Mendelian Genetics: How Are Traits Inherited?

It requires indeed some courage to undertake a labor of such far-reaching extent; this appears, however, to be the only right way by which we can finally reach the solution of a question, the importance of which cannot be overestimated, in connection with the history of the evolution of organic forms.

—Gregor Mendel, 1866

Chapter opening photo
Portrait of Gregor Mendel, the founder of genetics. Mendel’s largely misunderstood paper was published in 1866, less than a decade after Darwin’s book, The Origin of Species.

Overview
In this chapter, we will examine how traits are passed from generation to generation—a branch of biology called classical, or Mendelian, genetics. We will see that a modest garden, growing within the walls of a
Moravian monastery at about the same time that Darwin was writing *The Origin of Species*, was to change forever our understanding of how traits are inherited. From that same garden would come answers to some of the nagging questions about Darwin’s controversial new theory, evolution by the mechanism of natural selection.

Darwin’s revolutionary insight was immediately recognized by some as a powerful explanation for the variety of species on Earth. Many people, however, remained unconvinced. For those who held certain religious beliefs, including one stating that all species were put on Earth by a supreme being during one week of creation as set forth in Genesis, no amount of scientific evidence could be convincing. But even those who searched for naturalistic explanations for the diversity of life found reason to criticize Darwin. Some features of natural selection were readily accepted; they were obvious and verifiable by observation and study. For example, one could easily see that most organisms produced more offspring than could possibly survive. And it was evident that traits that enhance the ability of individuals to survive and reproduce are passed on to the next generation. But Darwin’s critics were quick to point out that there was no satisfactory explanation for how traits were passed from parents to offspring. The ideas that had been proposed about the mechanism of heredity were highly improbable and not verifiable. Many, including Darwin, mistakenly believed that traits from two parents blended together in their offspring. Thus, the children of a blue-eyed man and a brown-eyed woman would have bluish-brown eyes. Likewise, if the pollen of a red flower landed on a white-flowered plant, the flowers of the offspring should all be pink. But clearly blending does not happen—at least not all the time. Traits of parents may occasionally appear as blended intermediates in their children (more on this in Section 3-3), but more often they do not. Some traits are passed on apparently unaltered from parent to offspring; others hide for generations at a time, only to reappear at unpredictable times in
family histories. What could account for the seemingly unpredictable behavior of heritable traits as they are passed from generation to generation?

Another problem for Darwin and his supporters was their inability to explain the source of variation among individuals in natural populations. Variation, like heredity, is an essential element of Darwinian selection. In light of the erroneous theory of blending, all organisms of a population should appear quite similar. In fact, if blending were indeed occurring, then all variation within a given population would be obliterated within about 10 generations; all individuals would be identical, and evolution would cease. But that is not the case.

Unbeknownst to Darwin and his critics, these problems were being addressed in a series of ingenious experiments carried out by an Austrian monk, Gregor Mendel. (See the chapter opening photograph.) Mendel’s work was published in 1866. Unfortunately, although Darwin lived until 1881, he was unaware of these experiments or their lasting importance to his theory of evolution by natural selection.

3-1 How Are Traits Passed from Generation to Generation?

Do you look more like your mother or your father? Perhaps you are the spitting image of your Great Uncle Horace. Chances are, while you share some characteristics or traits with each of your parents, you are not a perfect blend of the two. You may even have characteristics that appear in neither of your parents. Clearly, different forms of traits can persist in populations for many generations. They remain whole and unaltered by both time and their passage through the individuals that carry them and pass them on. Hereditary traits in all of their varied forms behave as units, moving through time as bits of information.

But living things, be they people, oak trees, grizzly bears, mushrooms, slime molds, or pea plants, are each combinations of perhaps hundreds of thousands of traits. To study them all would have been a monumental task indeed. It would be nearly impossible to find consistencies or rules that govern the inheritance of all of them at once. Gregor Mendel was the first to recognize that traits in individuals are controlled by some type of hereditary units, which he called “factors.” He was also the first to describe the passage of these factors through the generations. There were at least three reasons for Mendel’s success: (1) He focused on just a few traits—seven to be exact—instead of many traits as others did; (2) he thoroughly documented and quantified all of his experimental results; (3) he chose to study these traits in the garden pea, Pisum sativum.
Mendel Discovered That Traits Are Inherited in Discrete Units

Gregor Mendel, born Johann Mendel, was the son of peasant farmers. From a childhood spent on a farm, Mendel understood the value of plant breeding in developing productive varieties of crops. This undoubtedly contributed to his lifelong interest in gardening and horticulture. At the age of 21, Mendel entered the priesthood, taking the clerical name of Gregor by which he is now remembered. In the remote monastery in what is now the Czech Republic, Mendel had time to indulge his love of plant breeding. He read widely, especially the natural sciences. He was quite aware of the controversial new theory of evolution proposed by his British contemporary, Charles Darwin. He knew of the unanswered questions about heredity arising from Darwin’s theory, the very topic Mendel sought to understand. He made the fortuitous choice to study the pea, which is an organism that can be easily manipulated in breeding experiments. Even in Mendel’s time, pea plants came in many distinct strains or varieties.

Mendel studied traits that each occur in two distinct forms (Figure 3-1). The color of the pea flower, for example, is either purple or white, never purplish white. The shape of the pea pod is either puffy and inflated or narrow and constricted, never partly puffy, and so on with each of the seven traits he studied. He began by developing true-breeding varieties for each of the seven traits; that is, when bred among themselves, all of the offspring of a given variety were identical to the parent for that trait. For example, one variety produced only purple blooms for many generations, another only white blooms. One variety produced only puffy pods for many generations, another only constricted pods. There were 14 varieties in all. When he was certain that all of his varieties bred true, he carefully engineered matings between pairs of plants showing different forms of each trait.

In addition to this focused approach, Mendel added yet another new twist: Mathematical analysis. He counted the number of young plants that developed the parental forms of each trait and calculated the numerical ratios of offspring showing each form of a trait. In Mendel’s day, this application of mathematics to plant breeding experiments was uncommon, to say the least. Let’s start with just one trait that Mendel studied and carefully follow his reasoning.

Mendel’s First Discovery
When organisms reproduce sexually, both parents produce specialized reproductive cells called gametes. Male gametes are sperm, and female gametes are eggs. When egg and sperm fuse—a process called fertilization—a new individual is produced. In flowering plants such as the garden pea, sperm are contained in pollen. Eggs are contained in ovules, which when fertilized, mature into seeds. Ovules are contained within a structure in the flower called the carpel (Figure 3-2). Pea plants are often (but not always) self-fertilizing; that is, the sperm-carrying pollen usually lands on the top of the egg-carrying carpel of the same plant. If the flowers are covered to ensure that insects cannot carry pollen from one flower to another, the sperm and eggs from the same plant combine within the bud to give rise to peas—the seeds of the next generation of pea plants.

Mendel manipulated this process by opening the flower buds and cutting off the pollen-bearing structures, called anthers, from some flowers. Using anthers taken from different flowers, Mendel could control exactly which sperm was used to fertilize which eggs (Figure 3-2). He started with two varieties of plants, one whose ancestors produced only round, smooth peas and another from a long line of plants that produced only wrinkled peas. He cross-fertilized the two varieties. In other words, he used the pollen of one variety to fertilize the egg of the other variety, creating hybrid offspring. This was done by brushing the female parts of flowers of the round-seeded line with the male pollen from the wrinkled-seeded variety, and vice versa. If blending were indeed the basis of heredity, as discussed earlier, all of the hybrid seeds from these experimental crosses would have been partially wrinkled in texture, intermediate between the two parental forms. That did not happen. Remarkably, the hybrid peas of this first generation, called the F₁, or first filial, generation, were all round.
### Table of Traits Studied by Mendel

<table>
<thead>
<tr>
<th>Trait</th>
<th>Form 1</th>
<th>Form 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plant Height</td>
<td>Tall (6–7 feet)</td>
<td>Dwarf (9–18 inches)</td>
</tr>
<tr>
<td>Flower Color</td>
<td>Purple</td>
<td>White</td>
</tr>
<tr>
<td>Flower Position</td>
<td>At leaf junctions (axial)</td>
<td>At tips of branches (terminal)</td>
</tr>
<tr>
<td>Pod Color</td>
<td>Green</td>
<td>Yellow</td>
</tr>
<tr>
<td>Pod Shape</td>
<td>Inflated</td>
<td>Constricted</td>
</tr>
<tr>
<td>Seed Color</td>
<td>Yellow</td>
<td>Green</td>
</tr>
<tr>
<td>Seed Shape</td>
<td>Round</td>
<td>Wrinkled</td>
</tr>
</tbody>
</table>

**Figure 3-1** The seven traits that Mendel studied. Note that each trait appears in one of two distinct forms.

When these hybrid round peas grew into mature plants and were permitted to self-fertilize, some of the many “grandchildren” of the original pure-breeding varieties—the $F_2$, or second filial, generation—were round and some were wrinkled. In fact, 5,474 of the $F_2$ generation were round, and 1,850 were wrinkled, a ratio of about three round
Mendel took pollen from the anthers of a plant exhibiting one form of a trait. He brushed the pollen onto the stigma of a plant showing a different form of the trait. The anthers of the second plant were first removed to prevent self-fertilization.

