MIMOJADERNÁ DĚDIČNOST

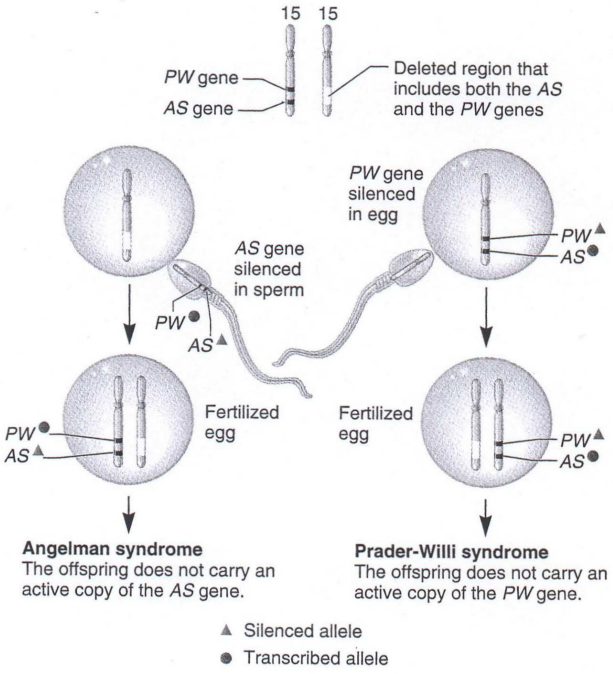


FIGURE 7.12 The role of imprinting in the development of Angelman and Prader-Willi syndromes.

GENES→TRAITS A small region on chromosome 15 contains two different genes designated the *AS* gene and *PW* gene in this figure. If a chromosome 15 deletion is inherited from the maternal parent, it leads to Angelman syndrome. This phenotype occurs because the offspring does not inherit an active copy of the *AS* gene. Alternatively, the chromosome 15 deletion may be inherited from the male parent, leading to Prader-Willi syndrome. The phenotype of this syndrome occurs because the offspring does not inherit an active copy of the *PW* gene.

in PWS is a gene designated *SNRPN*. The gene product is part of a small nuclear ribonucleoprotein polypeptide N, which is a complex that controls gene splicing and is necessary for the synthesis of critical proteins in the brain. The maternal allele of *SNRPN* is silenced.

7.3 EXTRANUCLEAR INHERITANCE

Thus far, we have considered several types of non-Mendelian inheritance patterns. These include maternal effect genes, dosage compensation, and genomic imprinting. All of these inheritance patterns involve genes found on chromosomes in the cell nucleus. Another cause of non-Mendelian inheritance patterns concerns genes that are not located in the cell nucleus. In eukaryotic species, the most biologically important example of extranuclear inheritance involves genetic material in cellular organelles. Since these organelles are found within the cytoplasm of the cells, the inheritance of organellar genetic material is called **extranuclear inheritance** (the prefix *extra-* means outside of) or **cytoplasmic inheritance.** In addition to the cell nucleus, where the linear chromosomes reside, the mitochondria and plastids (e.g., chloroplasts) contain their own genetic material.

In this section, we will examine the genetic composition of mitochondria and plastids and explore the pattern of transmission of these organelles from parent to offspring. We will also consider a few other examples of inheritance patterns that cannot be explained by the transmission of nuclear genes.

Mitochondria and Chloroplasts Contain Circular Chromosomes with Many Genes

In 1951, Y. Chiba was the first to suggest that chloroplasts contain their own DNA. He based his conclusion on the staining properties of a DNA-specific dye known as Feulgen. Researchers later developed techniques to purify organellar DNA. In addition, electron microscopy studies provided interesting insights into the organization and composition of mitochondrial and chloroplast chromosomes. More recently, the advent of molecular genetic techniques in the 1970s and 1980s has allowed researchers to determine the DNA sequences of organellar DNAs. From these types of studies, the chromosomes of mitochondria and chloroplasts were found to resemble smaller versions of bacterial chromosomes.

The genetic material of mitochondria and chloroplasts is located inside the organelle in a region known as the **nucleoid** (fig. 7.13). The genome is a single circular chromosome (composed of double-stranded DNA), although a nucleoid contains several copies of this chromosome. In addition, a mitochondrion or chloroplast often contains more than one nucleoid. In mice, for example, each mitochondrion has one to three nucleoids, with each nucleoid containing two to six copies of the circular mitochondrial genome. On average, each mouse mitochondrion contains five to six copies of the mitochondrial genome. However, this number is variable and depends on the type of cell and the stage of development. In comparison, the plastids of algae and higher plants tend to have more nucleoids per organelle. Table 7.3 describes the genetic composition of mitochondria and chloroplasts for a few selected species.

Besides variation in copy number, the sizes of mitochondrial and plastid genomes also vary greatly among different species. For example, there is a 400-fold variation in the size of the mitochondrial chromosomes. In general, the mitochondrial genomes of animal species tend to be fairly small; those of fungi, algae, and protists are intermediate in size; and those of plant cells tend to be fairly large. Among algae and more complex plants, there is substantial variation in the size of plastid chromosomes.

