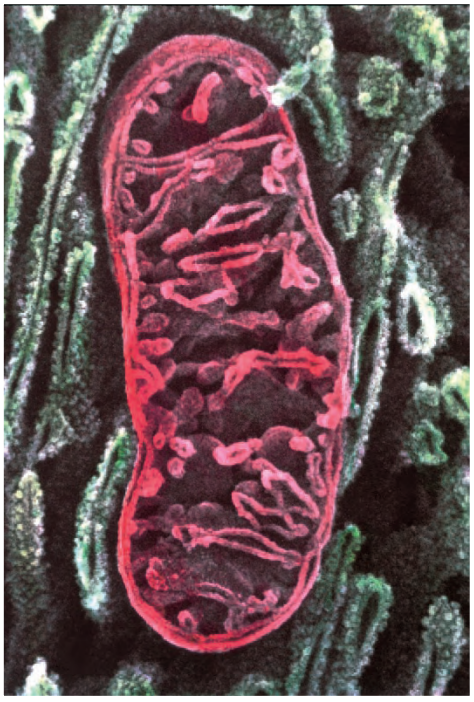
17

NON-MENDELIAN INHERITANCE

STUDY OBJECTIVES

1. To analyze the inheritance patterns of maternal effects 509
2. To analyze the patterns of cytoplasmic inheritance 511
3. To analyze the patterns of imprinting 524

STUDY OUTLINE



Artificially colored scanning electron micrograph of a mitochondrion in the cytoplasm of an intestinal epithelial cell. (© Professors P. Motta & T. Naguro/ SPL/Photo Researchers, Inc.)

The phenotype can be controlled by chromosomal genes behaving according to Mendelian rules and the environment. In this chapter, we deal with another mode of inheritance, non-Mendelian inheritance (also called extrachromosomal, cytoplasmic, and nonchromosomal inheritance; maternal effects; or imprinting). **Maternal effects** are the influences of a mother's genotype on the phenotype of her offspring; examples include snail coiling and moth pigmentation (we started a discussion of maternal effects in chapter 16, when we looked at development in *Drosophila*). **Cytoplasmic inheritance** is controlled by nonnuclear genomes found in chloroplasts, mitochondria, infective agents, and plasmids. And *imprinting* is a process in which gene expression depends on the parent from which the gene came. None of these modes of inheritance follow the usual Mendelian rules and ratios.

Maternal effects result from the asymmetric contribution of the female parent to the development of zygotes. Although both male and female parents contribute equally to the zygote in terms of chromosomal genes (with the exception of sex chromosomes), the sperm rarely contributes anything to development other than chromosomes. The female parent usually contributes the zygote's initial cytoplasm and organelles. Zygotic development, therefore, usually begins within a maternal milieu, so that the maternal cytoplasm directly affects zygotic development (see chapter 16).

Cytoplasmic inheritance refers to the inheritance pattern of organelles and parasitic or symbiotic particles that have their own genetic material. Chloroplasts, mitochondria, bacteria, viruses, and, of course, plasmids all have their own genetic material. These genomes are open to mutation. As we shall see, their inheritance pattern does not follow Mendel's rules for chromosomal genes.

Imprinting occurs in more than twenty genes and is responsible for several human diseases.

DETERMINING NON-MENDELIAN INHERITANCE

How does one determine that a trait is inherited? The question does not have as obvious an answer as we might expect. Environmentally induced traits can mimic inherited phenotypes, as with the phenocopies we discussed in chapter 5. For example, the inheritance of vitamin D-resistant rickets is mimicked by lack of vitamin D in the diet. It is possible to determine that the rickets is not inherited by simply administering adequate quantities of vitamin D. Inherited rickets does not respond to vitamin D until about 150 times the normally adequate amount is administered.

Some environmentally induced traits persist for several generations. For example, a particular *Drosophila* strain that normally grows at 21° C was exposed to 36° C for twenty-two hours. Dwarf progeny were produced. When they were mated among themselves, fewer and fewer dwarfs appeared in each generation, but smaller-than-normal flies were produced as late as the fifth generation. The appearance of an environmentally induced trait that persists for several generations has been termed **dauermodification.**

Extrachromosomal inheritance is usually identified by the odd results of reciprocal crosses. If the progeny of reciprocal crosses are not followed for several generations, the results can be misleading when extrachromosomal inheritance is involved. Where feasible, nuclear transplantation has proved useful in identifying extrachromosomal inheritance. In this technique, the nucleus of a cell, such as an amoeba or frog egg, is removed by microsurgery or destroyed by radiation, and another nucleus substituted. Thus, not only can a nucleus be isolated from its cytoplasm, but various nuclei can be implanted in the same cytoplasm.

A similar experiment, called a *heterokaryon test,* can be done with various fungi such as *Neurospora* and *Aspergillus:* Mycelia can fuse and form a heterokaryon, a cell containing nuclei from different strains. Thus, nuclei of both strains exist in the mixed cytoplasm. Subsequently, spores (conidia) that have one or the other nucleus in the mixed cytoplasm can be isolated. The phenotype of the colonies produced from these isolated conidia show whether the trait under observation is controlled by the nucleus or the cytoplasm.

Chromosomal genes in a particular cytoplasm can also be isolated by repeated backcrossing of offspring with the male-parent type. In each cross, the content of the female chromosomal genes is halved, but, presumably, the cytoplasm remains similar to the female line. Thus, after several generations, male genes can be isolated in female cytoplasm. The phenotypic results of the final cross will indicate whether inheritance was chromosomal or extrachromosomal.

MATERNAL EFFECTS

Snail Coiling

Snails are coiled either to the right (dextrally) or to the left (sinistrally) as determined by holding the snail with the apex up and looking at the opening. The snail is dextrally coiled if the opening comes from the right-hand side and sinistrally coiled if it comes from the left-hand side (fig. 17.1). The inheritance pattern of the coiling is at first perplexing.