Flower of a pea plant (a) Cross-fertilization (b)

Figure 3-2 (a) Flower of a pea plant, cut to show male and female flower parts. (b) Using artificial cross-fertilization, Mendel controlled matings between plants.

peas for every one wrinkled pea. Within each pea pod of this F₂ generation (a single pod contains about six to nine peas), about 75%, or three-fourths, of the peas were round, and about 25%, or one-fourth, were wrinkled (Figure 3-3).

What happened when this second generation was allowed to grow and self-fertilize? Mendel planted both the round and wrinkled peas and observed that the wrinkled peas bred true, producing only wrinkled offspring. Likewise, approximately one-third of the round peas bred true, producing only round offspring. Two thirds of the round F₁ peas, however, gave rise to both round and wrinkled peas in the third, or F₃, generation. The results were similar for all seven paired characters. For every cross between parents showing alternate forms of a single trait, the F₁ offspring plants all exhibited just one form of the trait. When the F₁ plants underwent self-fertilization, about 75% of the resulting F₂ generation showed one form of the trait, and about 25% exhibited the alternate form (Figure 3-3). On the BioInquiry web site, you can try this experiment by crossing white-flowered peas and purple-flowered peas. What color are the blooms of the generation? Which form of the flower color trait occurs in about 75% of the generation?

Mendel’s Interpretations Perhaps Mendel’s real genius was in how he interpreted the results of his experiments. Mendel imagined that each of the contrasting forms of a trait, for example the “roundness” or “wrinkledness” of seeds, was controlled by a hereditary factor. He realized that his results could be best explained by supposing these factors occur in pairs within the individual pea plants. A pea arising from a long line of plants producing only wrinkled seeds has two factors for wrinkled seed texture; likewise, a pea from a family lineage that produces only round seeds has two factors for round seed texture.

When organisms breed, hereditary factors are passed on whole, and usually unaltered, to the offspring. Mendel realized that during reproduction, each parent contributes one hereditary factor for each trait to the offspring. Thus for every trait, each individual has one maternally derived factor and one paternally derived factor—one factor from its mother and one from its father.
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Mendel grew pea plants from true-breeding wrinkled-seeded and true-breeding round-seeded varieties.

When these plants matured, he used pollen taken from the anthers of the wrinkled-seeded variety to fertilize the plant grown from the round-seeded variety. He removed the anthers of the round-seeded plant to prevent self-fertilization.

The carpel of the round-seeded plant matured into a pea pod containing all round peas. These peas were the seeds of the F1 generation.

Mendel planted the F1 peas and allowed them to grow into mature plants.

These plants were allowed to self-fertilize. Pollen from the anthers of the F1 plants fell directly onto the tops of the carpels of the same flower.

The carpels of the F1 plants matured into pea pods containing peas—the seeds of the F2 generation. About 75% of these peas were round and about 25% were wrinkled.

Figure 3-3 = One of Mendel’s crosses between smooth round-seeded and wrinkled-seeded pea plants.
When an organism has two identical factors for a trait, as in true-breeding varieties, it is said to be **homozygous** for that trait. (The prefix *homo-* means “the same.”) If the two factors are different, the organism is said to be **heterozygous** for that trait. (The prefix *hetero-* means “different.”) Mendel’s true-breeding varieties were homozygous; the hybrid offspring he created were heterozygous.

Mendel’s results and interpretations are still relevant today, although our vocabulary is slightly different from his. We use the term **gene** to describe the hereditary information that determines a single trait. Seed texture in peas, for example, is a trait determined by a gene. Flower color is another trait determined by a gene. The different forms that a gene might take—what Mendel referred to as factors—are called **alleles**. Wrinkled and round are alternate alleles for the gene for seed texture; purple and white are different alleles for the gene for flower color. *The relationship between genes and alleles is a fundamental concept of biology.*

In Mendel’s peas, the presence of the allele for round seeds was quite visible in the F1 generation. Indeed all of the peas were round. But what of the allele for wrinkled seeds that later appeared in the F2? Where was it hiding in the F1 peas?

**Dominant Traits Mask the Presence of Recessive Alleles**

Let’s call the allele for round seeds *R*, and the allele for wrinkled seeds *r*. Now, if both parents carry two identical alleles for wrinkled seeds, *rr*, each of the offspring will get an *r* allele for wrinkled seeds from mother and another wrinkled-seed *r* allele from father. All of the offspring will have a double dose of wrinkled-seed alleles, *rr*, and will have wrinkled seeds, just like the parents. These peas, as well as their parents, are homozygous for the gene for seed texture. But in Mendel’s first experimental cross, one parent had only wrinkled-seed alleles to give, *rr*, and the other parent had only round-seed alleles, *RR*. One parent could contribute only *r* alleles and the other could contribute only *R* alleles to the offspring. When the peas reproduced, the F1 generation ended up with two different alleles, *Rr*. They were heterozygous peas, with a wrinkled allele from one parent and a round allele from the other.

Yet in Mendel’s experiments, all the F1 hybrids produced round seeds. There was no sign of wrinkled seeds, even though one of the parents had wrinkled seeds. The seven traits that Mendel studied all showed the same pattern. Mendel called the trait that appeared in the F1 generation the dominant trait and the trait that was hidden the recessive trait. The allele for the hidden trait was there, whole and unchanged, in the heterozygous individuals, but it was completely masked by the presence of the dominant allele. The recessive form of a trait is only seen when both of the alleles are recessive.

Because some alleles are dominant and some are recessive, you cannot always tell the genetic makeup of an individual by looking at its traits. There may be recessive alleles in the genes masked by their dominant counterparts. For example, a round pea with two *R* alleles for round seeds would look the same as a round pea with one *R* allele and one *r* allele for wrinkled seeds. We call the forms of traits that an individual expresses—those we can see or otherwise detect—its **phenotype**. The combination of the expressed and hidden alleles in an individual’s genes we refer to as its **genotype**.

While we cannot always tell by looking, it is sometimes possible to learn the genotype of an individual by using a **testcross**. In a testcross, an individual of unknown genotype is mated with one that is homozygous for the recessive trait. In our example, a pea plant grown from a round seed whose genotype is *R*? is mated with a plant grown from a wrinkled seed, an *rr* individual. If all the offspring have round seeds, the parent of unknown genotype is most likely *RR*. What would happen if that parent were heterozygous for the seed texture gene? Try a testcross on the BioInquiry web site.

Try describing your own phenotype with regard to some traits. Do you have a widow’s peak or a dimple in your chin? Are your earlobes attached, or are they free? Now try to describe your genotype. You will find that you need more information to accurately assess
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Figure 3-4

Actors (a) Leonardo DiCaprio, (b) Matt Damon, and (c) Parker Posey illustrate some examples of human traits governed by single genes. A widow’s peak, seen in all three, is a dominant genetic trait. Compare Leonardo’s detached earlobes with Matt’s attached earlobes. Detached earlobes are the dominant form of the trait. Other single gene traits in humans include the ability to roll the tongue, hair on middle finger segments, dimples, and the ability to wiggle one’s ears.

which alleles you may be carrying. You need to know which alleles are dominant and which are recessive. You need to know which alleles your parents, and perhaps even your grandparents and great grandparents, possessed. If you have children, you can learn more about your genotype by seeing which traits are expressed in them, but even that may not be enough (Figure 3-4). We can learn about the genotypes underlying different phenotypes in plants, flies, even mice by performing controlled crosses between individuals, then calculating the ratio of offspring showing different forms of traits, in much the same way Mendel did. In human populations, where it is impossible to perform controlled crosses, we rely on family trees, called pedigrees, to follow the pathways of alleles through generations. Using the BioInquiry web site, you can practice working out the genotypes of individuals by performing controlled virtual crosses.

