## Geneticists Use a Variety of Symbols for Alleles

A standard convention used to symbolize alleles for very simple Mendelian traits is that the initial letter of the name of a recessive trait, lowercased and italicized, denotes the recessive allele, and the same letter in uppercase refers to the dominant allele. Thus, in the case of tall and dwarf, where dwarf is recessive, *D* and *d* represent the alleles responsible for these respective traits. Mendel used upper- and lowercase letters such as these to symbolize his unit factors.

Another useful system was developed in genetic studies of the fruit fly *Drosophila melanogaster* to discriminate between wild-type and mutant traits. This system uses the initial letter, or a combination of several letters, from the name of the mutant trait. If the trait is recessive, lowercase is used; if it is dominant, uppercase is used. The contrasting wild-type trait is denoted by the same letters, but with a superscript $^{+}$. For example, *ebony* is a recessive body color mutation in *Drosophila*. The normal wild-type body color is gray. Using this system, we denote *ebony* by the symbol *e*, while gray is denoted by $e^{+}$. The responsible locus may be occupied by either the wild type allele (*e*+) or the mutant allele (*e*). A diploid fly may thus exhibit one of three possible genotypes (the two phenotypes are indicated parenthetically):

$e^{+}/ e^{+}$ gray homozygote (wild type)
$e^{+}/ e$ gray heterozygote (wild type)
*e* /*e* ebony homozygote (mutant)

The slash between the letters indicates that the two allele designations represent the same locus on two homologous chromosomes. If we instead consider a mutant allele that is dominant to the normal wild-type allele, such as *Wrinkled* wing in *Drosophila*, the three possible genotypes are *Wr*/*Wr*, *Wr*/*Wr*+, and *Wr*+/*Wr*+. The initial two genotypes express the mutant wrinkled-wing phenotype. One advantage of this system is that further abbreviation can be used when convenient: The wild-type allele may simply be denoted by the + symbol. With *ebony* as an example, the designations of the three possible genotypes become:

+/+ gray homozygote (wild type)

+/*e* gray heterozygote (wild type)

*e*/*e* ebony homozygote (mutant)

Another variation is utilized when no dominance exists between alleles. We simply use uppercase letters and superscripts to denote alternative alleles (e.g., $R^1$ and $R^2$, $L^M$ and $L^N$, and $I^A$ and $I^B$).

Many diverse systems of genetic nomenclature are used to identify genes in various organisms. Usually, the symbol selected reflects the function of the gene or even a disorder caused by a mutant gene. For example, in yeast, *cdk* is the abbreviation for the *c*yclin-*d*ependent *k*inase gene, whose product is involved in the cell-cycle regulation mechanism. In bacteria, $leu^-$ refers to a mutation that interrupts the biosynthesis of the amino acid leucine, and the wild-type gene is designated $leu^+$.