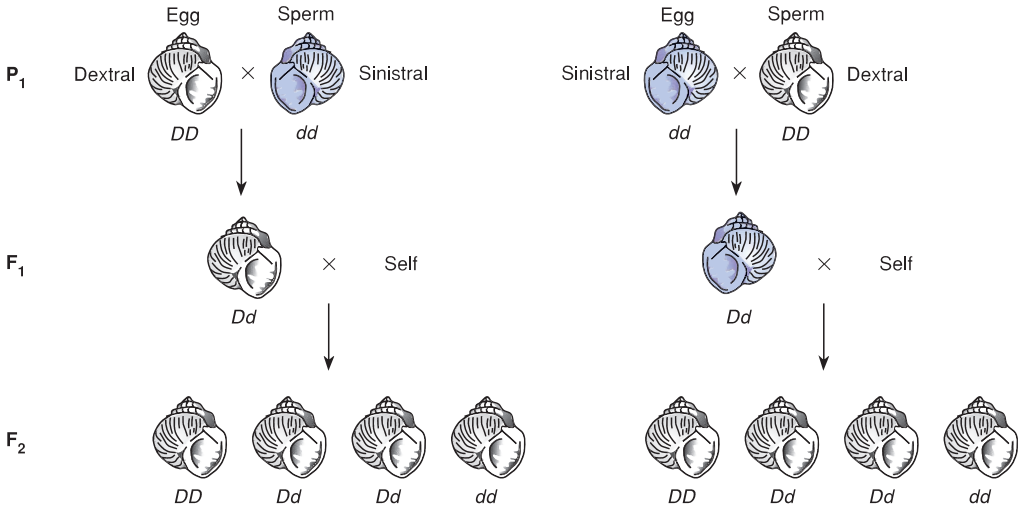


Figure 17.1 Inheritance of coiling in the pond snail, *Limnaea peregra.* Reciprocal crosses (*D,* dominant dextral; *d,* recessive sinistral coiling) are shown (*DD* mated with *dd* in each case). The F_1 individuals in both crosses have the *Dd* genotype but reflect the mother's genotype in respect to coiling; *DD* mothers produce dextrally coiled offspring, whereas *dd* mothers produce sinistrally coiled offspring. The F_2 individuals in both cases are identical because the genotypes of the F_1 mothers are identical (*Dd*). The coiling of a snail's shell is determined by its mother's genotype, not phenotype.

In the left half of figure 17.1, a dextral snail provides the eggs, and a sinistral snail provides the sperm. The offspring are all dextral; presumably, therefore, dextral coiling is dominant. When the F_1 are self-fertilized (snails are hermaphroditic), all the offspring are dextrally coiled. The result is unexpected. Nevertheless, when the F_2 are self-fertilized, one-fourth produce only sinistral offspring, and three-fourths produce only dextral offspring. If self-fertilization is continued through ensuing generations, this 3:1 phenotypic ratio will be revealed as a Mendelian 1:2:1 genotypic ratio, thereby reaffirming the notion of a single locus with two alleles, and dextral dominant. However, something interfered with the expected phenotypic pattern.

When the reciprocal cross is made (fig. 17.1, *right*), the F_1 have the same genotype as just described but are coiled sinistrally, as is the female parent. From here on, the results are exactly the same for both crosses. In both cases, the F_1 are phenotypically similar to the female parent even though the offspring in both crosses have the same genotype (*Dd*). The explanation is that the genotype of the maternal parent determines the phenotype of the offspring, with dextral dominant. Thus, the *DD* mother in figure 17.1 produces F_1 progeny that are dextral with a *Dd* genotype, and the *dd* mother produces progeny that are sinistral with the same *Dd* genotype. Why does this pattern occur?

A process of **spiral cleavage** takes place in the zygotes of mollusks and some other invertebrates. The spindle at mitosis is tipped in relation to the axis of the egg. If the spindle is tipped one way, a snail will be coiled sinistrally; if it is tipped the other way, the snail will be coiled dextrally. The direction of tipping is determined by the maternal cytoplasm, which is under the control of the maternal genotype. Obviously, maternal control affects only one generation—in each generation, the coiling is dependent on the maternal genotype.

Moth Pigmentation

There are other examples of maternal effects in which the cytoplasm of the mother, under the control of chromosomal genes, controls the phenotype of her offspring. In the flour moth, *Ephestia kühniella,* kynurenin, which is a precursor for pigment, accumulates in the eggs. The recessive allele, *a,* when homozygous, results in a lack of kynurenin. Reciprocal crosses give different results for larvae and adults. When a nonpigmented female is crossed with a pigmented male, the results are strictly Mendelian; but when the mother is pigmented (a^+a), all the larvae are pigmented regardless of genotype (fig. 17.2). The initial larval pigmentation comes from residual kynurenin in the eggs, which is then diluted out so that an adult's pigmentation conforms to its own genotype.

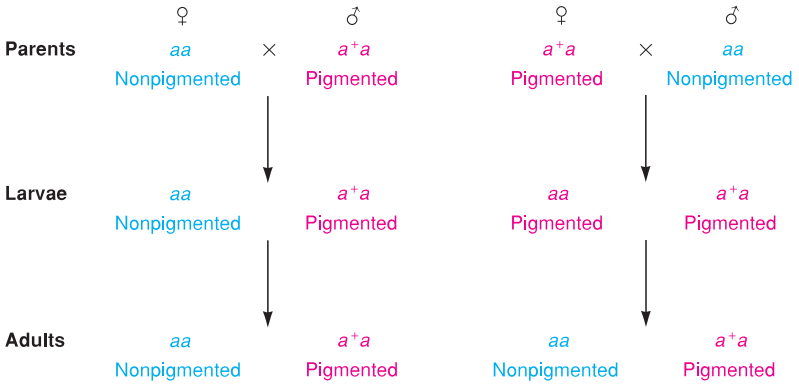


Figure 17.2 Inheritance pattern of larval and adult pigmentation in the flour moth, *Ephestia kühniella.* A single locus controls the presence (a^+) or absence (a) of kynurenin. In the cross on the *left,* the mother is *aa* (nonpigmented). Her *aa* offspring, in both the larval and adult stages, are also nonpigmented. In the reciprocal cross (*right),* the mother has the a^+a genotype and is pigmented. Her *aa* offspring are nonpigmented as adults but are pigmented as larvae because of residual kynurenin from the egg, which eventually dilutes out.

CYTOPLASMIC INHERITANCE

Mitochondria

The **mitochondrion** is an organelle in eukaryotic cells in which the electron transport chain takes place. The actual number of mitochondria per cell can be determined by serial sectioning of whole cells and examination under the electron microscope. This is a tedious and difficult procedure. Estimates range between ten and ten thousand per cell, depending on the organism and cell type. As far as we are concerned, the most interesting aspect of the mitochondrion is that it has its own DNA. In most animal cells, the mitochondrial DNA (mtDNA) is a circle of about sixteen thousand base pairs (fig. 17.3). However, some organisms (yeast, higher plants) have mitochondrial DNAs five to twenty-five or more times larger than in animals. And some organisms have linear mitochondrial chromosomes.

