1 green.

Finally, epistasis can be reciprocal: either gene, when present in the dominant (or recessive) form, expresses the same phenotype. In the shepherd's purse plant (*Capsella bursa-pastoris*), the characteristic of seed shape is controlled by two genes in a dominant epistatic relationship. When the genes A and B are both homozygous recessive (aabb), the seeds are ovoid. If the dominant allele for either of these genes is present, the result is triangular seeds. That is, every possible genotype other than aabb results in triangular seeds; a cross between heterozygotes for both genes (AaBb × AaBb) would yield offspring with a phenotypic ratio of 15 triangular:1 ovoid.

Keep in mind that any single characteristic that results in a phenotypic ratio that totals 16 is typical of a two-gene interaction. Recall the phenotypic inheritance pattern for Mendel's dihybrid cross, which considered two non-interacting genes: 9:3:3:1. Similarly, we would expect interacting gene pairs to also exhibit ratios expressed as 16 parts. Note that we are assuming the interacting genes are not linked; they are still assorting independently into gametes.