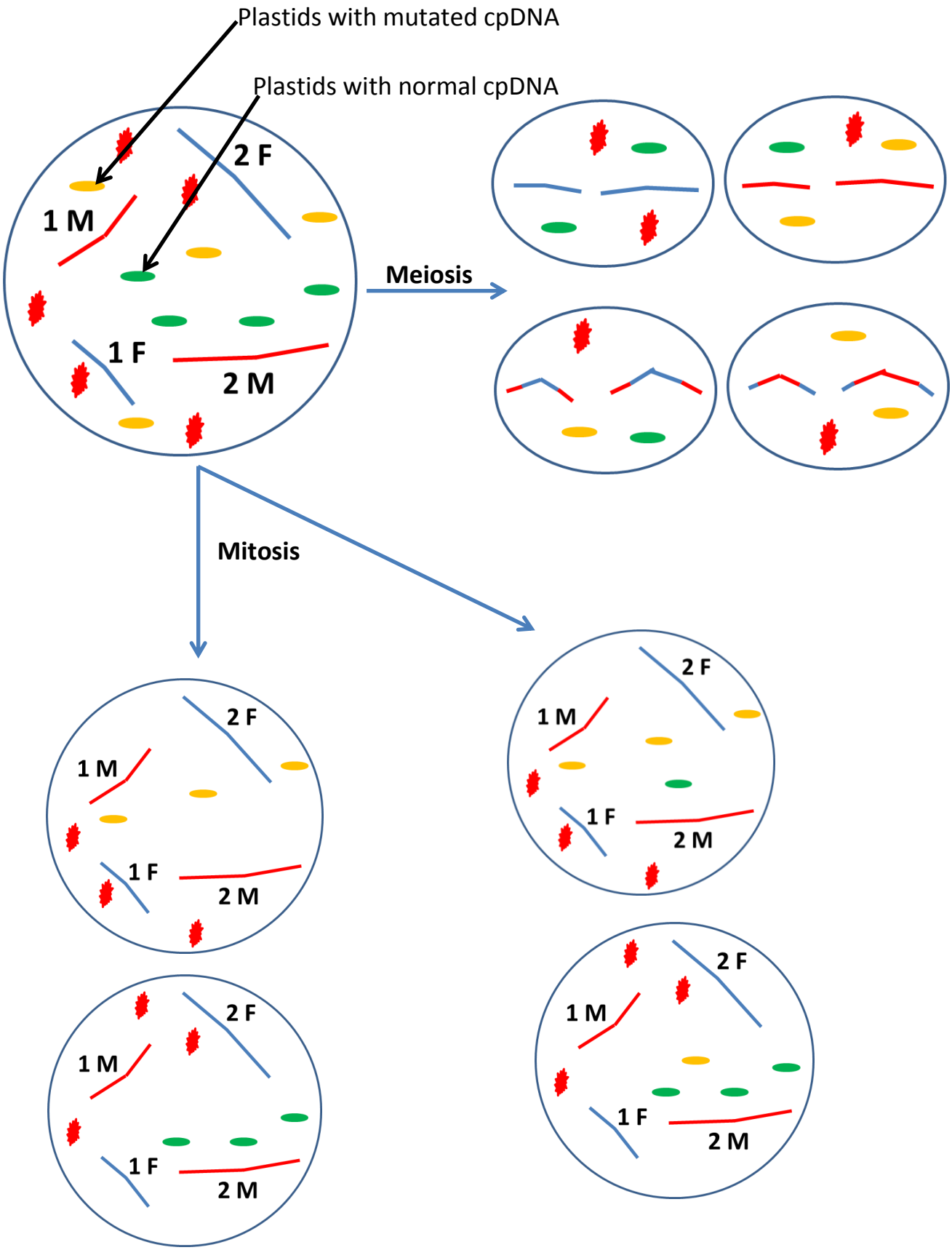
There are several different ways to record genotypes for X-linked traits. Sometimes the genotypes are recorded in the same fashion as they are for autosomal characteristics. In this case, the hemizygous males are simply given a single allele: the genotype of a female *Drosophila* with white eyes is *ww*, and the genotype of a white-eyed hemizygous male is *w*. Another method is to include the Y chromosome, designating it with a diagonal slash (/). With this method, the white eyed female's genotype is still *ww* and the white-eyed male's genotype is *w*/. Perhaps the most useful method is to write the X and Y chromosomes in the genotype, designating the X-linked alleles with superscripts, as is done in this chapter. With this method, a white-eyed female is $X^wX^w$ and a white eyed male is $X^wY$.