Two general patterns are found in mitochondrial inheritance in animals. First, the mitochondria are generally inherited in a maternal fashion; that is, the male gamete usually does not contribute mitochondria to the zygote. However, a small amount of "leakiness" occurs in this process. For example, it has recently been shown that about one mitochondrion per thousand is of paternal origin in mice. In some species, such as mussels, it appears that mitochondrial inheritance is biparental. That is, the population of mitochondria in an offspring derives almost equally from the male and female parent. In some gymnosperm plants, such as coastal redwoods, mitochondria are inherited paternally—only paternal mitochondria are passed into the zygote. However, these are all exceptions to the general rule of maternal inheritance of mitochondria.

The second general pattern of mitochondrial inheritance is **homoplasmy,** the existence of a uniform population of mitochondria within an organism. In general, all the mitochondria within an individual are genetically identical. Certainly, biparental inheritance and leakiness of paternal mitochondria violate that principle, resulting in **heteroplasmy,** a heterogeneity of mitochondria within a cell or organism.

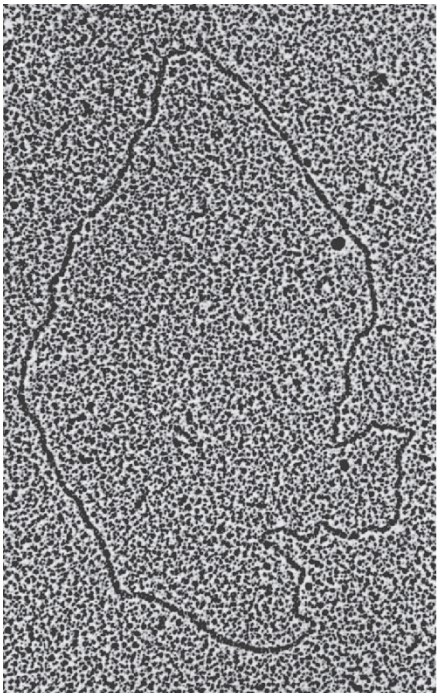


Figure 17.3 Electron micrograph of the circular DNA from within a mouse cell mitochondrion. Magnification 48,000×. (M. M. K. Nass, "The circularity of mitochondrial DNA," *Proceedings of the National Academy of Sciences, USA,* 56 (1966):1215–22. Reproduced by permission of the author.)

Mitochondrial Genomes

Numerous mitochondrial DNAs have been sequenced, including the human mitochondrial DNA, which is 16,569 base pairs long. It is a model of economy, with very few noncoding regions and no introns (fig. 17.4). Each strand of the duplex is transcribed into a single RNA product that is then cut into smaller pieces, primarily by freeing the twenty-two transfer RNAs interspersed throughout the genome. Also formed are a 16S and a 12S ribosomal RNA. Although proteins and small molecules such as ATP and tRNAs can move in and out of the mitochondrion, large RNAs cannot. Thus, the mitochondrion must be relatively self-sufficient in terms of the RNAs needed for protein synthesis. We previously discussed mitochondrial protein synthesis when we looked at unique attributes of the mitochondrial genetic code in chapter 11.

Oxidative phosphorylation, the process that occurs within the mitochondrion, requires at least sixty-nine polypeptides. The human mitochondrion has the genes for thirteen of these: cytochrome b, two subunits of ATPase, three subunits of cytochrome-c oxidase, and seven subunits of NADH dehydrogenase. The remaining polypeptides needed for oxidative phosphorylation are transported into the mitochondrion; they are synthesized in the cytoplasm under the control of nuclear genes. Proteins targeted for entry into the mitochondrion have special signal sequences (see chapter 11).

The signal sequences range up to eighty-five amino acids long. Signal sequences examined so far do not have consensus amino acids but do have certain attributes (fig. 17.5), including a somewhat regular alternation of basic (positively charged) and hydrophobic (negatively charged) residues. In addition, they form α helices with opposite hydrophobic and hydrophilic faces that must somehow be important in the protein's ability to enter the mitochondrion. When a signal sequence (such as that in fig. 17.5) is attached to nonmitochondrial proteins by DNA manipulations, those proteins are transported into the mitochondrion.

The mitochondrial ribosomal RNA is more similar to prokaryotic ribosomal RNA than to eukaryotic ribosomal RNA. The mitochondrial ribosome, although constructed of imported cellular proteins, is sensitive to prokaryotic antibiotics; for example, streptomycin and chloramphenicol inhibit their function. This affinity (close resemblance) between mitochondria and prokaryotes is strong support for the symbiotic origin of mitochondria. That is, we now accept the model advocated by L. Margulis that organelles such as mitochondria and chloroplasts were originally free-living bacteria and cyanobacteria, respectively. These prokaryotes invaded or were eaten by early cells and, over evolutionary time, became the organelles we see today. Since they arose as prokaryotes, these organelles retain certain evolutionary similarities to other prokaryotes.