Figure 7.14 illustrates the genome of a human mitochondrion; this genetic material is called **mtDNA.** Each copy of the mitochondrial chromosome consists of a circular DNA molecule that is only 17,000 base pairs (bp) in length. This size is less than 1% of a typical bacterial chromosome. The mtDNA carries relatively few genes. There are genes that encode ribosomal RNA and

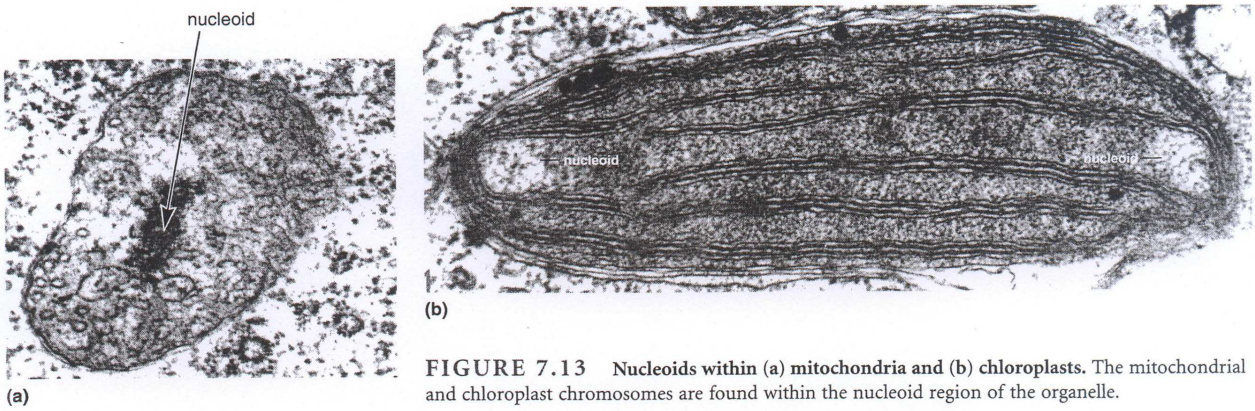


FIGURE 7.13 Nucleoids within (a) mitochondria and (b) chloroplasts. The mitochondrial and chloroplast chromosomes are found within the nucleoid region of the organelle.

TABLE 7.3
Genetic Composition of Mitochondria and Chloroplasts

Species	Organelle	Nucleoids per Organelle	Total Number of Chromosomes per Organelle
Tetrahymena	Mitochondrion	1	6–8
Mouse	Mitochondrion	1–3	5–6
Chlamydomonas	Chloroplast	5–6	~80
Euglena	Chloroplast	20–34	100–300
Higher plants	Chloroplast	12–25	~60

Data from: Gillham, N. W. (1994). *Organelle Genes and Genomes.* Oxford University Press, New York.

transfer RNA. These RNAs are necessary for the synthesis of proteins inside the mitochondrion. In addition, there are 13 genes encoding proteins that function within the mitochondrion. The primary functional role of mitochondria is to provide cells with the bulk of their ATP (adenosine triphosphate), which is used as an energy source to drive cellular reactions. These 13 polypeptides function in a process known as oxidative phosphorylation, which enables the mitochondrion to synthesize ATP. However, mitochondria require many additional proteins to carry out oxidative phosphorylation and other mitochondrial functions. Most mitochondrial proteins are encoded by genes within the cell nucleus. When these nuclear genes are expressed, the mitochondrial proteins are first synthesized outside the mitochondrion in the cytosol of the cell. After synthesis, nuclearly encoded mitochondrial proteins are then transported into the mitochondria.

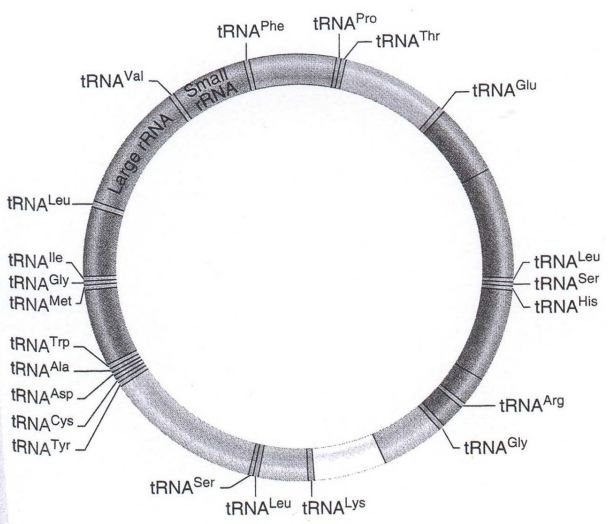


FIGURE 7.14 A genetic map of the human mitochondrial genome. This diagram illustrates the locations of many genes along the circular mitochondrial chromosome. The genes shown in *red* are genes that encode tRNAs. For example, tRNA^{arg} encodes the tRNA that carries arginine. The genes that encode ribosomal RNA are shown in *pale orange*. The remaining genes encode proteins that function within the mitochondrion. The mitochondrial genomes from numerous species have been determined.