Family Matters

Suppose you are interested in studying human traits, but performing genetic crosses is impossible. How can you learn about the genotypes of humans by studying the phenotypes of extended families? Will such family studies always establish genotypes with certainty?

Mendel’s Observations Are Widely Applicable

The principles of classical genetics, established in the mid-19th century by Mendel, are broad in their application and fundamental to our understanding of inheritance. Were they all of what Mendel discovered, his honored position in the history of ideas would be firmly established. But there was more to his work, and that, too, was far reaching. Let us leave the monastery garden for now, and apply Mendel’s principles to more immediate issues of human health and well-being, using as an example the human genetic disease, sickle cell anemia.

Sickle cell anemia is a hereditary disease in which the blood of affected individuals has a reduced capacity for delivering oxygen to tissues. The gene involved in sickle cell anemia encodes information for making part of the hemoglobin molecule, the oxygen-carrying
protein that gives our red blood cells their color. In people with normal hemoglobin, these cells assume the shape of a biconcave disk, as seen in Figure 3-5, and they travel easily through arteries, veins, and capillaries, carrying oxygen to the tissues. The red blood cells of people with sickle cell disease appear normal if oxygen is plentiful, but when oxygen levels decline, as they do in blood that is exiting tissues through capillaries and veins, the hemoglobin in their red blood cells forms insoluble fibrous strands that distort the shape of the cells into long, thin sickles. Even slightly lower levels of oxygen are enough to cause sickling. These distorted cells cannot easily pass through the narrow capillaries of the tissues. Capillaries become clogged, and the tissues are starved for oxygen. These cells may rupture, causing severe anemia, great pain, and serious tissue damage. Without medical attention, sufferers may die.

We can analyze the inheritance of sickle cell anemia by using the same approach that Mendel used for garden peas. We cannot, however, engineer crosses among human beings. Instead, we must rely on family pedigrees to establish inheritance patterns. We will consider two alleles for hemoglobin: The allele for the normal hemoglobin protein, called \( HbA \), and the allele for sickle cell anemia, called \( HbS \). Individuals homozygous for normal hemoglobin, designated \( HbA \) \( HbA \), have no disease. Homozygotes for the sickle cell gene, \( HbS \) \( HbS \), are afflicted with the disease. In heterozygotes, \( HbA \) \( HbS \), about 1% of red blood cells exhibit the sickling trait. These individuals, called sickle cell carriers, show no symptoms of the disease under normal circumstances. Carriers lead normal lives as long as they avoid strenuous exercise, high altitudes, and other situations in which oxygen levels in their blood might get very low.

What would happen if a woman who carries two normal alleles for hemoglobin and a man who suffers from sickle cell anemia had children? The children born to this couple would be analogous to the \( F_1 \) hybrids from Mendel’s first experimental crosses. Each child would receive one \( HbA \) allele from its mother and one \( HbS \) allele from its father. Each child would be heterozygous for the sickle cell gene. Each would be a sickle cell carrier.

**Punnett Squares Predict Possible Genotypes** A clever way of envisioning how alleles are distributed during reproduction, the Punnett square was developed in the early 20th century by the British geneticist Reginald C. Punnett. For a cross involving a single trait such as sickle cell anemia, the alleles of the parents are arranged on the top and sides of a matrix as shown in Figure 3-6.

Each block of the square represents a possible combination of alleles, a genotype, that could occur in the \( F_1 \) generation. Each egg produced by the mother contains one of the maternal alleles. With regard to the gene for hemoglobin, all the possible eggs...
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Figure 3-6 = Punnett square illustrating possible genotypes of the offspring of a father suffering from sickle cell anemia and a normal mother. All children born to this couple are sickle cell carriers.

that this mother can produce with regard to the \textit{Hb} gene are listed at the far left of the rows. Because this mother is homozygous and has only \textit{HbA} alleles to contribute, all of her eggs contain the \textit{HbA} allele. Likewise, the father is homozygous for the \textit{HbS} allele, so all of his sperm contain the \textit{HbS} allele. At the heads of the columns of the Punnett square, all of the possible types of sperm with regard to the \textit{Hb} gene are listed. In each box, we insert the name of the allele at the head of that column and at the left of that row. For this match, regardless of which egg and which sperm join at conception, all the offspring will be heterozygous, which is shown by the \textit{HbA} \textit{HbS} genotypes in each of the boxes of the square. This Punnett square clearly illustrates that all children in this family have a 100\% chance of being heterozygous for the sickle cell trait, with one \textit{HbA} and one \textit{HbS} allele. All of them would be carriers of the allele for sickle cell anemia.

What happens when these children mature, marry, and have children of their own? We can envision several possible matches with different outcomes, depending on the genotypes of their spouses. First, let’s assume that a boy of the previously described family grows up and marries a woman who is homozygous for the dominant normal allele (\textit{HbA} \textit{HbA}). The possibilities for their children are illustrated on the Punnett square in Figure 3-7a.

The maternal eggs all carry the \textit{HbA} alleles because the mother is homozygous. But the heterozygous father can produce two different kinds of sperm with regard to the gene for hemoglobin: Either \textit{HbA} or \textit{HbS}. Of the four possible combinations of alleles that could occur in the children, two, or 50\%, are heterozygous, and two, the other 50\%, are homozygous for the dominant trait. Thus, each child from this union would have a 50\% chance of inheriting one copy of the sickle cell allele.

Now consider the possibility that a man of the F\textsubscript{1} generation chose a wife who was also heterozygous for the sickle cell trait (Figure 3-7b). Of the four possible genotypes that could occur in their children, two are heterozygous (\textit{HbA} \textit{HbS}). Each child in this family would have a 50\% chance of being a carrier of the sickle cell trait. The two other possible genotypes include homozygous dominant (\textit{HbA} \textit{HbA}), in which case the child would have neither the disease nor the allele for the disease, and homozygous recessive (\textit{HbS} \textit{HbS}), in which case the child would be afflicted with sickle cell anemia. Each child in this family would have a 25\% chance of each of the homozygous genotypes: They would have a 75\% chance of leading a normal life and a 25\% chance of suffering from the disease. Note that the ratio of genotypes exhibiting the two phenotypes, 3:1 normal/afflicted, corresponds exactly to the 3:1 dominant/recessive ratio that Mendel described in his experimental crosses. Were these parents to have lots and lots of children, we could reasonably predict that about 75\% of them could lead normal or nearly normal lives and about 25\% would suffer from sickle cell anemia.
Alleles Are Randomly Donated from Parents to Offspring

Using all seven of the traits he studied in peas, Mendel found that the F₂ generation averaged about three offspring exhibiting the dominant trait for each one exhibiting the recessive trait. Punnett squares illustrate that underlying the 3:1 ratio for phenotypes is a 1:2:1 ratio of genotypes—one homozygous dominant to two heterozygotes to one homozygous recessive. Mendel recognized that the 3:1 ratio of phenotypes from so many different crosses, and the 1:2:1 ratio of genotypes, imply that heterozygous parents are equally likely to donate either of their two different alleles to their offspring. Were this not the case—if, for example, only the dominant allele could be passed on—then 100% of the offspring would exhibit the dominant phenotype. Likewise, if the recessive allele were favored, offspring would all exhibit the recessive trait. The allele donated by a heterozygous parent is random. This simple but elegant insight is the best explanation of the experimental results—the 3:1 ratio of phenotypes and the 1:2:1 ratio of genotypes—from a cross between hybrids. This is called Mendel's law of segregation. Formally stated, it says that a parent contributes only one of its two alleles for a trait to each offspring, and if the parent is heterozygous for that trait, the particular allele that is donated to the offspring is random. Thus each embryo has exactly the same chance of receiving a particular allele from each parent. Assuming all combinations of alleles are equally likely to survive, the offspring of crosses between heterozygous parents will exhibit a 3:1 phenotypic ratio of dominant/recessive. If the phenotypic ratio resulting from a hybrid cross differs significantly from 3:1 (as we shall see in some special situations explained in Section 3-3), other forces must be operating.
Mendel’s Factors Can Act Independently . . . Sometimes

Thus far, we have considered the inheritance of a single characteristic, seed texture in peas or the gene for hemoglobin in humans, much as Mendel did at the beginning of his plant breeding experiments. But organisms are combinations of many traits, all of which are derived from the genes of their parents. Do Mendel’s laws apply if two or more traits are considered simultaneously? When Mendel performed crosses in which he followed two traits at a time, he found that all of his original conclusions applied to both traits. Remarkably, the two different traits appeared to be operating utterly independently of one another as they passed from parents to offspring. In his words, “the relation of each pair of different characters in hybrid union is independent of the other differences in the two original parental stocks.” This important observation is called Mendel’s law of independent assortment. It states that the alleles of one gene are passed to offspring independently of the alleles of other genes.