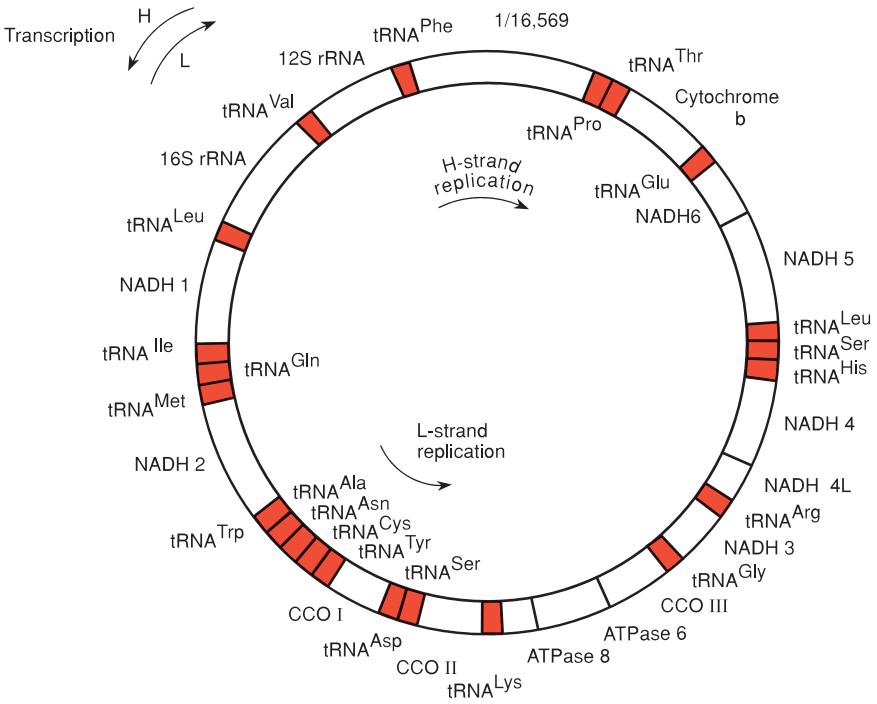


Figure 17.4 Gene map of the human mitochondrial chromosome. All but nine loci are on the heavy (H) strand. The light-strand (L) loci are labeled inside the circle; the H-strand loci are labeled on the outside. Also shown are the origins of H- and L-strand replication and the directions of transcription. The twenty-two tRNA genes are colored *red.* NADH refers to NADH dehydrogenase (subunits 1–4, 4L, 5, and 6); CCO refers to cytochrome-c oxidase (subunits I–III). (Source: Data from V. McKusick, *Mendelian Inheritance in Man,* 7th edition, 1986.)

Lynn Margulis (1938–). (Courtesy of Lynn Margulis, Boston University Photo Services.)

Among the mitochondrial DNAs that have been sequenced from different organisms, we see great variation in content and organization. Yeast mitochondrial DNA, for example, is not as economical as human mitochondrial DNA. Yeast mitochondrial DNA, about five times larger than human mitochondrial DNA, has noncoding regions as well as introns. Because mitochondria are similar in structure and biochemistry to prokaryotic cells, given the general lack of introns in prokaryotic genes, it was surprising to find introns in yeast mitochondrial DNA. These genes most probably arose later as nuclear genes that were then "captured" by the mitochondria, possibly by recombination with nuclear DNA.

Of the many mitochondria sequenced to date (about 175 at the beginning of 2001), the sizes range from less than 6 to more than 200 kilobases and from 3 to 97 genes. With this wide range of genes present, the only generality we can make about mitochondrial DNA is that the large and small segments of the mitochondrial ribosomal RNA, as well as most of the mitochondria's transfer RNAs, are usually coded by the mitochondria's own genome, as are several proteins in respiratory complexes III and IV (cytochrome c oxidase and cytochrome c oxidoreductase). Once the interaction within the mitochondrial-nuclear genetic system is clearly understood, we might expect to see several different inheritance patterns—following either cytoplasmic or nuclear lines—for the genetic defects that lead to interruption of cellular respiration. Among the best-studied phenotypes with such inheritance patterns are the *petite* mutations of yeast.

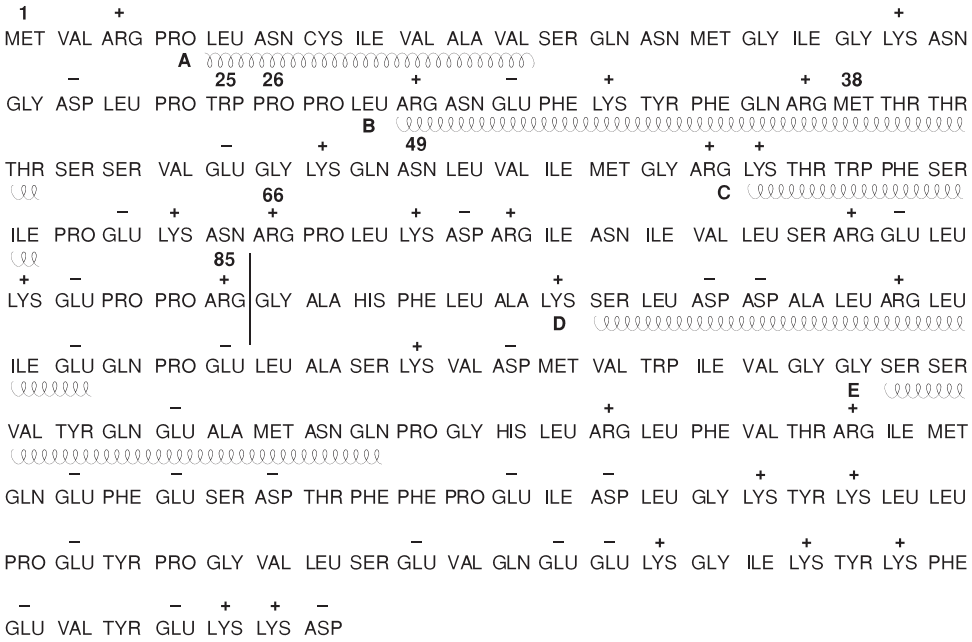


Figure 17.5 The amino acid sequence of mouse dihydrofolate reductase. Numbers refer to sequential amino acids. The first eighty-five amino acids serve as the signal sequence for transport into mitochondria. Five α-helical regions exist in the protein (A–E). Positively and negatively charged amino acids are marked with (+) and (−) signs. (Reprinted by permission from E. C. Hurt and G. Schatz, "A cytosolic protein contains a cryptic mitochondrial targeting signal," *Nature,* Volume 325, p. 499, 1987. Copyright © 1987 Macmillan Magazines, Ltd.)

Petites

Under aerobic conditions, yeast grows with a distinctive colony morphology. Under anaerobic conditions, the colonies are smaller, and the structures of the mitochondria are reduced. Occasionally, when growing aerobically, small, anaerobiclike colonies appear; but in these colonies, the mitochondria appear perfectly normal. These colonies are caused by **petite mutations.** When petites are crossed with the wild-type, three modes of inheritance emerge (fig. 17.6). The *segregational petite,* caused by mutation of a chromosomal gene, exhibits Mendelian inheritance. The *neutral petite* is lost immediately upon crossing to the wild-type. The *suppressive petite* shows variability in expression from one strain to the next but is able to convert the wild-type mitochondria to the petite form. All petites represent failures of mitochondrial function, whether the function is controlled by the mitochondria themselves or by the cell's nucleus; they usually lack one or another cytochrome.

