# GENETICS NOTES-1

**The Birth of Genetics:** A Scientific Revolution Science is a complex endeavor involving careful observation of natural phenomena, reflective thinking about these phenomena, and formulation of testable ideas about their causes and effects. Progress in science often depends on the work of a single insightful individual. Consider, for example, the effect that Nicolaus Copernicus had on astronomy, that Isaac Newton had on physics, or that Charles Darwin had on biology. Each of these individuals altered the course of his scientific discipline by introducing radically new ideas. In effect, they began scientific revolutions. In the middle of the nineteenth century, the Austrian monk Gregor Mendel, a contemporary of Darwin, laid the foundation for another revolution in biology, one that eventually produced an entirely new science—genetics. Mendel's ideas, published in 1866 under the title "Experiments in Plant Hybridization," endeavored to explain how the characteristics of organisms are inherited. Many people had attempted such an explanation previously but without much success. Indeed, Mendel commented on their failures in the opening paragraphs of his article: To this object, numerous careful observers, such as Kölreuter, Gärtner, Herbert, Lecoq, Wichura and others, have devoted a part of their lives with inexhaustible perseverance. . . . [However,] Those who survey the work in this department will arrive at the conviction that among all the numerous experiments made, not one has been carried out to such an extent and in such a way as to make it possible to determine the number of different forms under which the offspring of the hybrids appear, or to arrange these forms with certainty according to their separate generations, or definitely to ascertain their statistical relations.1 He then described his own efforts to elucidate the mechanism of heredity: 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.

## Mendel's Study of Heredity

The life of Gregor Johann Mendel (1822–1884) spanned the middle of the nineteenth century. His parents were farmers in Moravia, then a part of the Hapsburg Empire in Central Europe. A rural upbringing taught him plant and animal husbandry and inspired an interest in nature. At the age of 21, Mendel left the farm and entered a Catholic monastery in the city of Brünn (today, Brno in the Czech Republic). In 1847 he was ordained a priest, adopting the clerical name Gregor. He subsequently taught at the local high school, taking time out between 1851 and 1853 to study at the University of Vienna. After returning to Brünn, he resumed his life as a teaching monk and began the genetic experiments that eventually made him famous. Mendel performed experiments with several species of garden plants, and he even tried some experiments with honeybees. His greatest success, however, was with peas. He completed his experiments with peas in 1864. In 1865, Mendel presented the results before the local Natural History Society, and the following year, he published a detailed report in the society's proceedings. Unfortunately, this paper languished in obscurity until 1900, when it was rediscovered by three botanists—Hugo de Vries in Holland, Carl Correns in Germany, and Erich von Tschermak-Seysenegg in Austria. As these men searched the scientific literature for data supporting their own theories of heredity, each found that Mendel had performed a detailed and careful analysis 35 years earlier. Mendel's ideas quickly gained acceptance, especially through the promotional efforts of a British biologist, William Bateson. This champion of Mendel's discoveries coined a new term to describe the study of heredity: genetics, from the Greek word meaning "to generate." MENDEL'S EXPERIMENTAL ORGANISM, THE GARDEN PEA One reason for Mendel's success is that he chose his experimental material astutely. The garden pea, Pisum sativum, is easily grown in experimental gardens or in pots in a greenhouse. Pea flowers contain both male and female organs. The male organs, called anthers, produce sperm-containing pollen, and the female organ, called the ovary, produces eggs. One peculiarity of pea reproduction is that the petals of the flower close down tightly, preventing pollen grains from entering or leaving. This enforces a system of self-fertilization, in which male and female gametes from the same flower unite with each other to produce seeds. As a result, individual pea strains are highly inbred, displaying little if any genetic variation from one generation to the next. Because of this uniformity, we say that such strains are true-breeding. At the outset, Mendel obtained many different true-breeding varieties of peas, each distinguished by a particular characteristic. In one strain, the plants were 2 meters high, whereas in another they measured only a half meter. Another variety produced green seeds, and still another produced yellow seeds. Mendel took advantage of these contrasting traits to determine how the characteristics of pea plants are inherited. His focus on these singular differences between pea strains allowed him to study the inheritance of one trait at a time—for example, plant height. Other biologists had attempted to follow the inheritance of many traits simultaneously, but because the results of such experiments were complex, they were unable to discover any fundamental principles about heredity. Mendel succeeded where these biologists had failed because he focused his attention on contrasting differences between plants that were otherwise the same—tall versus short, green seeds versus yellow seeds, and so forth. In addition, he kept careful records of the experiments that he performed.