## F) Cytoplasmic Inheritance

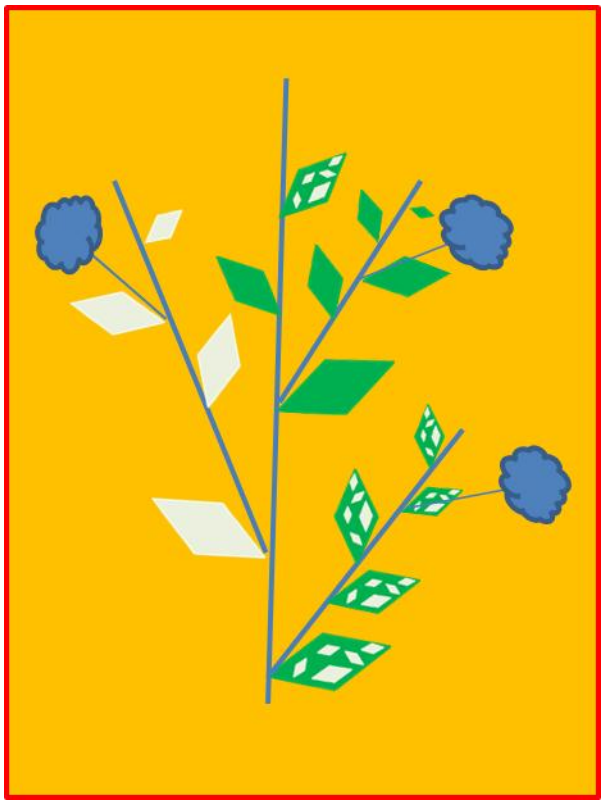
Mendel's principles of segregation and independent assortment are based on the assumption that genes are located on chromosomes in the nucleus of the cell. For most genetic characteristics, this assumption is valid, and Mendel's principles allow us to predict the types of offspring that will be produced in a genetic cross. However, not all the genetic material of a cell is found in the nucleus; some characteristics are encoded by genes located in the cytoplasm. These characteristics exhibit **cytoplasmic inheritance**.

A few organelles, notably chloroplasts and mitochondria, contain DNA. The human mitochondrional genome contains about 15,000 nucleotides of DNA, encoding 37 genes. Compared with that of nuclear DNA, which contains some 3 billion nucleotides encoding some 20,000 to 25,000 genes, the size of the mitochondrial genome is very small; nevertheless, mitochondrial and chloroplast genes encode some important characteristics.

Cytoplasmic inheritance differs from the inheritance of characteristics encoded by nuclear genes in several important respects. A zygote inherits nuclear genes from both parents; but, typically, all its cytoplasmic organelles, and thus all its cytoplasmic genes, come from only one of the gametes, usually the egg. A sperm generally contributes only a set of nuclear genes from the male parent. In a few organisms, cytoplasmic genes are inherited from the male parent or from both parents; however, for most organisms, all the cytoplasm is inherited from the egg. In this case, cytoplasmically inherited traits are present in both males and females and are passed from mother to offspring, never from father to offspring. Reciprocal crosses, therefore, give different results when cytoplasmic genes encode a trait. Cytoplasmically inherited characteristics frequently exhibit extensive phenotypic variation because no mechanism analogous to mitosis or meiosis ensures that cytoplasmic genes are evenly distributed in cell division. Thus, different cells and individual offspring will contain various proportions of cytoplasmic genes. Consider chloroplast genes. Suppose that half of the chloroplasts in a cell contain a normal wild-type copy of cpDNA and the other half contain a mutated copy. In cell division, the chloroplasts segregate into progeny cells at random. Just by chance, one cell may receive mostly mutated cpDNA and another cell may receive mostly wild-type cpDNA. In this way, different progeny from the same mother and even cells within an individual offspring may vary in their phenotypes. Traits encoded by mitochondrial DNA (mtDNA) are similarly variable.


Plastids with mutated cpDNA
Plastids with normal cpDNA
2 F
1 M
1 F
2 M
Meiosis
Mitosis
2 F
1 M
1 F
2 M
2 F
1 M
1 F
2 M
2 F
1 M
1 F
2 M
2 F
1 M
1 F
2 M

Correns, one of the biologists who rediscovered Mendel's work, studied the inheritance of leaf variegation in the four-o'clock plant, *Mirabilis jalapa.* Correns found that the leaves and shoots of one variety of four-o' clock were variegated, displaying a mixture of green and white splotches. He also noted that some branches of the variegated strain had all-green leaves; other branches had all-white leaves. Each branch produced flowers; so Correns was able to cross flowers from variegated, green, and white branches in all combinations. The seeds from green branches always gave rise to green progeny, no matter whether the pollen was from a green, white, or variegated branch. Similarly, flowers on white branches always produced white progeny. Flowers on the variegated branches gave rise to green, white, and variegated progeny, in no particular ratio.