Although the mechanisms that produce neutral and suppressive petites are not known with certainty, their DNA has supplied some interesting information. In some petites, no change in the buoyant density of the DNA is found. (*Buoyant density,* a term that describes the position at which the DNA equilibrates during density-gradient centrifugation, is a measure of the composition of the molecule; see chapter 15.) In other petites, changes in buoyant density range from very small to the complete absence of DNA.

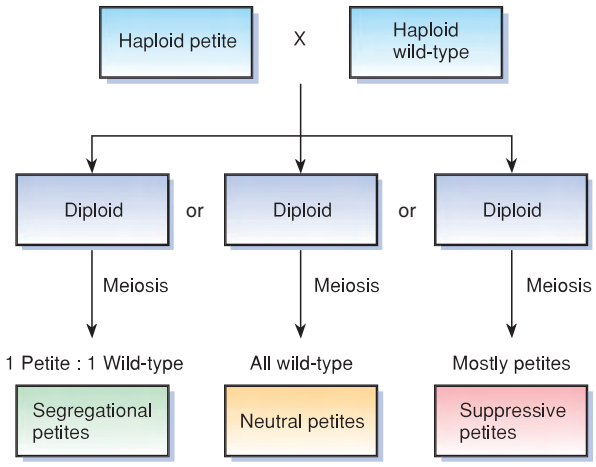


Figure 17.6 Petite yeasts categorized on the basis of segregation patterns. Three types of petites are recognized (segregational, neutral, and suppressive), depending on the meiotic segregation pattern of petite × wild-type diploids. Segregational petite heterozygotes segregate a 1:1 ratio of spores; neutral petites are lost when heterozygous; and suppressive petites act in a dominant fashion under the same circumstances.

Petites, therefore, can be the result of an approximation to a point mutation (with no measurable change in the buoyant density of the DNA), marked changes in the DNA, or the total absence of DNA. In most petites, protein synthesis within the mitochondrion is lacking. Any and all of these changes produce the petite (anaerobiclike) phenotype.

Neutral petites seem to have mitochondria that entirely lack DNA. When neutral petites are crossed with the wild-type to form diploid cells, the normal mitochondria dominate. During meiosis, virtually every spore receives large numbers of normal mitochondria; the progeny are, therefore, all normal.

Suppressive petites could exert their influence over normal mitochondria in one of two ways. The suppressive mitochondria might simply out-compete the normal mitochondria and take over; they might simply reproduce faster within a cell. Alternatively, crossing over between the DNA of the suppressive petite and the wild-type might affect the normal DNA if the suppressive petite's DNA were severely damaged. Presumably, recombination in mitochondrial DNAs occurs when two or more mitochondria fuse, bringing the two different sets of DNA in contact within the same organelle. Recombination would presumably take place by normal crossover mechanisms.

If large portions of the DNA from the suppressive mitochondria were missing or altered, recombination with the normal mitochondria's DNA might exchange some of this damaged DNA. Several experiments have crossed a suppressive petite and a wild-type, each with mitochondrial DNA of known buoyant density. The DNAs of the offspring colonies, which were petites, were of various buoyant densities. For example, when a normal strain with mitochondrial DNA with a buoyant density of 1.684 g/cm^3 was crossed with a suppressive petite with a buoyant density of 1.677 g/cm^3, the offspring colonies' mitochondrial DNA had buoyant densities of 1.671, 1.674, and 1.683 g/cm^3. Such information supports the notion that the suppressive character takes over a colony by way of recombination.

Human Mitochondrial Inheritance

In human beings, certain diseases trace their dysfunction to mitochondrial pathologies. The first such disease, Luft disease, characterized by excessive sweating and general weakness, was reported in 1962. In 1988, Douglas Wallace and his colleagues showed that *Leber optic atrophy* is a cytoplasmically inherited disease. This disease causes blindness, with a median age of onset of twenty to twenty-four years. The onset age and phenotype are variable, depending on the degree of heteroplasmy in the in-

dividual. Apparently, defects in mitochondria are not tolerable in the optic nerve, which demands a great deal of energy. The disease also does some damage to the heart. Pedigrees showed that Leber optic atrophy is transmitted only maternally. Sequencing of mitochondrial DNAs in affected families pinned down the disease to a point mutation, a change in nucleotide 11,778, which is in the gene for NADH dehydrogenase subunit 4 (see fig. 17.4). A guanine is changed to an adenine at codon 340, which converts an arginine to a histidine. This is the first human disease traced to a specific mitochondrial DNA mutation. Since 1962, over one hundred diseases, including some of the general symptoms of aging and cancer, have been attributed to mitochondrial pathology.

Antibiotic Influences

Since the machinery of mitochondrial protein synthesis is prokaryotic in nature, antibiotics such as chloramphenicol and erythromycin can inhibit it. These antibiotics elicit a petite-type growth response in yeast. Antibiotic-resistant strains can be obtained by growing yeast on the antibiotic; only resistant mutants will grow. The resistance appears to be inherited in the mitochondrial, not the cellular, DNA. A mitochondrial inheritance pattern results, with crosses between a resistant and a sensitive (wild-type) yeast, as shown in figure 17.7. The resulting diploid colonies segregate both resistant and sensitive cells. Although not expected on the basis of a chromosomal gene, the random sorting of mitochondria through cell division could result in a wild-type cell containing only sensitive mitochondria. Since some yeast have only one to ten mitochondria per cell, this random assortment of sensitive mitochondria can be expected to occur at a relatively high rate.

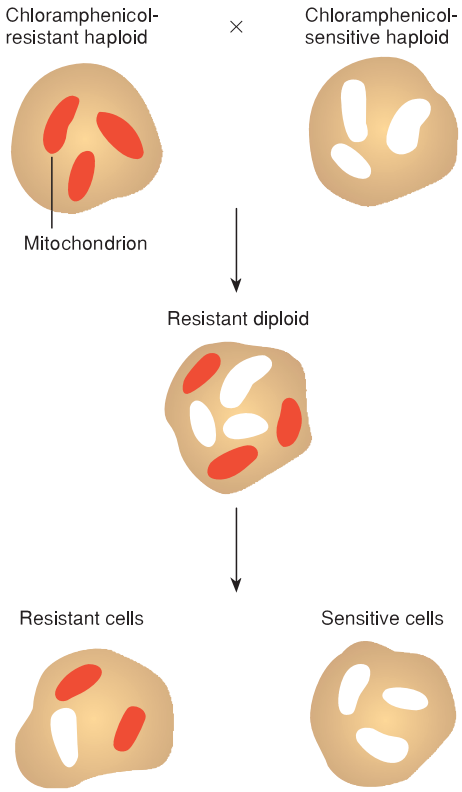


Figure 17.7 Inheritance of antibiotic (chloramphenicol) resistance in yeast. Resistant and sensitive cells are produced by a diploid cell that resulted from a cross of resistant and sensitive haploids. The segregation is not in a simple Mendelian ratio, but depends on the random assortment of mitochondria. Sensitive cells have no resistant mitochondria. Resistant cells have resistant mitochondria.