## MONOHYBRID CROSSES: THE PRINCIPLES OF DOMINANCE AND SEGREGATION

In one experiment, Mendel cross-fertilized—or, simply, crossed— tall and dwarf pea plants to investigate how height was inherited ( ■ Figure 3.1). He carefully removed the anthers from one variety before its pollen had matured and then applied pollen from the other variety to the stigma, a sticky organ on top of the pistil that leads to the ovary. The seeds that resulted from these cross-fertilizations were sown the next year, yielding hybrids that were uniformly tall. Mendel obtained tall plants regardless of the way he performed the cross (tall male with dwarf female or dwarf male with tall female); thus, the two reciprocal crosses gave the same results. Even more significantly, however, Mendel noted that the dwarf characteristic seemed to have disappeared in the progeny of the cross, for all the hybrid plants were tall. To explore the hereditary makeup of these tall hybrids, Mendel allowed them to undergo self-fertilization— the natural course of events in peas. When he examined the progeny, he found that they consisted of both tall and dwarf plants. In fact, among 1064 progeny that Mendel cultivated in his garden, 787 were tall and 277 were dwarf—a ratio of approximately 3:1. Mendel was struck by the reappearance of the dwarf characteristic.

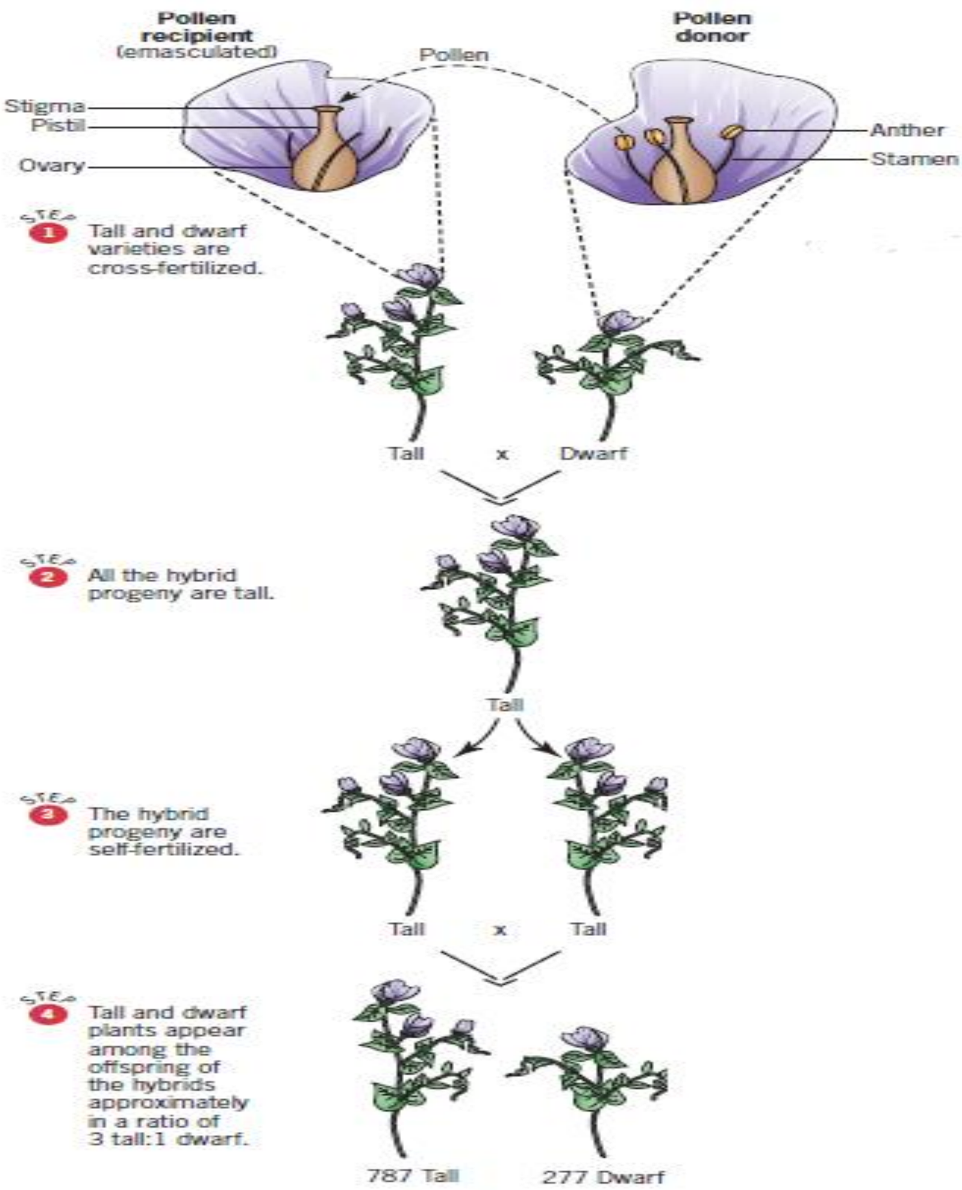
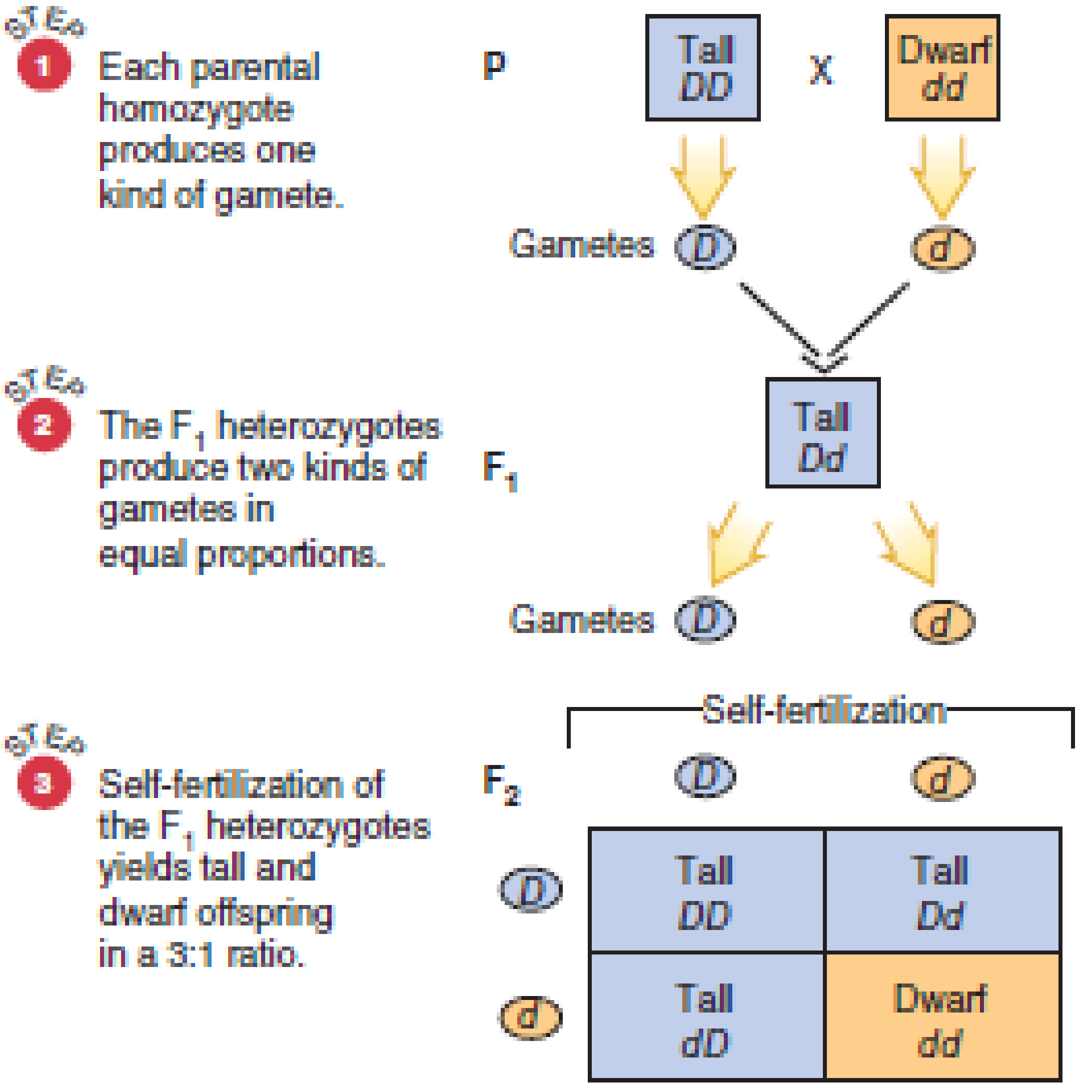