Correns's crosses demonstrated cytoplasmic inheritance of variegation in the four-o clocks. The phenotypes of the offspring were determined entirely by the maternal parent, never by the paternal parent (the source of the pollen). Furthermore, the production of all three phenotypes by flowers on variegated branches is consistent with cytoplasmic inheritance. Variegation in these plants is caused by a defective gene in the cpDNA, which results in a failure to produce the green pigment chlorophyll. Cells from green branches contain normal chloroplasts only, cells from white branches contain abnormal

chloroplasts only, and cells from variegated branches contain a mixture of normal and abnormal chloroplasts. In the flowers from variegated branches, the random segregation of chloroplasts in the course of oogenesis produces some egg cells with normal cpDNA, which develop into green progeny; other egg cells with only abnormal cpDNA develop into white progeny; and, finally, still other egg cells with a mixture of normal and abnormal cpDNA develop into variegated progeny.

## G) Impact of genetic background and environmental factors on Phenotypic Expression

In the previous part we assumed that the genotype of an organism is always directly expressed in its phenotype. For example, pea plants homozygous for the recessive *d* allele (*dd*) will always be dwarf. We discussed gene expression as though the genes operate in a closed system in which the presence or absence of functional products directly determines the phenotype of an individual. The situation is actually much more complex. Most gene products function within the cell, and cells interact with one another in various ways. Furthermore, the organism exists under diverse environmental influences. Thus, gene expression and the resultant phenotype are often modified through the interaction between an individual's particular genotype and the external environment. In this section, we will deal with some of the variables that are known to modify gene expression.

### Penetrance and Expressivity

In the genetic crosses presented thus far, we have considered only the interactions of alleles and have assumed that every individual organism having a particular genotype expresses the expected phenotype. We assumed, for example, that the genotype *Rr* always produces round seeds and that the genotype *rr* always produces wrinkled seeds. For some characters, however, such an assumption is incorrect: the genotype does not always produce the expected phenotype, a phenomenon termed incomplete penetrance.

Incomplete penetrance is seen in human polydactyly, the condition of having extra fingers and toes. The trait is usually caused by a dominant allele. Occasionally, people possess the allele for polydactyly (as evidenced by the fact that their children inherit the

polydactyly) but nevertheless have a normal number of fingers and toes. In these cases the gene for polydactyly is not fully penetrant.

**Penetrance** is defined as the percentage of individual organisms having a particular genotype that express the expected phenotype. For example, if we examined 42 people having an allele for polydactyly and found that only 38 of them were polydactylous, the penetrance would be 38/42 = 0.90 (90%).

A related concept is that of **expressivity**, the degree to which a character is expressed. In addition to incomplete penetrance, polydactyly exhibits variable expressivity. Some polydactylous persons possess extra fingers and toes that are fully functional, whereas others possess only a small tag of extra skin. Incomplete penetrance and variable expressivity are due to the effects of other genes and to environmental factors that can alter or completely suppress the effect of a particular gene.

### 1) Position Effects

Although it is difficult to assess the specific effect of the genetic background and the expression of a gene responsible for determining a potential phenotype, one effect of genetic background has been well characterized, called the position effect. In such instances, the physical location of a gene in relation to other genetic material may influence its expression. For example, if a region of a chromosome is relocated or rearranged (called a translocation or inversion event), normal expression of genes in that chromosomal region may be modified. This is particularly true if the gene is relocated to or near certain areas of the chromosome that are condensed and genetically inert, referred to as heterochromatin.

## 2) Onset of Genetic Expression (Effect of age)

Not all genetic traits become apparent at the same time during an organism's life span. In most cases, the age at which a mutant gene exerts a noticeable phenotype depends on the stage of growth and development. In humans, the prenatal, infant, preadult, and adult phases require different genetic information. As a result, many severe inherited disorders are not manifested before certain age. For example:

- Tay–Sachs disease, inherited as an autosomal recessive, is a lethal lipid-metabolism disease involving an abnormal enzyme, hexosaminidase A. Newborns appear to be phenotypically normal for the first few months. Then, developmental retardation, paralysis, and blindness ensue, and most affected children die around the age of 3.
- Duchenne muscular dystrophy (DMD), an X-linked recessive disorder associated with progressive muscular wasting. It is not usually diagnosed until a child is 3 to 5 years old. Even with modern medical intervention, the disease is often fatal in the early 20s.