There are exceptions to the law of independent assortment, but the exceptions do not invalidate Mendel’s general conclusions. We shall see in Chapter 5 that the Mendelian factors, the genes, are carried on structures in cells called chromosomes. Each chromosome can carry many, many genes. When the genes for two different traits are found on the same chromosome, they have a tendency to travel together. But that does not minimize the importance of independent assortment. Genes that occur on different chromosomes do segregate independently, and even those that share a carrier chromosome may exhibit some degree of independence. It is well worth a closer look at independent assortment.

Whereas Mendel preferred to work with the accommodating garden pea, we can just as easily describe independent assortment by using another species that has played a starring role in the history of genetics: The fruit fly, Drosophila melanogaster (Figure 3-8). Fruit flies are tiny, are easy to keep, and have short life cycles, all characteristics that make them good candidates for studying the transmission of genetic traits. Females lay hundreds of eggs in a lifetime. When many offspring are produced from a single cross, it is easy to calculate the ratios of different phenotypes that result from that cross. Hundreds of different traits have been experimentally bred into the many strains of flies that inhabit genetics laboratories throughout the world. Let’s look at two of them simultaneously: Body color and wing size.

The Dihybrid Cross Most fruit flies that live in the wild have broad, straight wings and pale-colored bodies with dark transverse stripes. These traits are dominant to their alternatives, vestigial (shriveled) wings and ebony body color (Figure 3-9). A trait that is usually found in organisms in their natural, or wild, state is called the wild type. Thus, broad wings and pale, striped bodies are the wild-type forms of the traits for wing size and body color. Vestigial wings and ebony body color are recessive forms of the traits,
Dihybrid Cross:
Cross two traits simultaneously.

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called “mutant” forms.1 Fruit fly genes are usually named for the mutant form; uppercase letters designate the dominant alleles, and lowercase letters designate the recessive alleles. Starting with parents that are homozygous for both traits, let’s engineer a cross between a broad-winged (VV), striped (EE) parent (wild type for both traits) and a vestigial-winged (vv), ebony (ee) parent (mutant for both traits). Now our shorthand for the genotypes must include two sets of alleles, one for two different traits:

\[
P_1 \quad VV \quad EE \quad \times \quad vv \quad ee
\]

(broad-winged, striped) \times (vestigial-winged, ebony)

Compare this with the first parental crosses that Mendel made between parents showing different forms of a single trait. All the F1 of this cross will exhibit the dominant forms of both traits: Broad wings and pale, striped bodies. Their genotype is heterozygous for both traits:

\[
F_1 \quad Vv \quad Ee
\]

(broad-winged/striped)

Now engineer a cross between the members of the F1. Because the F1 flies are hybrids (heterozygous) for both traits and we are following the fate of two traits simultaneously, this experimental cross is called a dihybrid cross:

\[
F_1 \quad Vv \quad Ee \times Vv \quad Ee
\]

Each new fly receives one allele for wing shape and one allele for body color from each parent, but recall that the law of segregation states that the actual allele that an offspring receives for each trait is random. It is just as likely that a fly will inherit a V allele as it is that it will inherit a v allele for wing size. The same goes for the E and e alleles for body color.

The law of independent assortment also applies. Hence, these alleles can be inherited by the offspring in any combination, as long as each new fly receives two alleles for wing shape and two alleles for body color. The possible genotypes that can result from this cross can be examined by using a Punnett square, as shown in Figure 3-10.

These four alleles can combine to give a total of 16 genotypes, not all of them different, but each with equal likelihood. Of the 16 combinations, 9 are different. How many different phenotypes do these 16 genotypes represent? Recall that alleles designated with an uppercase letter are dominant to those designated with a lowercase letter. Figure 3-11 shows a Punnett square filled in with phenotypes instead of genotypes. From the 9 different genotypes, a total of 4 different phenotypes can occur, and they occur in a very specific ratio: 9:3:3:1, or 9 wild type for both traits to 3 wild-type wing size with mutant body color, to 3 mutant wing size with wild-type body color, to 1 mutant for both traits.

The 9:3:3:1 ratio is characteristic of the offspring of a dihybrid cross in which both traits follow Mendel’s laws of segregation and independent assortment. Mendel did many dihybrid crosses in which he chose several different pairs from the seven traits he studied in pea plants, and in every case, he found that the ratio of different phenotypes of the offspring approximated the predicted 9:3:3:1. For each pair of genes, the alleles segregated to the offspring independently of one another.

More Combinations
What general rule about the ratio of genotypes can you infer from a dihybrid cross? What would happen if three traits were considered simultaneously in a trihybrid cross? Is there a mathematical rule that can predict the number of possible genotypes and phenotypes that can occur when any number of traits are considered simultaneously?

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1In this particular example, the mutant forms are recessive to the wild-type forms. It is important to note, however, that there are many examples of mutant forms that are actually dominant to the more common wild-type alleles.
3-1 How Are Traits Passed from Generation to Generation?

**Figure 3-10** Genotypes of the F₂ generation of a dihybrid cross. Each parent fly is heterozygous for two traits, wing shape and body color. This kind of cross creates nine distinct genotypes.

**Figure 3-11** Phenotypes of the F₂ generation in a dihybrid cross. Four phenotypes result from this cross between flies heterozygous for both wing shape and body color. The ratio of phenotypes is nine wild-type flies (broad wings, striped body), to three flies with vestigial wings and striped bodies, to three flies with broad wings and ebony bodies, to one fly with vestigial wings and an ebony body.
CHAPTER 3  Mendelian Genetics: How Are Traits Inherited?

**Chance Determines Which Alleles an Individual Inherits**

A young couple anxiously awaits the arrival of their first child. Among the many things they wonder about before that child is born is whether their new baby will be healthy. One concern of prospective parents is cystic fibrosis, a genetic disease caused by a recessive allele of the \textit{CF} gene. The recessive allele is carried by about 1 of every 25 white North Americans, making cystic fibrosis the most common genetic disorder among this group. It affects about 1 in 2,500 babies in this population. The disease is characterized by production of a thick, sticky mucus in the lungs that is difficult to propel from the airways (Figure 3-12). Victims suffer from chronic infections that progressively destroy the lungs. It is not surprising that the disease is a concern of prospective parents.

Because the allele is recessive, parents may be carriers of the disease-causing \textit{CF} allele, but show no signs of the disease. In other words, healthy parents may be heterozygous for the \textit{CF} gene. Genetic testing can determine whether a person is a carrier of the recessive \textit{CF} allele. If a couple knows from genetic tests that the mother is heterozygous for the \textit{CF} gene and that the father does not carry the disease-causing allele, they can use a Punnett square to predict that the chances of having a child who is a carrier are equal to the chances of having a child who is not: 50% in each case. They can predict that if they had 10 children, about 5 of them would probably be \textit{CF} carriers and 5 would be homozygous for the normal allele. But until their baby is tested for the \textit{CF} allele, they cannot know for certain whether that child will be a carrier of cystic fibrosis. And even if they had 99 children, they could not predict whether or not child number 100 would carry the \textit{CF} allele.