**FIGURE 3.1** Mendel's crosses involving tall and dwarf varieties of peas.

Clearly, the hybrids that he had made by crossing tall and dwarf varieties had the ability to produce dwarf progeny even though they themselves were tall. Mendel inferred that these hybrids carried a latent genetic factor for dwarfness, one that was masked by the expression of another factor for tallness. He said that the latent factor was recessive and that the expressed factor was dominant. He also inferred that these recessive and dominant factors separated from each other when the hybrid plants reproduced. This enabled him to explain the reappearance of the dwarf characteristic in the next generation. Mendel performed similar experiments to study the inheritance of six other traits: seed texture, seed color, pod shape, pod color, flower color, and flower position (Table 3.1). In each experiment—called a monohybrid cross because a single trait was being studied—Mendel observed that only one of the two contrasting characteristics appeared in the hybrids and that when these hybrids were self-fertilized, they produced two types of progeny, each resembling one of the plants in the original crosses. Furthermore, he found that these progeny consistently appeared in a ratio of 3:1. Thus, each trait that Mendel studied seemed to be controlled by a heritable factor that existed in two forms, one dominant, the other recessive. These factors are now called genes, a word coined by the Danish plant breeder Wilhelm Johannsen in 1909; their dominant and recessive forms are called alleles—from the Greek word meaning "of one another." Alleles are alternate forms of a gene. The regular numerical relationships that Mendel observed in these crosses led him to another important conclusion: that genes come in pairs. Mendel proposed that each of the parental strains that he used in his experiments carried two identical copies of a gene—in modern terminology, they are diploid and homozygous. However, during the production of gametes, Mendel proposed that these two copies are reduced to one; that is, the gametes that emerge from meiosis carry a single copy of a gene—in modern terminology, they are haploid. Mendel recognized that the diploid gene number would be restored when sperm and egg unite to form a zygote. Furthermore, he understood that if the sperm and egg came from genetically different plants—as they did in his crosses—the hybrid zygote would inherit two different alleles, one from the mother and one from the father. Such an offspring is said to be heterozygous. Mendel realized that the different alleles that are present in a heterozygote must coexist even though one is dominant and the other recessive, and that each of these alleles would have an equal chance of entering a gamete when the heterozygote reproduces. Furthermore, he realized that random fertilizations with a mixed population of gametes—half carrying the dominant allele and half carrying the recessive allele—would produce some zygotes in which both alleles were recessive. Thus, he could explain the reappearance of the recessive characteristic in the progeny of the hybrid plants. Mendel used symbols to represent the hereditary factors that he postulated—a methodological breakthrough. With symbols, he could describe hereditary phenomena clearly and concisely, and he could analyze the results of crosses mathematically. He could even make predictions about the outcome of future crosses. Although the practice of using symbols to analyze genetic problems has been much refined since Mendel's time, the basic principles remain the same. The symbols stand for genes (or, more precisely, for their alleles), and they are