## 3) Genetic Anticipation

Some heritable disorders that exhibit a progressively earlier age of onset and an increased severity of the disorder in each successive generation. This phenomenon is referred to as genetic anticipation. Myotonic dystrophy (DM), the most common type of adult muscular dystrophy, clearly illustrates genetic anticipation. Individuals afflicted with this autosomal dominant disorder exhibit extreme variation in the severity of symptoms.

Mildly affected individuals develop cataracts as adults, but have little or no muscular weakness. Severely affected individuals demonstrate more extensive weakness, as well as myotonia (muscle hyperexcitability) and in some cases mental retardation. In its most extreme form, the disease is fatal just after birth. Increased severity and earlier onset of disease was recorded with successive generations of inheritance.

## 4) Genomic (Parental) Imprinting and Gene Silencing

The process of selective *gene silencing* occurs during early development, impacting on subsequent phenotypic expression. Examples involve cases where genes or regions of a chromosome are imprinted on one homolog but not the other.

An example in humans involves two distinct genetic disorders thought to be caused by differential imprinting of the same region of the long arm of chromosome 15. In both cases, the disorders are due to an identical deletion of this region in one member of the chromosome 15 pair:

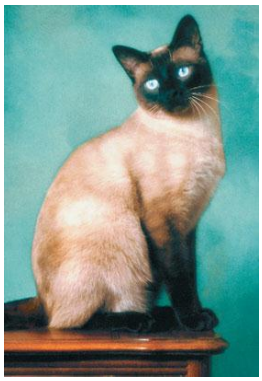
The first disorder, **Prader–Willi syndrome (PWS)**, results when the paternal segment is deleted and an undeleted maternal chromosome remains. If the maternal segment is deleted and an undeleted paternal chromosome remains, an entirely different disorder, **Angelman syndrome (AS)**, results.

These two conditions exhibit different phenotypes. PWS entails mental retardation, a severe eating disorder marked by an uncontrollable appetite, obesity, diabetes, and growth retardation. Angelman syndrome also involves mental retardation, but involuntary muscle contractions (chorea) and seizures characterize the disorder. We can conclude that the involved region of chromosome 15 is imprinted differently in male and female gametes and that both an undeleted maternal and a paternal region are required for normal development.

**Imprinting** is an example of the more general topic of **epigenetics**, where genetic expression is *not* the direct result of the information stored in the nucleotide sequence of DNA. Instead, the DNA is altered in a way that affects its expression. These changes are stable in the sense that they are transmitted during cell division to progeny cells, and often through gametes to future generations.

**5) Temperature Effects**

Chemical activity depends on the kinetic energy of the reacting substances, which in turn depends on the surrounding temperature. We can thus expect temperature to influence phenotypes. An example is seen in the evening primrose, which produces red flowers when grown at 23°C and white flowers when grown at 18°C. An even more striking example is seen in Siamese cats and Himalayan rabbits, which exhibit dark fur in certain regions where their body temperature is slightly cooler, particularly the nose, ears, and paws.

In these cases, it appears that the enzyme normally responsible for pigment production is functional only at the lower temperatures present in the extremities, but it loses its catalytic function at the slightly higher temperatures found throughout the rest of the body.

**6) Nutritional Effects**

In humans, the ingestion of certain dietary substances that normal individuals may consume without harm can adversely affect individuals with abnormal genetic constitutions. Often, a mutation may prevent an individual from metabolizing some substance commonly found in normal diets. For example:

**phenylketonuria** cannot metabolize the amino acid phenylalanine.

**galactosemia** cannot metabolize galactose.

**lactose intolerance** cannot metabolize lactose.

However, if the dietary intake of the involved molecule is drastically reduced or eliminated, the associated phenotype may be ameliorated.