Chloroplast genomes tend to be larger than mitochondrial genomes, and they have a correspondingly greater number of genes. A typical chloroplast genome is approximately 100,000 to 200,000 bp in length, which is about 10 times larger than the mitochondrial genome of animal cells. Figure 7.15 shows the chloroplast genome, called **cpDNA,** of the tobacco plant. It is a circular DNA molecule that contains 156,000 bp. It carries between 110 and 120 different genes. These include genes that encode ribosomal RNAs, transfer RNAs, and many proteins required for photosynthesis. As with mitochondria, many chloroplast proteins are encoded by genes found in the plant cell nucleus. These proteins contain chloroplast-targeting signals that direct them into the chloroplasts.

Extranuclear Inheritance Produces Non-Mendelian Results in Reciprocal Crosses

In a diploid eukaryotic species, most genes within the nucleus obey a Mendelian pattern of inheritance because the homologous pairs of chromosomes segregate during gamete formation. Except for sex-linked traits, offspring inherit one copy of each gene from both the maternal and paternal parents. By comparison, the inheritance pattern of extranuclear genetic material does not display a Mendelian pattern. This is because mitochondria and plastids do not segregate into the gametes in the same way as nuclear chromosomes.

Carl Correns discovered a trait that showed a non-Mendelian pattern of inheritance involving a pigmentation trait in *Mirabilis jalapa* (the four-o'clock plant). Leaves could be green, white, or variegated (with both green and white sectors). Correns discovered that the pigmentation of the offspring depended solely on the maternal parent and not at all on the paternal parent (fig. 7.16). If the female parent had white pigmentation, all the offspring had white leaves. Similarly, if the female was green, all the offspring were green. When the female was variegated, the offspring could be green, white, or variegated.

The pattern of inheritance observed by Correns is a type of extrachromosomal inheritance called **maternal inheritance** (not to be confused with maternal effect). In this example, maternal inheritance occurs because the chloroplasts (a type of plastid),

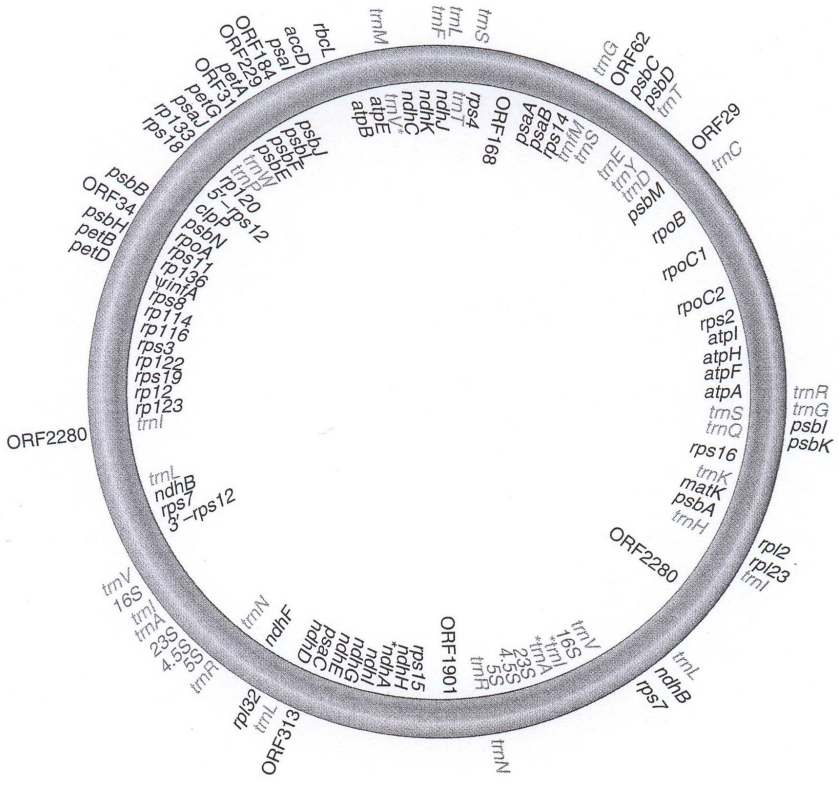


FIGURE 7.15 **A genetic map of the tobacco chloroplast genome.** This diagram illustrates the locations of many genes along the circular chloroplast chromosome. The genes shown in *blue* encode transfer RNAs. The genes that encode ribosomal RNA are shown in *red.* The remaining genes shown in *black* encode polypeptides that function within the chloroplast. The genes designated ORF (open reading frame) encode polypeptides with unknown functions.