manipulated according to the rules of inheritance that Mendel discovered. These manipulations are the essence of formal genetic analysis. As an introduction to this subject, let's consider the symbolic representation of the cross between tall and dwarf peas ( ■ Figure 3.2). The two true-breeding varieties, tall and dwarf, are homozygous for different alleles of a gene controlling plant height. The allele for dwarfness, being recessive, is symbolized by a lowercase letter d; the allele for tallness, being dominant, is symbolized by the corresponding uppercase letter D. In genetics, the letter that is chosen to denote the alleles of a gene is usually taken from the word that describes the recessive trait (d, for dwarfness). Thus, the tall and dwarf pea strains are symbolized by DD and dd, respectively. The allelic constitution of each strain is said to be its genotype. By contrast, the physical appearance of each strain—the tall or dwarf characteristic—is said to be its phenotype. As the parental strains, the tall and dwarf pea plants form the P generation of the experiment. Their hybrid progeny are referred to as the first filial generation, or F1, from a Latin word meaning "son" or "daughter." Because each parent contributes equally to its offspring, the genotype of the F1 plants must be Dd; that is, they are heterozygous for the alleles of the gene that controls plant height. Their phenotype, however, is the same as that of the DD parental strain because D is dominant over d. During meiosis, these F1 plants produce two kinds of gametes, D and d, in equal proportions. Neither allele is changed by having coexisted with the other in a heterozygous genotype; rather, they separate, or segregate, from each other during gamete formation. This process of allele segregation is perhaps the most important discovery that Mendel made. Upon self-fertilization, the two kinds of gametes produced by heterozygotes can unite in all possible ways. Thus, they produce four kinds of zygotes (we write the contribution of the egg first): DD, Dd, dD, and dd. However, because of dominance, three of these genotypes have the same phenotype. Thus, in the next generation, called the F2, the plants are either tall or dwarf, in a ratio of 3:1. Mendel took this analysis one step further. The F2 plants were selffertilized to produce an F3. All the dwarf F2 plants produced only dwarf offspring, demonstrating that they were homozygous for the d allele, but the tall F2 plants comprised two categories. Approximately one-third of them produced only tall offspring, whereas the other two-thirds produced a mixture of tall and dwarf offspring. Mendel concluded that the third that were true-breeding were DD homozygotes and that the two-thirds that were segregating were Dd heterozygotes. These proportions, 1/3 and 2/3, were exactly what his analysis predicted because, among the tall F2 plants, the DD and Dd genotypes occur in a ratio of 1:2. We summarize Mendel's analysis of this and other monohybrid crosses by stating two key principles that he discovered: 1. The Principle of Dominance: In a heterozygote, one allele may conceal the presence of another. This principle is a statement about genetic function. Some alleles evidently control the phenotype even when they are present in a single copy. We consider the physiological explanation for this phenomenon in later chapters. 2. The Principle of Segregation: In a heterozygote, two different alleles segregate from each other during the formation of gametes. This principle is a statement about genetic transmission. An allele is transmitted faithfully to the next generation, even if it was present with a different allele in a heterozygote.