Chloroplasts

The **chloroplast** is the chlorophyll-containing organelle that carries out photosynthesis and starch-grain formation in plants (fig. 17.8). Chloroplasts are referred to as **plastids** before chlorophyll develops. However, when grown in the dark (and under some other circumstances), plastids do not develop into chloroplasts, but remain reduced in size and complexity. These undeveloped plastids, referred to as **proplastids,** are each about the size and shape of a mitochondrion.

Like mitochondria, chloroplasts contain DNA and ribosomes, both with prokaryotic affinities. The DNA of chloroplasts (cpDNA) is a circle that ranges in size from 85 kilobases (kb) in the green alga *Codium* to as large as 2,000 kilobases in the green alga *Acetabularia.* Thus, chloroplast DNA is minimally about five times the size of an animal mitochondrial DNA. The chloroplast DNA, like mitochondrial DNA, controls the production of transfer RNAs, ribosomal RNAs, and some of the proteins found within the organelle. From the more than nineteen chloroplast DNAs that have been sequenced, there seem to be about one hundred genes in the chloroplast genome. About thirty code for the subunits of the five photosynthetic protein complexes: photosystem I, photosystem II, ribulose bisphosphate carboxylase-oxygenase, cytochrome *b6-f* complex, and ATP synthase. About sixty genes code for the protein synthesis apparatus of the chloroplast. Scientists believe that the chloroplast evolved from symbiotic cyanobacteria (blue-green algae), which have many affinities with the chloroplast: The ribosomal RNA of cyanobacteria will hybridize with the DNA of chloroplasts.

The similarities between mitochondria and chloroplasts make it possible to predict the inheritance patterns of chloroplast mutations on the basis of existing

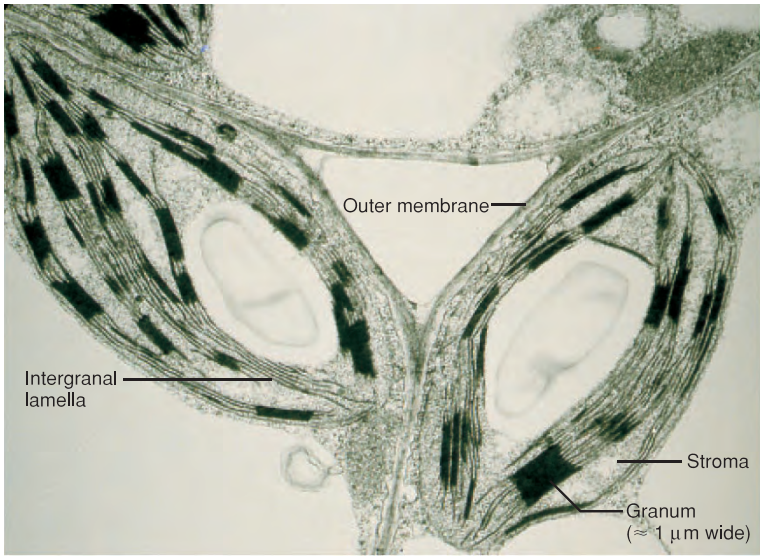


Figure 17.8 Electron micrograph of lettuce chloroplasts. The chloroplast consists of an outer membrane, stacks of grana, lamellae, and stroma. Magnification 3,570×. (© Dr. J. Burgess/Science Photo Library/Photo Researchers, Inc.)

knowledge of mitochondrial genetics: We should find both chromosomal and plastid mutants of chloroplast functions. Simple segregation should occur in the chromosomal mutations, and cytoplasmic patterns of inheritance should occur with the chloroplast DNA mutations. Investigation of these inheritance patterns is complicated by the fact that plant cells have both mitochondria and chloroplasts. Since both have prokaryotic affinities, it is sometimes difficult to determine whether a genetic trait is due to a defect in the genetic system of the chloroplast or the mitochondrion. Like mitochondria, chloroplasts generally show homoplasmy and maternal inheritance, although, as in mitochondria, there are exceptions. For example, gymnosperms usually have paternal inheritance of chloroplasts.

Lesions in the photosystems of the chloroplast result in proplastid formation, with a loss of green color. When proplastid formation occurs in a particular tissue of a plant, variegation results. That is, there are both green and white parts, often as stripes. Some interesting genetic studies have focused on the inheritance of variegation, especially in the interaction of chloroplast and chromosomal genes.

Zea mays

M. Rhoades worked on the variegation in corn (*Zea mays*) controlled by the *iojap* chromosomal locus, which, when homozygous, prevents proplastids from developing into chloroplasts and thus results in variegation. The *iojap*-affected plastids do not contain ribosomes or ribosomal RNA; they therefore lack protein synthesis.

Marcus M. Rhoades (1903–1991). (Courtesy of Indiana University Office of Communications and Marketing.)

The interaction of chromosomal and extrachromosomal inheritance is shown in the reciprocal crosses depicted in figure 17.9. One cross produces results exactly as would be predicted on the basis of simple Mendelian inheritance, with the homozygous recessive genotype (*ijij*) inducing variegation. When the reciprocal cross is carried out, blotch variegation is seen in both the F_1 and F_2 that carry the dominant *Ij* allele.