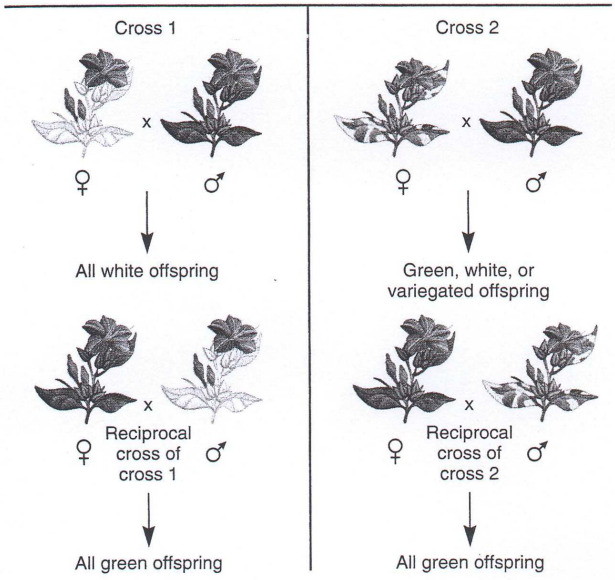


FIGURE 7.16 Maternal inheritance in the four-o'clock plant, *Mirabilis jalapa*. The reciprocal crosses of four-o'clock plants by Carl Correns. A pair of crosses between white-leaved and green-leaved plants. A pair of crosses between variegated- and green-leaved plants.

GENES→TRAITS In this example, the white phenotype is due to chloroplasts that carry a mutant allele that diminishes green pigmentation. The variegated phenotype is due to a mixture of chloroplasts, some of which carry the normal (green) allele and some of which carry the white allele. In the crosses shown here, the parent providing the eggs determines the phenotypes of the offspring. This is due to maternal inheritance. The egg contains the chloroplasts that are inherited by the offspring. If the plant providing the eggs has a white phenotype, all the offspring will inherit chloroplasts that carry the mutant allele and will have white leaves. Similarly, if the plant providing the eggs is green, all the offspring will inherit normal chloroplasts and will be green. If the plant providing the eggs is variegated, it can transmit normal chloroplasts, mutant chloroplasts, or a mixture of these to the offspring. This will produce green, white, or variegated offspring, respectively. Note: the defective chloroplasts that give rise to white sectors are not completely defective in chlorophyll synthesis. Therefore, entirely white plants can survive though they are smaller than green or variegated plants.

which are the site of green pigment synthesis, are inherited only through the cytoplasm of the egg. The pollen grains of *M. jalapa* do not transmit plastids to the offspring.

The phenotypes of leaves can be explained by the types of chloroplasts within the leaf cells. The green phenotype is the wild-type condition. It is due to the presence of normal chloroplasts that can make green pigment. By comparison, the white phenotype is due to a mutation in a gene within the chloroplast DNA that diminishes the synthesis of green pigment. It is possible for a cell to contain both types of chloroplasts, a condition known as **heteroplasmy.** If a leaf cell contained both types of chloroplasts, it would be green because the normal chloroplasts would produce green pigment.

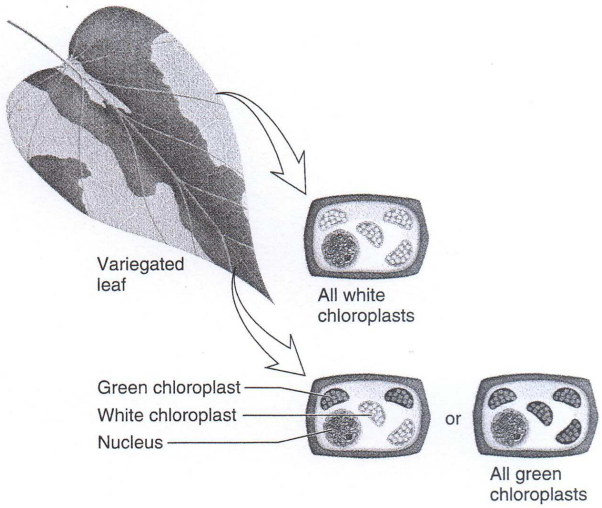


FIGURE 7.17 A cellular explanation of the variegated phenotype in *Mirabilis jalapa*. The plant shown originally inherited two types of chloroplasts: those that can produce green pigment and those that are defective. As this plant grows, the two types of chloroplasts are irregularly distributed to daughter cells. On occasion, a cell may receive only the chloroplasts that are defective at making green pigment. Such a cell continues to divide and produces a sector of the plant that is entirely white. Cells that contain both types of chloroplasts, or cells that contain only green chloroplasts, would produce green tissue, which may be adjacent to a sector of white tissue. This is the basis for the variegated phenotype of the leaves.

Figure 7.17 considers the leaf of a plant that began from a fertilized egg that contained both types of chloroplasts (i.e., a heteroplasmic cell). As a plant grows, the two types of chloroplasts are irregularly distributed to daughter cells. On occasion, a cell may receive only the chloroplasts that have a defect in making green pigment. Such a cell continues to divide and produce a sector of the plant that is entirely white. This is how the variegated phenotype is created. Similarly, if we consider the results of figure 7.16, a female parent that is variegated may transmit green, white, or a mixture of these types of chloroplasts to the egg cell and thereby produce green, white, or variegated offspring, respectively.