Donating alleles during reproduction is like tossing a coin. Both are random events. The best possible prediction of the outcome of a random event is nothing more than the probability that each of the possible outcomes will occur. To better understand segregation, independent assortment of alleles and the different ratios of phenotypes and genotypes predicted from hybrid crosses, it is useful to know some facts about probability.

**Probability**  Every time a coin is tossed, there are two possible and equally likely outcomes: Heads or tails. When a single die is tossed, there are six possible and equally likely outcomes: The numbers one through six. In any random event, the probability, or likelihood, that any single outcome will occur is equal to the number of times it can or actually does occur divided by the total number of possibilities. Thus, the probability of getting

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**Figure 3-12**  Cystic fibrosis treatment. In 1992, an experimental treatment was introduced in which the patient inhales a mist containing enzymes that thin the mucus that accumulates in the lungs.
heads in a single toss of a coin is $\frac{1}{2}$, or 0.5. Heads is one of two possible outcomes. Likewise, the probability of getting a specific number, say a four, on any given roll of the die is $\frac{1}{6}$, or 0.17. An event that always occurs has a probability of $\frac{1}{1}$, or 1.0. An impossible event has a probability of 0.

We can apply probability theory to the distribution of alleles at conception. Imagine a parent who is heterozygous for some hypothetical gene we will call $G$. Because the genotype is $Gg$, each gamete (egg or sperm) produced by that parent will contain one of the two alleles, either $G$ or $g$, but not both. If neither allele is favored when gametes are produced, as we predict, the basis of Mendel’s law of segregation, the probability $P$, that any one gamete will contain the $G$ allele and, hence be passed on, is $P(G) = \frac{1}{2}$, or 0.5. Likewise, the probability that the $g$ allele is passed on is $P(g) = \frac{1}{2}$, or 0.5. Notice that the probability that either the $G$ or the $g$ allele is passed on is equal to the sum of the probabilities of the two events:

$$P(G \text{ or } g) = 0.5 + 0.5 = 1.0$$

Either $G$ or $g$ is passed on by this parent, but not both. This is an example of a mutually exclusive event and is analogous to tossing a coin. Either heads or tails can occur, but never both from the same toss of the coin. The preceding equation illustrates the **sum rule** that applies to mutually exclusive events. The combined probability of two or more mutually exclusive events occurring is equal to the sum of their individual probabilities.

Now let’s consider two events that are not mutually exclusive, but instead are independent of one another and happen simultaneously. This is exactly the situation when the gametes of two heterozygous parents join at fertilization, each donating just one allele for each trait to a single offspring. For example, assume a $Gg$ mother and a $Gg$ father have one child. What is the probability of that child having a $gg$ genotype? The probability of the mother’s egg carrying a $g$ allele is 0.5. The probability of the father’s sperm containing a $g$ allele is also 0.5. The allele that the mother contributes has no effect on the one that the father contributes; thus, we are describing two independent events happening simultaneously. To calculate the probability that any two specific outcomes—say a $g$ from mother and a $g$ from father—will result, we must multiply the probabilities of each of the events that happen individually:

$$P(g \text{ from mother and } g \text{ from father}) = P(g \text{ from mother}) \times P(g \text{ from father})$$

or

$$P(gg \text{ genotype in offspring}) = 0.5 \times 0.5 = 0.25$$

This is known as the **product rule**. It states that the joint probability that both of two independent events will occur is the product of the individual probabilities of each. The joint probability in this case is equal to 0.25; in other words, there is a 25% chance that any given offspring of this union will be homozygous for the $g$ allele. This is precisely what we saw when we applied the Punnett analysis to a hybrid cross.

Probability is a more formal way of determining the likelihood that an individual conception will yield a specific genotype. Keep in mind that probability cannot determine the actual outcome of any single event; it can only give the odds that a given outcome might occur. Thus, our expectant parents can make an educated guess about the likelihood of each of their children inheriting a gene for cystic fibrosis, but they cannot know for sure until their baby is tested.

The more times an event occurs—the more times we toss a coin, or the more babies that are born to our heterozygous couple—the more likely it becomes that the ratio of different outcomes matches probabilities. Toss a coin 2 times or 4 times, and you may get two heads or four tails. But toss a coin 100 times, and the number of times you get heads will approach 50, approximately the probability of 0.5.
When Mendel crossed pea plants, he counted thousands of offspring. Because there were so many, the ratios of the different phenotypes were very close to the theoretical values that his laws of segregation and independent assortment predicted. They were close, but never exactly right on.

**Half Is Enough** The examples we have considered thus far apply to organisms, like humans, that spend most of their life history carrying two alleles for each gene. Only the gametes carry single alleles. Some organisms, however, such as algae and mosses, spend much of their lives carrying only a single copy of each gene. How do Mendel’s laws apply to these creatures?

**Piecing It Together**

Mendel’s principles, derived from his experiments with peas, are true of all sexually reproducing organisms—those that produce gametes that join at fertilization. Here, we summarize Mendel’s conclusions about the inheritance of traits, as well as some of the insights that have emerged from his work:

1. Hereditary characteristics are passed from parent to offspring as units or particles. We refer to the basic unit of inheritance for a given trait as a gene. The different forms of a gene are called alleles. Mendel’s factors correspond to alleles.

2. Individuals carry two alleles for every gene. The two alleles for a given trait may be identical, in which case the individual is said to be homozygous for that trait. Alternatively, the two alleles may differ, and hence, the individual is said to be heterozygous for that trait.

3. Prior to reproduction, pairs of alleles are separated so that specialized reproductive cells called gametes contain only one allele from each pair. At fertilization, gametes fuse, each contributing one allele for each trait to the new offspring.

4. Some genes show dominance; that is, heterozygous individuals may express only one allele—the dominant allele—while the other, the recessive allele, is masked. Thus, the phenotype—the traits that are expressed in an individual—may not always reveal the genotype, or the full complement of alleles that the individual carries. Recessive alleles remain hidden in the genes.

5. Mendel’s law of segregation states that heterozygous parents are equally likely to pass either of their two alleles on to their offspring. In other words, gametes combine at fertilization without regard to which alleles they carry. Because the alleles that an individual inherits are purely a matter of chance, the rules of probability can be used to determine the likelihood that any given allele is passed on. The Punnett square is a tool that illustrates the law of segregation.

6. Mendel’s law of independent assortment applies when two or more genes are considered simultaneously. It states that the alleles of one gene are passed to offspring independently of the alleles for other genes. The Punnett square illustrates this law, as well.

**3-2 Why Aren’t Members of the Same Species Identical?**

Like begets like. When pea plants are crossed, the resulting offspring are never roses or geraniums: They are always peas. When dogs are bred, the result is puppies, and when racehorses are bred, inevitably they bear foals. Each species is a particular combination
of genetic traits which characterize that species and make it different from all the others. But to anyone who has bred racehorses for competition or dogs for show, it is abundantly clear that there are differences among members of the same species. These differences among individuals in natural populations are at the very core of Darwinian evolution. Where do these differences come from? What is the source of variety among natural populations?

**Independent Assortment Is an Important Source of Variety**

Almost every organism, every phenotype, is the result of perhaps thousands or tens of thousands of genes working together. When we considered just two of those genes in our dihybrid cross, body color and wing shape in the fruit fly, and ignored all the other genes of fruit flies, we saw that a single breeding pair of flies, both heterozygous for those two genes, could produce offspring with as many as four different phenotypes. A mathematical rule that expresses the number of possible different phenotypes that can result from a cross between heterozygotes for any number of traits is

\[
\text{number of possible phenotypes} = 2^n
\]

where \( n \) is the number of traits, or genes, considered. The 2 represents the two different forms of each trait; there are two alleles possible. For a monohybrid cross, there can be \( 2^1 = 2 \) possible phenotypes (for example, round or wrinkled seed shape; ebony or pale striped body color; broad or vestigial wings). For a dihybrid cross, \( n \) is equal to 2 because we are considering two different genes simultaneously, each occurring in two forms. The number of possible phenotypes is \( 2^2 = 4 \). This is exactly the number of phenotypes we saw with regard to body color and wing shape in fruit flies.