This inheritance pattern is caused by the fact that the pollen grain in corn does not carry any chloroplasts, whereas the ovule does. Thus, the first cross in figure 17.9 deals with the passage of normal chloroplasts only into the F_2 generation. In the F_2, the *ijij* genotype then induces variegation. The chloroplasts of the pollen parent are unimportant because they do not enter the F_1. In the reciprocal cross, however, because the stigma parent is variegated, the F_1 is heterozygous but carries proplastids from the ovule that remain proplastids even under the dominant normal (*Ij*) allele. Therefore, regions of colorless cells produce white spots (blotchy variegation). Once the *ij* allele induces chloroplasts to become pro-

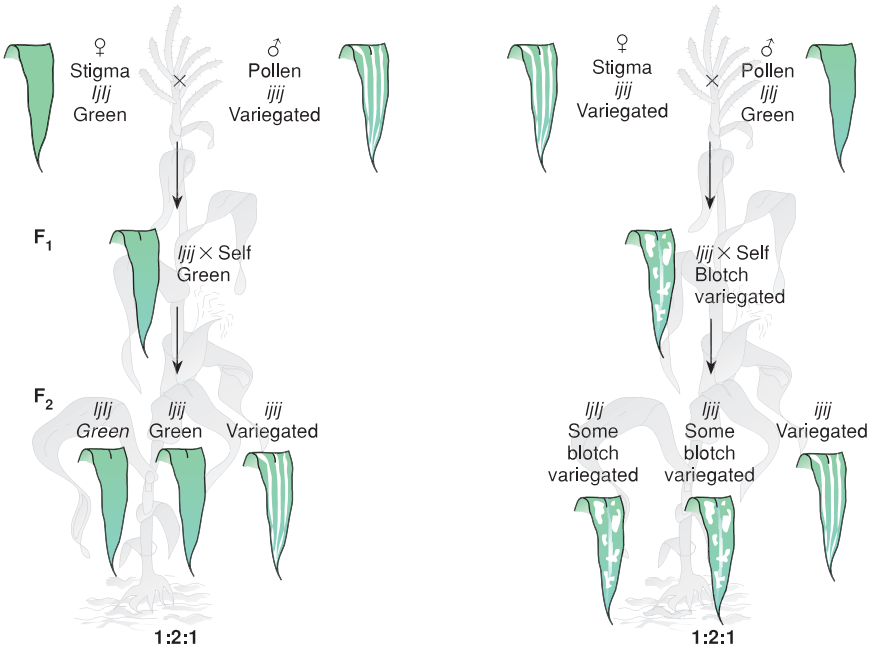


Figure 17.9 Reciprocal crosses involving the chromosomal gene *iojap* in corn. The homozygous recessive condition (*ijij*) induces variegation (representative corn leaves are shown). (Blotch variegation consists of irregularly shaped *white* areas rather than striping.) However, plants with the dominant allele (*Ijlj, Ijij*) can still be variegated if their mothers were variegated, since mothers pass on their chloroplasts to their offspring; males (pollen parents) do not pass on their chloroplasts. *Iojap* homozygotes induce variegation. The defective chloroplasts are then inherited in a cytoplasmic fashion.

plastids, they do not revert to normal type even under the *Ij* allele. Thus, we see the interaction of a chromosomal gene and the chloroplast itself, which "inherits" a changed condition.

There is some evidence that *iojap* may suppress the chloroplast rather than cause a mutation of some function. There are loci in corn and in other species that can induce back mutation in the chloroplasts. Removal of suppression rather than an actual reversion is more likely to occur because the reversion rate is too high to be due to simple back mutation.

Four-O'clocks

The first work with corn variegation was done by Carl Correns, one of Mendel's rediscoverers. Correns also found maternal inheritance of variegation in the four-o'clock plant, *Mirabilis jalapa.* He could predict color and variegation of offspring solely on the basis of the region of the plant on which the stigma parent was located. A flower from a white sector, when pollinated by any pollen, would produce white plants; a flower on a green sector or a variegated sector produced green or variegated plants, respectively, when pollinated by pollen from any region of a plant. We thus see the simple maternal nature of the inheritance of the variegation. A chromosomal gene, like *iojap,* induces variegation. Inheritance of this induced variegation follows the "maternal" pattern of chloroplast inheritance.

Chlamydomonas

The single-celled green alga, *Chlamydomonas reinhardi,* has been used in the study of extrachromosomal inheritance for several reasons. First, it has a single, large chloroplast; it can survive by culture technique even when the chloroplast is not functioning; and finally, it shows some interesting non-Mendelian inheritance patterns related to mating type. R. Sager has done extensive work on the inheritance of streptomycin resistance in *Chlamydomonas.*

Streptomycin resistance can be selected for in *Chlamydomonas* in several ways. Normal cells, sensitive to the antibiotic, are killed in its presence. If cells are grown in low levels of the antibiotic (100 g/ml), some cells show resistance to it. When these cells are crossed

Ruth Sager (1918–1997). (Courtesy of Dr. Ruth Sager.)

with the wild-type, the resistance segregates in a 1:1 ratio, indicating that streptomycin resistance is controlled by a chromosomal locus. The same experiment can be repeated using high levels of the antibiotic in the medium (500–1,600 g/ml). Again, resistant colonies grow. If they are crossed with the wild-type, a 1:1 ratio does not ensue.

Chlamydomonas does not have sexes but does have mating types mt^+ and mt^-. Only individuals of opposite type can mate. Mating type is inherited as a single locus with two alleles. When two haploid cells of opposite mating type fuse, they form a diploid zygote, which then undergoes meiosis to produce four haploid cells, two of mt^+ and two of mt^-. The high-level resistance always segregates with the mt^+ parent (fig. 17.10). It is as if the mt^+ parent were contributing the cytoplasm to the zygote in a manner similar to maternal plastid inheritance in plants. The mt^- parent acts like a pollen parent by making a chromosomal contribution but not a cytoplasmic one.

The mechanism of the extrachromosomal inheritance pattern of *Chlamydomonas* is the preferential digestion of the DNA of the chloroplast from the mt^- parent. Currently, we believe that streptomycin's target is the chloroplast.

More recent work has shown that the mt^+ inheritance is only 99.98% effective—that is, 0.02% of the offspring in crosses of the type shown in figure 17.10 have the streptomycin phenotype of the mt^- parent. Thus, we have the possibility of studying recombination in chloroplast genes. Although most of the evidence is only indirect and plagued by the previously mentioned problems of separating chloroplast and mitochondrial effects, some initial mapping studies have been done.