Studies in Yeast and *Chlamydomonas* Provided Genetic Evidence for Extranuclear Inheritance of Mitochondria and Chloroplasts

The studies of Correns and others indicated that some traits (e.g., leaf pigmentation) are inherited in a non-Mendelian manner. However, such studies did not definitively determine that maternal inheritance was due to genetic material within organelles. Further progress in the investigation of extranuclear inheritance

was provided by detailed genetic analyses of eukaryotic microorganisms such as yeast and algae by isolating and characterizing mutant phenotypes that specifically affected the chloroplasts or mitochondria.

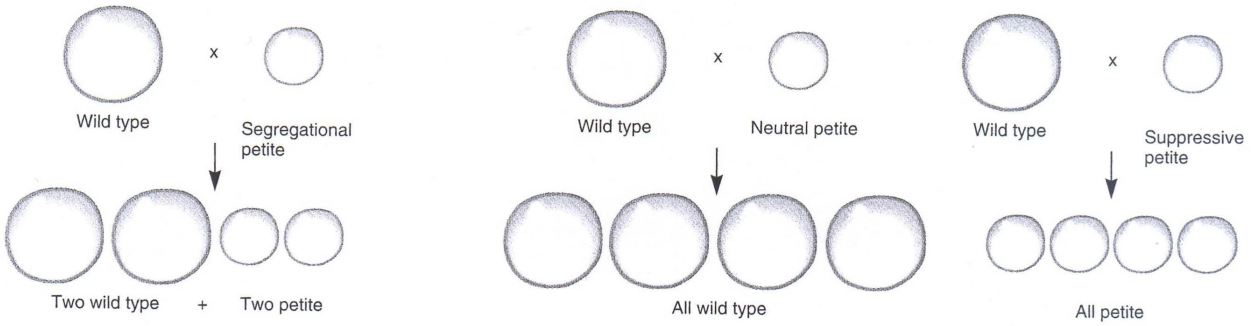
During the 1940s and 1950s, yeasts and molds became model eukaryotic organisms for investigating the inheritance of mitochondria. Because mitochondria produce energy for cells in the form of ATP, mutations that yield defective mitochondria are expected to make cells grow much more slowly. Boris Ephrussi and his colleagues identified mutations in *Saccharomyces cerevisiae* that had such a phenotype. These mutants were called **petites** to describe their formation of small colonies on agar plates (as opposed to wild-type strains that formed larger colonies). Biochemical and physiological evidence indicated that petite mutants had defective mitochondria. The researchers found that petite mutants could not grow when the cells only had an energy source requiring the metabolic activity of mitochondria, but they could form small colonies when grown on sugars that are metabolized by the glycolytic pathway, which occurs outside the mitochondria.

Genetic analyses showed that petite mutants are inherited in different ways. Segregational petite mutants were shown to have mutations in genes located in the nucleus. These mutations affect genes encoding proteins necessary for mitochondrial function. Many nuclear genes encode proteins that are synthesized in the cytosol and are then taken up by the mitochondria, where they perform their functions. Segregational petites get their name because they segregate in a Mendelian manner during meiosis (fig. 7.18*a*). By comparison, the second category of petite mutants, known as vegetative petite mutants, did not segregate in a Mendelian manner. This is because vegetative petites involve mutations in the mitochondrial genome itself.

Ephrussi identified two types of vegetative petites, called neutral petites and suppressive petites. Since yeast exist in two mating types designated a and α, he was able to cross vegetative petites to a wild-type strain. This revealed a non-Mendelian pattern of inheritance (fig. 7.18*b*). In a cross between a wild-type strain and a neutral petite, all four haploid progeny were wild type. This contradicts the normal 2:2 ratio expected for the segregation of Mendelian traits (see the discussion of tetrad analysis in chapter 5). By comparison, a cross between a wild-type strain and a suppressive petite yielded all petite colonies. Thus, vegetative petites are defective in mitochondrial function and show a non-Mendelian pattern of inheritance. Taken together, these results provided compelling evidence that the mitochondrion has its own genetic material.

Since these initial studies, researchers have found that neutral petites lack most of their mitochondrial DNA, whereas suppressive petites usually lack small segments of the mitochondrial genetic material. When two yeast cells are mated, the progeny inherit mitochondria from both parents. For example, in a cross between a wild-type and a neutral petite strain, the progeny inherit both types of mitochondria. Since wild-type mitochondria are inherited, the cells display a normal phenotype. The inheritance pattern of suppressive petites is more difficult to explain since the offspring inherit both normal and suppressive petite mitochondria. One possibility is that the suppressive petite mitochondria replicate more rapidly so that the wild-type mitochondria are not maintained in the cytoplasm for many doublings. Alternatively, some experimental evidence suggests that genetic exchanges between the genomes of wild-type and suppressive petites may ultimately produce a defective population of mitochondria.