Now consider the number of possible phenotypes that could result if we considered many traits simultaneously, say, 100 traits or 1,000 traits, each of which could occur in two different forms. It would be a daunting task to list all of the combinations, but we can easily calculate how many different ones are possible. For 100 traits,

\[
\text{the number of possible different phenotypes} = 2^{100} = 1.26765 \times 10^{30} = 1,267,650,000,000,000,000,000,000,000,000
\]

For 1,000 traits,

\[
\text{the number of possible different phenotypes} = 2^{1,000} = 11 \times 10^{300}
\]

or the number 11 followed by 300 zeros. That is more phenotypes than there are stars in the heavens or grains of sand on all the beaches of the world. The astonishingly large number of new combinations of alleles that can occur each time a breeding pair produces offspring is an important source of variety in populations—exactly the kind of variety that is required for evolution by natural selection. This is one example of *genetic recombination*, or the production of new combinations of genes not found in either parent. We will see other ways in which genetic recombination can be achieved in Chapter 5.

In fact, not all of the genes in living organisms have different forms, or alleles. It has been estimated that, on average, about 30% of human genes are actually heterozygous in a way that influences phenotypes and thus are a source of variety. If we assume that humans have about 30,000 genes, then 30% of 30,000 would be 9,000 heterozygous genes. To calculate the number of possible human phenotypes this could produce, you would raise 2 to the power of 9,000. Chances are you will exceed the capacity of your calculator. Even if 70% of the genes in humans are homozygous, and thus not a source
of genetic recombination, there is still sufficient variety to produce a nearly infinite number of different phenotypes—variety upon which natural selection can operate. It is no wonder that, aside from identical twins who begin life with all the same alleles, no two people present the same phenotype.

In our discussion of heredity thus far, we have considered only two different forms, or alleles, for each gene. Mendel’s peas were either smooth or wrinkled; the gene for one chain of the human hemoglobin protein was described as either normal or the sickle form. But whereas any individual can carry only two alleles for a given gene, there may be many different alleles for a trait in a population. Different combinations of these various alleles may produce more than two phenotypes for the trait. For example, there are three different alleles that determine blood type in human populations, namely A, B, and O. An individual can have only two of the three possible alleles, although a population of humans will have all three alleles represented. The possibilities for variety are endless.

Now imagine a certain combination of traits that bestows on its owner some competitive advantage. Imagine a desert plant, say a cactus, with an allele that creates a waxy coating on its surfaces. That trait alone would prevent water loss due to evaporation and help the plant to survive in the hot, arid environment of the desert. But living plants also need a mechanism for taking up carbon dioxide gas for photosynthesis. A waxy cuticle might be a barrier to carbon dioxide uptake. If that same cactus had the alleles that permitted it to take up carbon dioxide only at unwaxed entry points, the combination of a waxy cuticle and special carbon dioxide uptake sites would be a powerful advantage. That cactus would fare much better than one with only a waxy cuticle or one with specific gas exchange sites. Natural selection operates not on single traits, but on whole organisms, which are combinations of many, many traits.

**Sex among Microbes** Sexual reproduction allows members of the same species to create new combinations of genes by genetic recombination. But not all organisms reproduce sexually. Bacteria, for example, reproduce asexually by a process called binary fission. In binary fission, each bacterium makes a complete copy of all its genes, then splits, apportioning a complete copy of the genetic blueprint to each of the two new cells. Yet bacteria, too, exhibit genetic variety. Are there mechanisms by which organisms like bacteria that reproduce asexually can share genes?

**Mutations Are Another Source of Genetic Variety** Occasionally, when large numbers of plants or animals are grown domestically, an individual is born with an entirely new characteristic never before seen in that group or any of its ancestors. This phenomenon, which occurs in natural populations as well as domestic ones, was well known to Darwin. He referred to these rare individuals as “sports of nature”; we call them mutants. A long pedigree of red roses, for example, bred for many years to produce only crimson blooms, may suddenly produce a pink rose. Or within a herd of sheep, bred for many years with long legs, a single, short-legged lamb may appear. Darwin was at a loss to explain such phenomena, although he recognized the role these “sports” have in providing variety upon which natural selection can act. (Indeed, knowing nothing of genetic recombination, Darwin wondered if mutations alone could provide all of the necessary variety for natural selection.) Mendel’s laws do not explain the origin of these anomalies, although new features can often be propagated by careful breeding. Once present in a breeding population, a new trait obeys all of Mendel’s laws as if the allele that causes it had been present all along. What, in genetic terms, is a mutation, and how do mutants fit into our Mendelian view of inheritance?

A mutation is the sudden appearance of a new allele. Although mutations can occur at any time, they become heritable mutations when genes are copied and partitioned into gametes during sexual reproduction. When males and females make sperm and eggs
(the gametes that carry one allele for every gene into the next generation), they make copies of every single allele to be passed on. This process of gene replication has been studied extensively in the past several decades and is well understood, even at the level of the molecules involved; we'll focus more on that in Chapter 6. For now, suffice it to say that the copying process is pretty good, but not perfect. Occasionally a mistake slips in, and a new allele emerges as a result. Many times, errors in copying are fatal.

Imagine yourself as a maker of fine watches. Your timepieces are assembled from carefully designed parts that fit together to work harmoniously to keep time, much as the genes of a living thing work together to build a finely tuned organism. Each component of your watches is made by a different machine. Suddenly, a machine that makes a single part malfunctions, and the new versions of that part are somehow different from what they had been. Chances are the watches made with the “mutant” part will not keep time; after all, every part was carefully designed to fit with every other part. On rare occasions, however, the mutant part may have no effect on the functioning of your watches, or may cause them to work even better than the original. If that is the case, you would not be anxious to repair your part-making machine. Your new watches would be at least as good, perhaps even better, than your old watches.

The history of life on Earth is a history of random mutations, most lost forever due to their deleterious effects, many simply carried along from generation to generation because they have no effect on the survival or reproduction of their recipients. But occasionally a copying error has produced an organism better suited to survive the rigors of life. The lucky recipients of beneficial mutations have gone on to produce many offspring and left many copies of that new allele in the next generation. Mutations are the ultimate source of new alleles. If errors never occurred during gene replication, all of life on Earth would resemble the first living thing (whatever that was—a topic addressed in Chapter 9). Despite the mostly deleterious effects of mutations, evolution would be impossible without them.

### Mutations That Kill

Genes are copied during sexual reproduction, when gametes receive one copy of each allele, but they are also copied when organisms grow, making more cells that compose the living tissue. Can mutations occur in growing, nonreproductive tissues as well as reproductive tissues? What effect would mutations in nonreproductive tissues have on evolution and natural selection? How do mutations relate to cancer or other human diseases? Are you likely to be carrying any mutations in your genes?

### Exploration

### Piecing It Together

Variety is more than just the spice of life; it is the raw material upon which natural selection operates. Without it, there could be no evolution. Some of the genetic reasons for differences between individuals are summarized here:

1. The number of different phenotypes that can result from alleles coming together in new combinations as a result of sexual reproduction is essentially infinite. We can see this when we mathematically estimate the number of possible phenotypes arising from just a few traits.

2. Genetic traits can work together in combinations that enhance or hinder the survival and reproduction of their owners. In other words, having a certain trait may or may not provide an advantage, depending on the other traits that are present.
3. All genetic variety can ultimately be traced to mutation—the sudden appearance of new alleles in the genes of a population or species. Most mutations arise from errors that occur when the genetic information is copied.

4. Most mutations are deleterious or neutral. Because organisms are finely tuned combinations of traits, errors in the information encoding those traits are likely to do more harm than good. The occasional mutation that improves the functioning of an organism can be advantageous to its owner and may be passed on to future generations.

3-3 Do Mendel’s Laws Always Apply?

Mendel’s results were reported in 1865 as a series of lectures to the Brünn Society for the Study of Natural Science, and they were published in German in 1866 in a volume of proceedings of that society. Although the volume was widely distributed to libraries throughout Europe, few of Mendel’s contemporaries recognized the significance of his work. The quantitative approach that Mendel used, counting the number of offspring showing each trait and calculating ratios, is a hallmark of modern science, but it was virtually unknown and certainly unappreciated in the latter part of the 19th century. Then in the early part of the 20th century, three botanists—Carl Correns in Germany, Hugo de Vries in the Netherlands, and Erich von Tschermak in Austria—who were also conducting experiments in plant hybridization, all rediscovered Mendel’s original paper and realized its significance. Unfortunately, Mendel died in 1884, too soon to see his work assume its rightful place in the history of great discoveries.