| $F_2$ Phenotypes | Genotypes | Genotypic ratio | Phenotypic ratio |
|---|---|---|---|
| Tall | *DD* | 1 | 3 |
| | *Dd* | 2 | |
| Dwarf | *dd* | 1 | 1 |

**FIGURE 3.2** Symbolic representation of the cross between tall and dwarf peas.

## DIHYBRID CROSSES: THE PRINCIPLE OF INDEPENDENT ASSORTMENT

Mendel also performed experiments with plants that differed in two traits. He crossed plants that produced yellow, round seeds with plants that produced green, wrinkled seeds. The purpose of the experiments was to see if the two seed traits, color and texture, were inherited independently. Because the F1 seeds were all yellow and round, the alleles for these two characteristics were dominant. Mendel grew plants from these seeds and allowed them to self-fertilize. He then classified the F2 seeds and counted them by phenotype. The four phenotypic classes in the F2 represented all possible combinations of the color and texture traits. Two classes—yellow, round seeds and green, wrinkled seeds—resembled the parental strains. The other two—green, round seeds and yellow, wrinkled seeds—showed new combinations of traits. The four classes had an approximate ratio of 9 yellow, round:3 green, round:3 yellow, wrinkled:1 green, wrinkled (Figure 3.3).

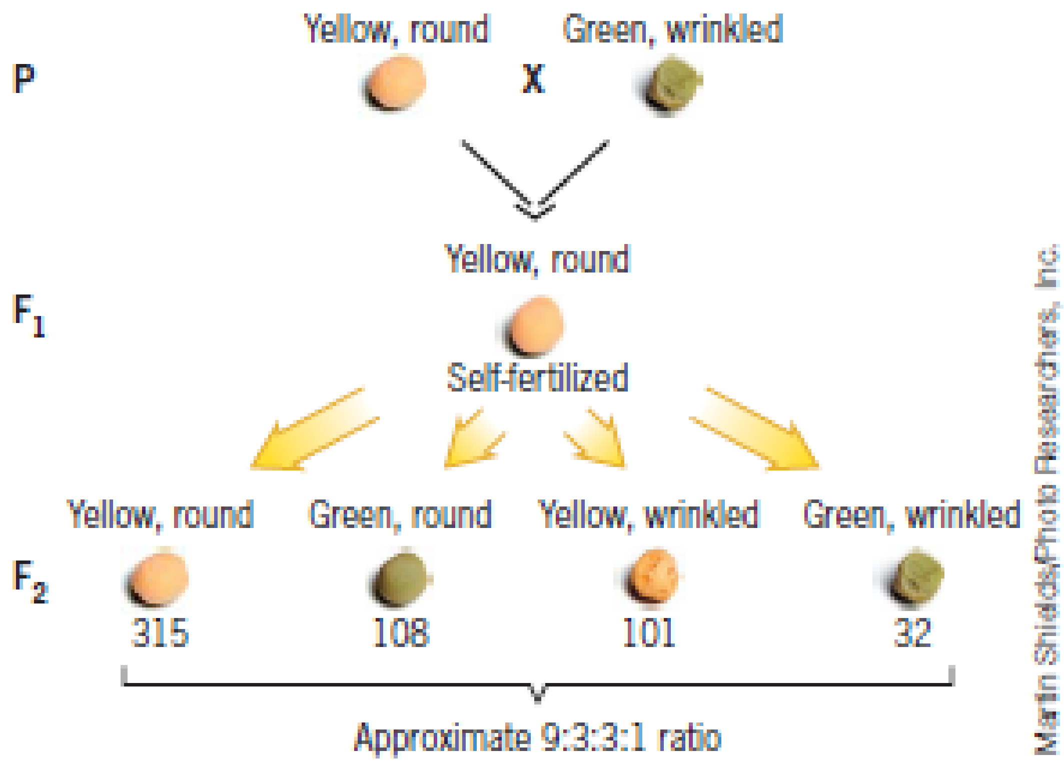
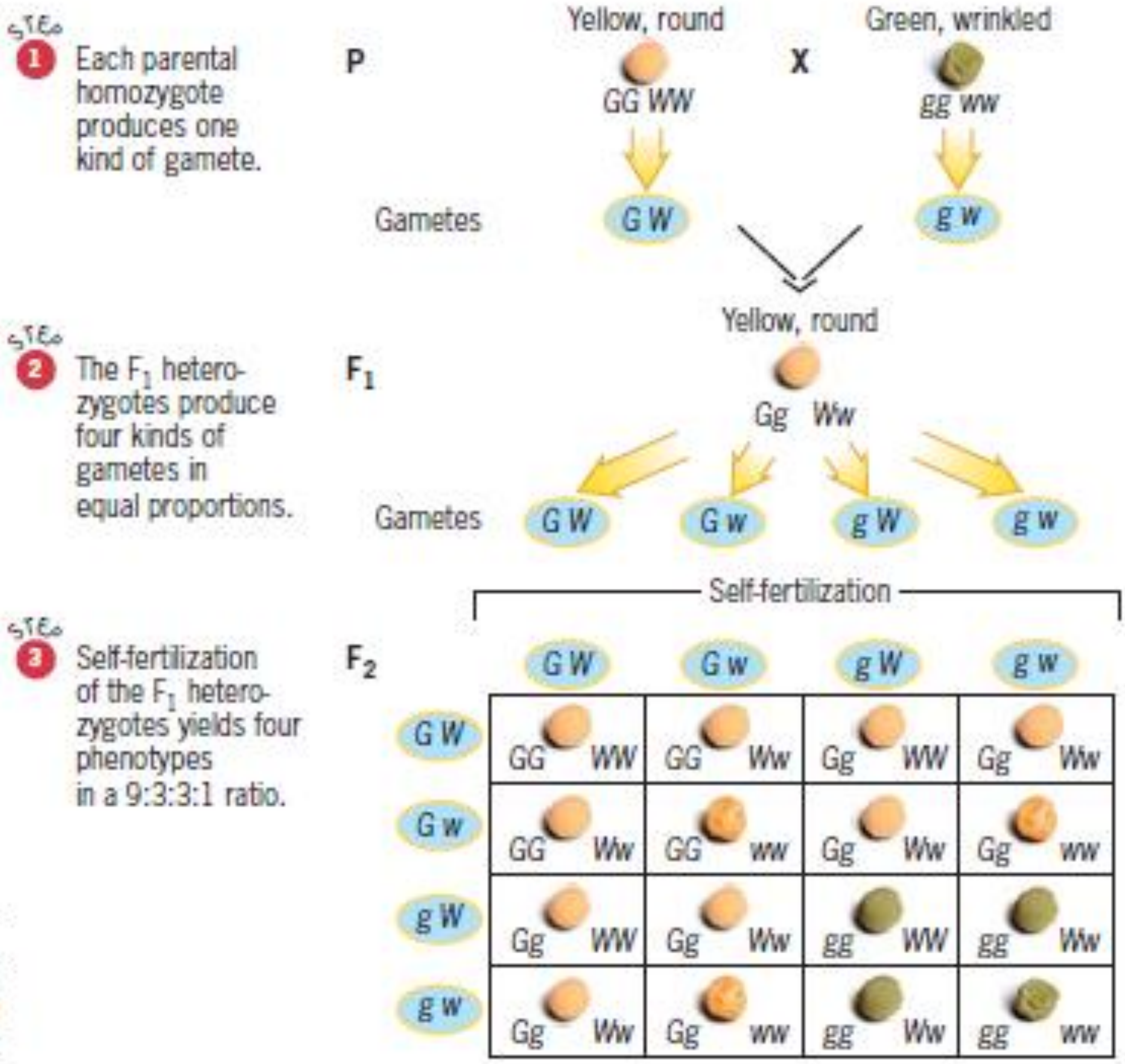