Let's now turn our attention to the inheritance of chloroplasts that are found in eukaryotic species capable of photosynthesis (namely, algae and higher plants). The unicellular alga *Chlamydomonas reinhardtii* has been used as a model organism to investigate the inheritance of chloroplasts. This organism contains a single chloroplast that occupies approximately 40% of the cell volume. Genetic studies of chloroplast inheritance began when Ruth Sager identified a mutant strain of *Chlamydomonas*



(a) A cross between a wild type and a segregational petite

(b) A cross between a wild type and a neutral or suppressive vegetative petite

FIGURE 7.18 **Transmission of the petite trait in *Saccharomyces cerevisiae*.** (**a**) A wild-type strain crossed to a segregational petite. (**b**) A wild-type strain crossed to a neutral and to a suppressive vegetative petite.

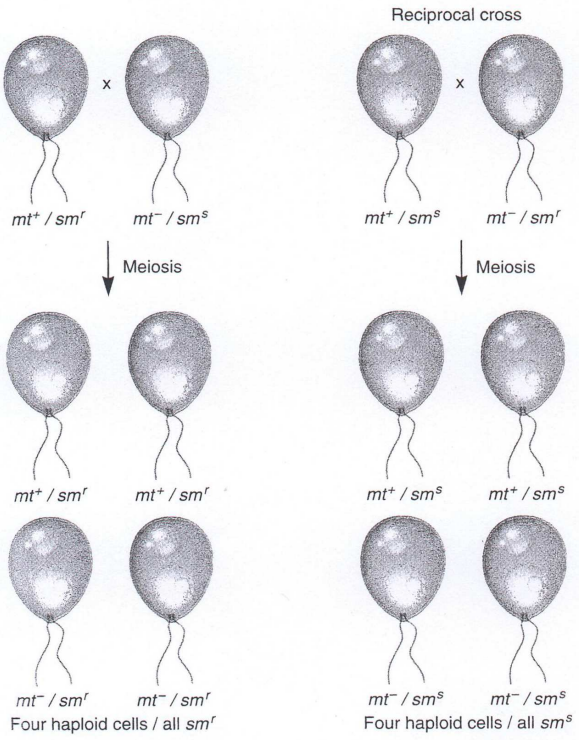


FIGURE 7.19 **Chloroplast inheritance in *Chlamydomonas*.** Mt^+ and mt^- indicate the two mating types of the organism. Sm^r indicates streptomycin resistance, whereas sm^s indicates sensitivity to this antibiotic.

with resistance to the antibiotic streptomycin (sm^r). By comparison, most strains are sensitive to killing by streptomycin (sm^s). In 1954, Sager isolated an sm^r mutant that was not inherited in a Mendelian manner (fig. 7.19). Like yeast, *Chlamydomonas* is an organism that can be found in two mating types, in this case, designated mt^+ and mt^-. Mating type is due to nuclear inheritance and segregates in a 1:1 manner. By comparison, Sager and her colleagues discovered that the sm^r trait was inherited from the mt^+ parent but not from the mt^- parent. In subsequent studies, they mapped several genes, including the sm^r gene, to a single chromosome that was not inherited in Mendelian manner. This linkage group is the chloroplast chromosome.

The Pattern of Inheritance of Mitochondria and Plastids Varies Among Different Species

The inheritance of traits via genetic material within mitochondria and plastids is now a well-established phenomenon that geneticists have investigated in many different species. In **heterogamous** species, two kinds of gametes are made. The female gamete tends to be large and provides most of the cytoplasm to the zygote, while the male gamete is small and often provides little more than a nucleus. Therefore, mitochondria and plastids are most often inherited from the maternal parent. However, this is not always the case. Table 7.4 describes the inheritance patterns of mitochondria and plastids in several selected species.

TABLE 7.4
Transmission of Organelles Among Different Species

Species	Organelle	Transmission
Mammals	Mitochondria	Maternal inheritance
Mussels	Mitochondria	Biparental
S. cerevisiae	Mitochondria	Biparental
Molds	Mitochondria	Usually maternal inheritance; paternal inheritance has been found in the genus *Allomyces*
Chlamydomonas	Mitochondria	Inherited from the parent with the mt^- mating type
Chlamydomonas	Chloroplasts	Inherited from the parent with the mt^+ mating type
Plants		
Angiosperms	Mitochondria and plastids	Often times maternally inherited although biparental inheritance is not uncommon among many species
Gymnosperms	Mitochondria and plastids	Usually paternal inheritance

Data from: Gillham, N. W. (1994). *Organelle Genes and Genomes.* Oxford University Press, New York.

In species where maternal inheritance is generally observed, the paternal parent may, on rare occasions, provide mitochondria via the sperm. This is called **paternal leakage.** It occurs in many species that primarily exhibit maternal inheritance of their organelles. In the mouse, for example, approximately one to four paternal mitochondria are inherited for every 100,000 maternal mitochondria per generation of offspring. This means that most offspring do not inherit any paternal mitochondria, but a rare individual may inherit a mitochondrion from the sperm.