Mendel’s Laws Are Extended by Experimental Evidence

In 1899, Carl Correns was performing controlled crosses by using a flowering plant called the four-o’clock. The blooms of the four-o’clock occur in three colors: White, red, and pink (Figure 3-13). When Correns crossed true-breeding red-flowered four-o’clocks with true-breeding white-flowered plants, the hybrid offspring all had pink flowers—a shade intermediate between those of the parents. If Correns had ended his experiments there, he, too, might have drawn the same erroneous conclusion that many of his predecessors, including Darwin, had drawn. He might have been fooled into thinking that the traits of offspring were blended averages of parental traits. But Correns went on to cross the pink-flowered plants of the F₁ with other pink F₁ plants and found that the F₂ plants exhibited all three traits: Some were white, others were pink, and still others were red.

Figure 3-13 The flowers of the four-o’clock plant. It appears that the flower color trait of the four-o’clock exhibits blending in the F₁ generation. However, when pink-flowered plants of the F₁ generation were crossed with each other, all three phenotypes illustrated here were present in the F₂ generation. Pink-flowered plants are heterozygous for flower color and exhibit incomplete dominance.
3-3 Do Mendel’s Laws Always Apply?

**Dominance Relations**

In Correns’s experiment, the ratio of phenotypes in the $F_2$ was one white to two pink to one red—exactly the ratio of genotypes that results from a monohybrid cross (a cross between two individuals, both heterozygous for a single trait). Four-o’clocks that were homozygous for the flower color gene were either red or white, depending on which allele was present. But when both the allele for red and the allele for white occurred in the same plant, neither the red allele nor the white allele masked the presence of the other. The alleles showed incomplete dominance, a condition in which all three genotypes are expressed. The phenotype of the heterozygote is intermediate between the phenotypes of the two homozygotes. The Punnett square for this cross, including both genotypes and phenotypes, illustrates it nicely (Figure 3-14). Because there is no truly dominant allele, we use the uppercase letter $R$ for both alleles, distinguishing white and red with either a 1 or a 2, respectively.

Do these results invalidate Mendel’s conclusions? At the level of the phenotype, the $F_1$ generation of the four-o’clock appears to be showing blending, contrary to what Mendel found. But at the level of the genes, each allele remains intact as it is passed from parent to offspring. Each allele is a discrete entity, capable of showing its true colors when it is paired with the same allele in a homozygous plant. Mendel’s laws are not invalidated.

**What’s Your Type?**

In the four-o’clock, each allele is fully expressed in the homozygote and partially expressed in the heterozygote. But are there genes in which both alleles can be fully expressed in the same individual, neither one being dominant or even partially dominant? This occurs in the gene that codes for human blood groups. What is this relationship among alleles called? How are human blood group designations inherited?

**Lethality**

Mendel made much of the ratios of different phenotypes he found in the offspring of his crosses between heterozygotes. The ratio of dominant to recessive phenotypes, 3:1, gave him the idea that factors occur in pairs, that alleles show dominance, and that alleles segregate during reproduction. The 9:3:3:1 ratio of phenotypes that is characteristic of a dihybrid cross between individuals which are heterozygous for two traits was the basis for his law of independent assortment. But what would happen to the...
CHAPTER 3  Mendelian Genetics: How Are Traits Inherited?

Figure 3-15 Mice with agouti (brown) and yellow fur. The agouti mice are homozygous for the recessive allele encoding coat color. The yellow mouse is heterozygous. None of these mice is homozygous for the dominant allele, because the combination of two dominant alleles is lethal.

Figure 3-16 Inheritance of coat color in mice. The phenotypic ratio in the offspring of a cross between heterozygous yellow mice is closer to 2:1 than to the 3:1 ratio predicted by Mendelian genetics. The difference between the observed ratio and the predicted ratio is due to the recessive lethality of having two yellow Y alleles.

ratio of phenotypes if certain combinations of alleles were deadly to the newly formed embryo? Because each unlucky embryo receiving a lethal combination of alleles dies, that phenotype would not be represented in the next generation at all. Such a condition, called lethality, was first documented soon after Mendel’s groundbreaking paper was rediscovered in the early part of the 20th century. A dominant lethal allele is one that kills its recipient. A recessive lethal allele is only deadly when it is paired with another recessive lethal in a homozygote.

In 1904, the French geneticist Lucien Cuenot was performing experiments on the inheritance of coat color in mice. He found that the yellow coat color was dominant to the wild-type brownish color called agouti (Figure 3-15). When heterozygous mice, yellow in color, but each carrying an allele for the agouti color, were bred, the phenotypic ratio of offspring was 2:1 yellow/agouti, instead of the 3:1 dominant/recessive predicted by Mendel's laws. Furthermore, testcrosses between yellow mice and homozygous agouti mice proved that all yellow mice were heterozygous. (How can a testcross prove that individuals showing the dominant trait are heterozygous and not homozygous? Check the BioInquiry web site to remind yourself of how a testcross works.) Cuenot could not find a single mouse that was homozygous for the dominant allele.

Where were all the homozygous yellow mice? Later experiments showed that a double dose of the yellow allele is a deadly combination. All such embryos die early in development, skewing the ratio of offspring away from 3:1 dominant/recessive and toward the observed 2:1 outcome (Figure 3-16).

The yellow allele in mice, although dominant in its effect on coat color, is an example of an allele that is recessive in its lethality. It may seem that recessive lethals would be the victims of natural selection, quickly eliminated from populations by their deleterious effects. But because the carriers of many recessive lethals can survive and reproduce normally, such alleles can remain hidden within the genes of a population for many generations, only killing their carriers when, by random chance, they are paired with similar alleles in deadly combination.

But what of dominant lethals, or alleles that kill when present in a single copy? Common sense might lead us to conclude that a dominant lethal allele could not possibly survive in a population. After all, any individual unfortunate enough to acquire even a single lethal dominant would surely die, eliminating the deadly allele from the population. That is certainly the case with many lethal dominants, but not all. Huntington’s disease is an example of a deadly human disease caused by a dominant lethal allele. The disease is characterized by uncontrolled movements and mental deterioration, followed by death. Individuals need inherit only one copy of the Huntington’s gene to exhibit the lethal phenotype. Because the onset of the disease occurs late in life, usually between the ages of 30 and 60, an afflicted person may already have passed on the allele to
3-3 Do Mendel’s Laws Always Apply? 85

children before he or she is even aware of its presence. On average, about half of the offspring of an afflicted person inherit the disease. In this manner, a lethal allele can have a long history within a population.

One Gene Can Influence Two or More Traits  Just for a moment, let’s go back to the Moravian garden and take a closer look at the wrinkled and smooth peas that inspired Mendel to derive his laws of inheritance. While he was focusing on the texture of the seed coat, he most likely was not aware that another trait of pea seeds was also affected by the coat texture gene. If he had examined smooth and wrinkled peas in a microscope, he would have seen that the tiny starch grains that provide food for the developing pea plant were different in these two varieties. The same gene that influences seed texture also affects starch grain shape and size. This single gene has multiple effects. The phenomenon whereby a single gene affects two or more traits is called pleiotropy.

Sometimes pleiotropy is explained by examining a gene’s effect at an early stage of life. For example, cats that are either homozygous or heterozygous for a certain allele called W have pure white fur. These same cats are also deaf in one or both ears. What is the connection between the W allele, white fur, and deafness? The answer has to do with a particular kind of cell called the melanocyte. Melanocytes produce the pigmentation of the fur, and they also play a role in the inner ear of the animal where they contribute to the hair cells that sense sounds. When a cat inherits a W allele, its melanocytes fail to develop properly. Although deafness and white coat color appear to be unrelated phenomena, both phenotypic manifestations are attributed to this same failure. These are pleiotropic manifestations of a single allele.