**FIGURE 3.3** Mendel's crosses between peas with yellow, round seeds and peas with green, wrinkled seeds.

To Mendel's insightful mind, these numerical relationships suggested a simple explanation: Each trait was controlled by a different gene segregating two alleles, and the two genes were inherited independently. Let's analyze the results of this two-factor, or dihybrid cross, using Mendel's methods. We denote each gene with a letter, using lower case for the recessive allele and uppercase for the dominant ( ■ Figure 3.4). For the seed color gene, the two alleles are g (for green) and G (for yellow), and for the seed texture gene, they are w (for wrinkled) and W (for round). The parental strains, which were true-breeding, must have been doubly homozygous; the yellow, round plants were GG WW and the green, wrinkled plants were gg ww. Such two-gene genotypes are customarily written by separating pairs of alleles with a space. The haploid gametes produced by a diploid plant contain one copy of each gene. Gametes from GG WW plants therefore contain one copy of the seed color gene (the G allele) and one copy of the seed texture gene (the W allele). Such gametes are symbolized by G W. By similar reasoning, the gametes from gg ww plants are written g w. Cross-fertilization of these two types of gametes produces F1 hybrids that are doubly heterozygous, symbolized by Gg Ww, and their yellow, round phenotype indicates that the G and W alleles are dominant. The Principle of Segregation predicts that the F1 hybrids will produce four different gametic genotypes: (1) G W , (2) G w, (3) g W , and (4) g w. If each gene segregates its alleles independently, these four types will be equally frequent; that is, each will be 25 percent of the total. On this assumption, selffertilization in the F1 will produce an array of 16 equally frequent zygotic genotypes. We obtain the zygotic array by systematically combining the gametes, as shown in Figure 3.4. We then obtain the phenotypes of these F2 genotypes by noting that G and W are the dominant alleles. Altogether, there are four distinguishable phenotypes, with relative frequencies indicated by the number of positions occupied in the array. For absolute frequencies, we divide each number by the total, 16: yellow, round 9/16 yellow, wrinkled 3/16 green, round 3/16 green, wrinkled 1/16 This analysis is predicated on two assumptions: (1) that each gene segregates its alleles, and (2) that these segregations are independent of each other. The second assumption implies that there is no connection or linkage between the segregation events of the two genes. For example, a gamete that receives W through the segregation of the texture gene is just as likely to receive G as it is to receive g through the segregation of the color gene. Do the experimental data fit with the predictions of our analysis? ■ Figure 3.5 compares the predicted and observed frequencies of the four F2 phenotypes in two ways—by proportions and by numerical frequencies. For the numerical frequencies, we calculate the predicted numbers by multiplying the predicted proportion by the total number of F2 seeds examined. With either method, there is obviously good agreement between the observations and the predictions. Thus, the assumptions on which we have built our analysis—independent segregation of the seed color and seed texture genes—are consistent with the observed data. Mendel conducted similar experiments with other combinations of traits and in each case he observed that the alleles of different genes assorted independently. The results of these experiments led him to a third key principle: 3. The Principle of Independent Assortment: The alleles of different genes assort independently of each other. This principle is another rule of genetic transmission, based, on the behavior of different pairs of chromosomes during meiosis. However, not all genes abide by the Principle of Independent Assortment.




| $F_2$ Phenotypes | Genotypes | Genotypic ratio | Phenotypic ratio |
|---|---|---|---|
| Yellow, round | GG WW | 1 | 9 |
| | GG Ww | 2 | |
| | Gg WW | 2 | |
| | Gg Ww | 4 | |
| Yellow, wrinkled | GG ww | 1 | 3 |
| | Gg ww | 2 | |
| Green, round | gg WW | 1 | 3 |
| | gg Ww | 2 | |
| Green, wrinkled | gg ww | 1 | 1 |

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■ **FIGURE 3.4** Symbolic representation of Mendel's dihybrid cross.