A Few Rare Human Diseases Are Caused by Mitochondrial Mutations

The human mitochondrial genome has 13 genes that encode polypeptides necessary for the synthesis of ATP. In addition, the mtDNA has genes that encode ribosomal RNA and transfer RNA molecules. Human mtDNA is maternally inherited, since it is transmitted from mother to offspring via the cytoplasm of the egg. Therefore, the transmission of human mitochondrial diseases follows a strict maternal inheritance pattern.

TABLE 7.5
Examples of Human Mitochondrial Diseases

Disease	Mitochondrial Gene Mutated
Leber's hereditary optic neuropathy	A mutation in one of several mitochondrial genes that encode respiratory proteins: *ND1, ND2, CO1, ND4, ND5, ND6,* and *cytb*
Neurogenic muscle weakness	A mutation in the *ATPase6* gene that encodes a subunit of the mitochondrial ATP-synthetase, which is required for ATP synthesis
Mitochondrial encephalomyopathy, lactic acidosis, and strokelike episodes	A mutation in genes that encode tRNAs for leucine and lysine
Mitochondrial myopathy	A mutation in a gene that encodes a tRNA for leucine
Maternal myopathy and cardiomyopathy	A mutation in a gene that encodes a tRNA for leucine
Myoclonic epilepsy and ragged-red muscle fibers	A mutation in a gene that encodes a tRNA for lysine

Data from: Wallace, D. C. (1993). Mitochondrial diseases: genotype versus phenotype. *Trends Genet. 9,* 128–33.

Table 7.5 describes several mitochondrial diseases that have been discovered in humans and are caused by mutations in mitochondrial genes. These are usually chronic degenerative disorders that affect the brain, heart, muscles, kidneys, and endocrine glands. For example, Leber's hereditary optic neuropathy (LHON) affects the optic nerve. It may lead to the progressive loss of vision in one or both eyes. LHON can be caused by a defective mutation in one of several different mitochondrial genes. However, it is still unclear how a defect in these mitochondrial genes produces the symptoms of this disease.

Extranuclear Genomes of Mitochondria and Chloroplasts Evolved from an Endosymbiotic Relationship

The idea that the nucleus, mitochondria, and chloroplasts all contain their own separate genetic material may at first seem puzzling. It would appear simpler to have all the genetic material in one place in the cell. The underlying reason for distinct genomes of mitochondria and chloroplasts can be traced back to their evolutionary origin, which is thought to involve a symbiotic association.

A symbiotic relationship occurs when two different species live together in direct contact with each other in a mutually beneficial relationship. The symbiont is the smaller of the two species. The term **endosymbiosis** describes a symbiotic relationship in which the symbiont actually lives inside (*endo-*, inside) the larger of the two species. In 1883, Andreas Schimper proposed that plastids were descended from an endosymbiotic relationship between cyanobacteria and eukaryotic cells. This idea, now known as the **endosymbiosis theory,** suggested that the ancient origin of plastids was initiated when a cyanobacterium took up residence within a primordial eukaryotic cell (fig. 7.20). Over the course of evolution, the characteristics of the intracellular bacterial cell gradually changed to those of a plastid. In 1922, Ivan Wallin also proposed an endosymbiotic origin for mitochondria.

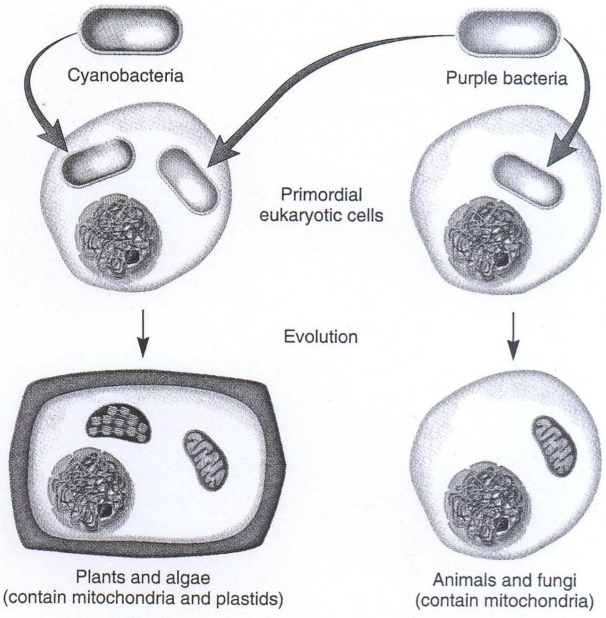


FIGURE 7.20 The endosymbiotic origin of mitochondria and chloroplasts. According to the endosymbiotic theory, plastids descended from an endosymbiotic relationship between cyanobacteria and eukaryotic cells. This arose when a bacterium took up residence within a primordial eukaryotic cell. Over the course of evolution, the intracellular bacterial cell gradually changed its characteristics, eventually becoming a plastid. Similarly, mitochondria were derived from an endosymbiotic relationship between purple bacteria and eukaryotic cells.