Two or More Genes Can Influence a Single Trait  If all the students in your class formed a line with the shortest person at one end and the tallest person at the other, we would see a continuum of heights from short to tall (Figure 3-17). Even in this small subset of the population, human heights do not fall into discrete categories. Part of the variation can be attributed to factors such as nutritional status and childhood diseases, among others. But much of what determines an individual’s height has an underlying genetic cause. Even with the powerful tools of modern molecular biology, no single gene for human height has been identified.2 Human height is an example of a trait that is affected by many genes—it is a polygenic trait. Traits that are determined by a single gene with two alleles—monogenic traits such as seed texture in peas or flower color in the four-o’clock plant—will occur as two or three distinct phenotypes. If as few as three different genes work together to determine a single trait, each represented by only two alleles, the distribution of phenotypes within a population becomes continuous. Other examples include weight, human skin color, coat color in many mammals, and even some traits that do form discrete phenotypes, such as the number of whiskers on the face of a mouse.

Mendel’s Work Generated New Fields of Inquiry

At the turn of the 20th century, when Mendel’s laws were gaining new adherents in the scientific community, it was not entirely clear how Darwin’s theory and Mendel’s laws complemented one another. Many who read Mendel’s work believed that genetic traits must occur as discrete, all-or-none phenotypes, such as the purple versus white flower color in peas, or yellow versus agouti coat color in mice. The way in which polygenic traits can create a continuum of phenotypes was unknown. Darwin’s champions pointed to the many traits that formed a continuum of phenotypes and insisted that although such gradual differences between individuals could not be explained by Mendelian genetics, they were

2 The exception to this rule is achondroplasia, or dwarfism. In this genetic condition, a single dominant allele prevents its carrier from growing to normal adult heights.
necessary for natural selection. Many believed that the two theories were incompatible; contentious, even vitriolic disagreements developed. In the 1930s, the controversy was finally put to rest. A new field of biology emerged, called population genetics, which employed mathematics and statistics to prove that the variety required for natural selection could arise from Mendelian genetics. Instead of focusing on just one or a few genes occurring in individuals, the population geneticists used mathematical models to study the movements of many genes through entire populations over time. Population genetics is an exciting field that has continued to grow and provide answers to evolutionary questions ever since. We will take up the topic of population genetics again in Chapter 8.

Recall that, to Mendel, the hereditary “factors” were nothing more than theoretical entities. His theories did not require the ability to visualize genes moving from parent to gamete then to offspring. But the question remained, what exactly are these mysterious hereditary factors? And how are they copied, passed on, and expressed in their carriers? The answers to these questions have a fascinating history, leading up to the development of modern molecular biology. While Mendel was cultivating peas, others in Europe and elsewhere were learning that all living things are composed of fundamental units called cells. The hereditary factors, as we will learn in Chapter 4, were found in cells.
Piecing It Together

In the century that has elapsed since Mendel’s work was rediscovered by Correns, de Vries, and Tschermak, new experimental evidence has provided the exceptions that prove the rules. Each new discovery can be explained in the context of the laws of inheritance as set forth so many years ago by this humble priest:

1. Alleles occurring together in heterozygotes do not always exhibit true dominance, but instead may be incompletely dominant.
2. Some alleles are lethal. Most lethal alleles that survive in populations are recessive. Other lethals are dominant, killing their carriers with a single copy, such as the one that causes Huntington’s disease.
3. Pleiotropic genes exert two or more effects on the phenotype.
4. Polygenic traits are influenced by two or more genes. These traits often do not occur as discrete phenotypes, but rather form continuous distributions of phenotypes in populations.
5. Mendelian genetics, originally thought to be incompatible with Darwinian evolution, was reconciled with natural selection in the 1930s. This synthesis of Darwinian evolution and Mendelian genetics gave rise to the modern science of population genetics.

WHERE ARE WE NOW?

Some of the most exciting discoveries of recent years have come from the field of genetics. In the past few decades, we have identified the genes that cause many human genetic disorders, developed tests for detecting these disorders both prenatally and in prospective parents, and engineered therapies to minimize or eliminate many genetic diseases.

Among the most surprising recent discoveries in genetics is a class of genes that “remember” their parental origins—imprinted genes. Usually, once fertilization has taken place, the maternal and paternal alleles for most genes cannot be distinguished. Mendel’s peas were just as round when the round allele came from the egg as when it came from the sperm. But for imprinted genes, alleles of maternal origin act differently from those of paternal origin.

Two Cambridge University researchers, Eric Keverne and Azim Surani, have discovered that, in mice, certain alleles from the mother contribute more to the development of the brain’s reasoning portion, the cortex. The same alleles from the father have a greater impact on the development of the brain region responsible for more primitive functions such as feeding, fighting, and reproduction. Paternal alleles also do the work of building the placenta and making the hormones responsible for the growth of the fetus. The alleles of certain genes that contribute to cortex development are “silenced” if they come from the sperm—they are chemically modified so that they are unable to function. Likewise, maternal alleles that contribute to growth hormones and placenta development are similarly silenced.

While neither researcher is willing to speculate on how human intelligence and behavior might be affected by imprinted genes, some human genetic disorders hint that we are not entirely dissimilar to the mouse. For example, children suffering from Prader-Willi syndrome have brain disorders that cause overeating, obesity, a placid personality, mild retardation, and a reduced sexual drive. These behaviors are under the control of
the brain’s primitive regions, the areas whose development can be traced to paternal alleles. Maternal alleles for these brain areas are normally silenced. Prader-Willi syndrome sufferers lack the paternal allele due to a deleterious mutation. Their abnormal phenotype implies that the maternal alleles for these brain areas cannot make up for the absence of the alleles from the father.

In addition, another human genetic disorder called Angelman syndrome occurs when a baby is born lacking a certain maternal allele that resides on chromosome number 15. Children with Angelman syndrome have defects in activities controlled by the higher brain centers. These defects include mental retardation, speech deficiencies, and jerky movements. The symptoms occur even though the chromosome 15 of paternal origin is present and intact. The abnormal phenotype of children with Angelman syndrome implies that the paternal alleles on chromosome 15 cannot substitute for the absence of those of maternal origin. While it is too soon to say whether human intelligence is maternal in origin, these exciting discoveries may give new insights into why we are the way we are.

**REVIEW QUESTIONS**

1. How did Mendel’s approach to answering scientific questions differ from that of his contemporaries? How did his novel approach contribute to his success in describing how traits are inherited? What advantages did he gain by choosing to study the garden pea?

2. When Mendel crossed plants that bred true for round pea seeds with those that bred true for wrinkled seeds, what was the phenotype of the F1 generation? What was the genotype of the F1 generation?

3. What is a gamete? In terms of the number of alleles for each gene, what general statement can you make about how gametes differ from other cells in a mature pea plant?

4. In a cross between a pea plant that breeds true for purple flowers and one that breeds true for white flowers, the F1 generation has all purple flowers. Draw a Punnett square showing how the alleles for flower color are combined in the F1. Then draw a Punnett square showing the genotypes that can result in the F2 generation.

5. The presence of freckles is a dominant trait in humans. What can you say about the genotype of a person with freckles? How could you find out for sure what that person’s genotype is?

6. You are a genetic counselor, and a married couple comes to you for advice. The man’s father suffers from sickle cell anemia. No one in the family history of the woman has ever had the disease. What would you tell this couple about the probability that their children will have the disease? What would you tell them about the probability that their children will be carriers of the disease?

7. What is an allele? How is an allele different from a gene? Give an example of a gene. Now give an example of two alleles for that gene.

8. In a dihybrid cross between individuals heterozygous for both traits, how many different genotypes are possible in the F2 generation? Assuming that both traits show dominance, how many different phenotypes are possible?

9. How many different types of gametes can be formed by individuals with a genotype of AAbb? With a genotype of AaBb?

10. Which of Mendel’s laws is illustrated by a dihybrid cross? What does the law state?

11. How many different phenotypes can result from a cross between individuals heterozygous for five different traits? How are these different phenotypes important to the process of evolution by natural selection?

12. Assume a new allele, called q, arises by a mutation in the Q gene. A gamete that acquires the mutant q allele dies. Will this allele show up in the next generation? Illustrate your answer with a Punnett square.

13. In Mendel’s crosses, one of the two forms of the traits he studied was dominant to the other. Are all traits inherited in this way? Support your answer with an example.

14. In genetic terms, what does it mean to be “true breeding”? Use the information in Section 3-3 to determine whether mice with yellow fur could be true breeding. Why or why not?

15. Suppose Mendel had decided to study inheritance by using the trait of human height. How would his methods have been different? Do you think he could have derived his principles of inheritance by using this trait? Why or why not?