In spite of these hypotheses, the question of endosymbiosis was largely ignored until researchers in the 1950s discovered that chloroplasts and mitochondria contain their own genetic material. The issue of endosymbiosis was hotly debated after Lynn Margulis published a book entitled *Origin of Eukaryotic Cells.* During the 1970s and 1980s, the advent of molecular genetic techniques allowed researchers to analyze genes from chloroplasts, mitochondria, bacteria, and eukaryotic nuclear genomes. They found that genes in chloroplasts and mitochondria are very similar to bacterial genes but not as similar to those found within the nucleus of eukaryotic cells. This observation provided strong support for the endosymbiotic origin of mitochondria and chloroplasts.

Symbiosis occurs because the relationship is beneficial to one or both species. In the case of the endosymbiosis theory, the relationship provided eukaryotic cells with useful cellular characteristics. Plastids were derived from cyanobacteria, a bacterial species that is capable of photosynthesis. The ability to carry out photosynthesis is beneficial to plant cells, providing them with the ability to use the energy from sunlight. It is less clear how the relationship would have been beneficial to a cyanobacterium. By comparison, mitochondria are thought to have been derived from a different type of bacteria known as Gram-negative nonsulfur purple bacteria. In this case, the endosymbiotic relationship enabled eukaryotic cells to synthesize greater amounts of ATP.

During the evolution of eukaryotic species, most genes that were originally found in the genome of the primordial cyanobacteria and purple bacteria have been lost or transferred from the organelles to the nucleus. The sequences of certain genes within the nucleus are consistent with their origin within an organelle. Such genes are more similar in DNA sequence to known bacterial genes than to their eukaryotic counterparts. Therefore, researchers have concluded that these genes have been removed from the mitochondrial and chloroplast chromosomes and relocated to the nuclear chromosomes. This has occurred many times throughout evolution, so that modern mitochondria and chloroplasts have lost most of the genes that are still found in present-day purple bacteria and cyanobacteria.

Most of this gene transfer occurred early in mitochondrial and chloroplast evolution. It appears that the functional transfer of mitochondrial genes has ceased in animals, but gene transfer from mitochondria and chloroplasts to the nucleus continues to occur in plants at a low rate. The molecular mechanism of gene transfer is not entirely understood, but the direction of transfer is well established. During evolution, gene transfer has occurred primarily from the organelles to the nucleus. Transfer of genes from the nucleus to the organelles has almost never occurred, although there is one example of a nuclear gene in plants that has been transferred to the mitochondrial genome. This unidirectional gene transfer from organelles to the nucleus partly explains why the organellar genomes now contain relatively few genes. In addition, gene transfer can occur between organelles. It can happen between two mitochondria, between two chloroplasts, and between a chloroplast and mitochondrion. Overall, the transfer of genetic material between the nucleus, chloroplasts, and mitochondria is an established phenomenon, although its biological benefits remain unclear.

Eukaryotic Cells Occasionally Contain Symbiotic Infective Particles

Other unusual endosymbiotic relationships have been identified in eukaryotic organisms. There are a few rare cases where infectious particles establish a symbiotic relationship with their host. In some cases, research indicates that symbiotic infectious particles are bacteria that exist within the cytoplasm of eukaryotic cells. While examples of symbiotic infectious particles are relatively rare, they have provided interesting and even bizarre examples of the extranuclear inheritance of traits.

In the 1940s, Tracy Sonneborn studied a trait in the protozoan *Paramecia aurelia* known as the killer trait. Killer paramecia secrete a substance called paramecin, which kills some but not all strains of paramecia. The killer strains themselves are resistant to paramecin. Sonneborn found that killer strains contain particles in their cytoplasm known as kappa particles. Each kappa particle is 0.4 μm long and has its own DNA. Genes within the kappa particle encode the paramecin toxin. In addition, other kappa particle genes provide the killer paramecia with resistance to paramecin. When nonkiller strains are mixed with a cell extract derived from killer paramecia, the kappa particles within the extract can infect the nonkiller strains and convert them into killer strains. In other words, the extranuclear particle that determines the killer trait is infectious.

Infectious particles have also been identified in fruit flies. P. l'Heritier identified strains of *Drosophila melanogaster* that are highly sensitive to killing by CO_2. Reciprocal crosses between CO_2-sensitive and normal flies revealed that the trait is inherited in a non-Mendelian manner. Furthermore, cell extracts from a sensitive fly can infect a normal fly and make it sensitive to CO_2.

Another example of an infectious particle in fruit flies involves a trait, known as sex ratio, that was discovered by Chana Malogolowkin and D. Poulson. This trait was found in one strain of *Drosophila willistoni* where most of the offspring of female flies were daughters; nearly all the male offspring died. The sex ratio trait is transmitted from mother to offspring. The rare surviving males do not transmit this trait to their male or female offspring. This result indicates a maternal inheritance pattern for the sex ratio trait. The agent in the cytoplasm of female flies was found to be a symbiotic microorganism. Its presence is usually lethal to males but not to females. This infective agent can be extracted from the tissues of adult females and used to infect the females of a normal strain of flies.