Infective Particles

Paramecium

Tracy Sonneborn discovered the killer trait in *Paramecium.* Before analyzing this trait, we must digress a moment to look at the life cycle of *Paramecium,* a ciliated

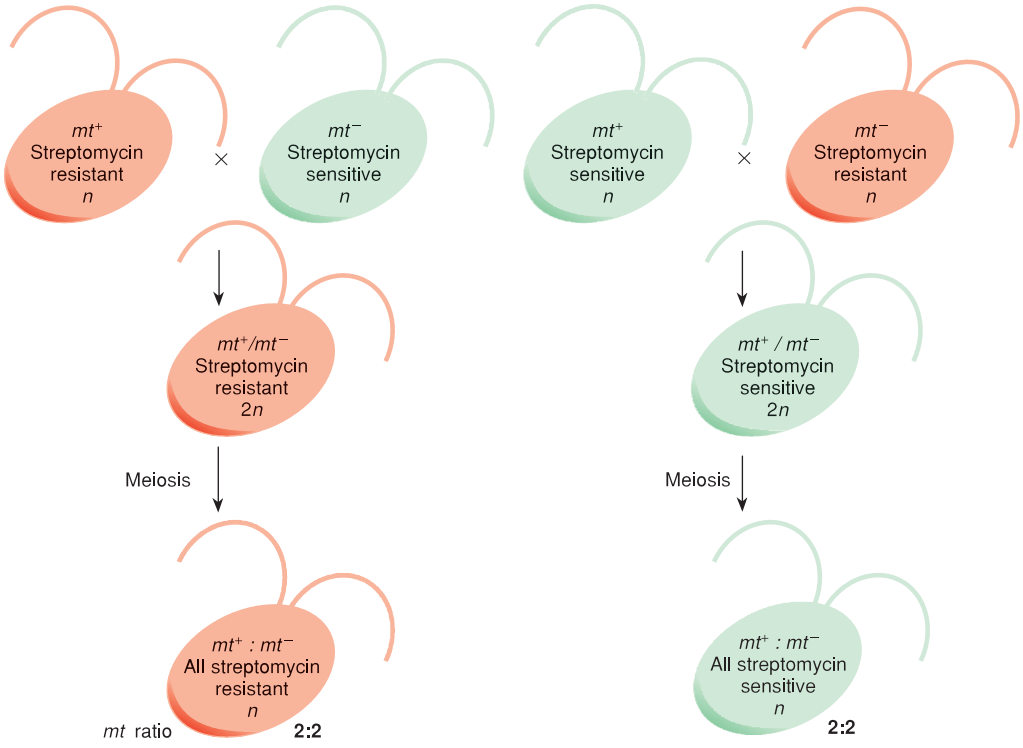


Figure 17.10 Inheritance pattern of streptomycin resistance in *Chlamydomonas* is dependent on the genotype of the mt^+ parent. (The *n* and *2n* refer to the ploidy of the cells.) If the mt^+ parent is streptomycin resistant *(red),* then the diploid heterozygote, as well as the meiotic products, will be streptomycin resistant. If, however, the mt^+ parent is streptomycin sensitive (*green),* the diploid heterozygote, as well as the meiotic products, will be streptomycin sensitive.

Tracy M. Sonneborn (1905–1981). (Courtesy: Indiana University Archives.)

protozoan familiar to most biologists. Ciliates have two types of nuclei: macronuclei and micronuclei. In *Paramecium,* there are two micronuclei, which are primarily reproductive nuclei, and one macronucleus, which is a polyploid nucleus concerned with the vegetative functions of the cell. During cell division, termed **binary fission,** the micronuclei divide by mitosis and the macronucleus constricts and is pulled in half.

Paramecium undergoes two types of nuclear rearrangements, during conjugation and **autogamy.** In conjugation, individuals of two mating types come together and form a connecting bridge. The nuclear events are shown in figure 17.11. Briefly, the macronucleus of each cell disintegrates while the micronuclei undergo meiosis. Of the resulting eight micronuclei per cell, seven disintegrate and one remains; this one undergoes mitosis to form two haploid nuclei per cell. A reciprocal exchange of nuclei across the bridge then occurs. Each cell now has two haploid nuclei, one original and one migrant. The two nuclei fuse to form a diploid nucleus. The diploid nuclei in the two conjugating cells are genetically identical because of the reciprocity of the process. These nuclei then undergo two mitoses each to form four diploid nuclei per cell. Two nuclei become macronuclei, which separate at the next cell division; two remain as micronuclei that divide by mitosis at the next cell division. The two cells that separate are known as **exconjugants.** Depending primarily on the amount of time conjugating cells remain united, an exchange of cytoplasm may occur along with the exchange of nuclei.

In the second type of process, autogamy, only one *Paramecium* is involved (fig. 17.12). The nuclear events are the same as in conjugation except that, at the point where a reciprocal exchange of nuclei would take place, the two haploid nuclei within the cell fuse. All cells after autogamy are homozygous.

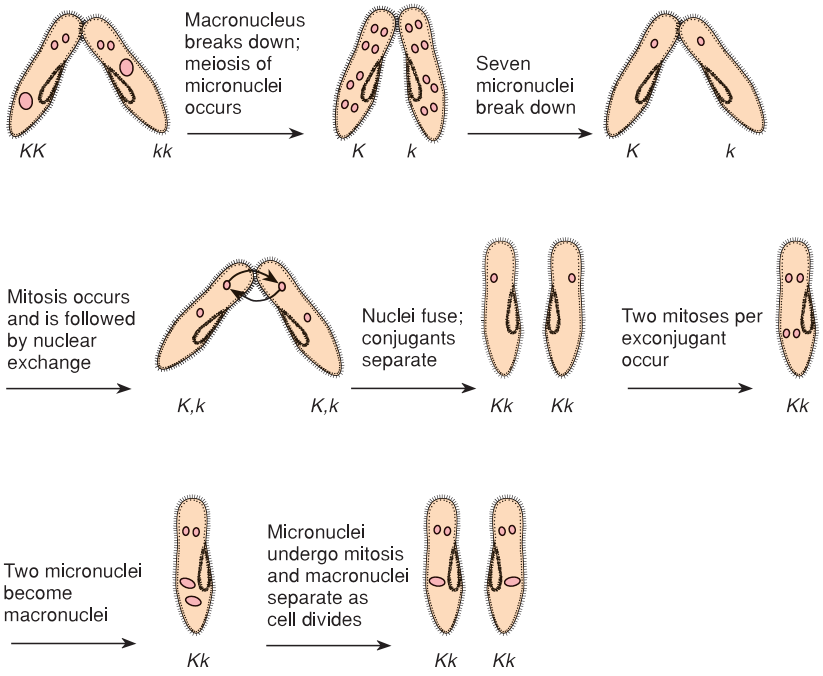


Figure 17.11 Conjugation in *Paramecium.* The letters *K* and *k* represent alleles of a gene in each micronucleus. When a *KK* and a *kk* individual conjugate, the exconjugants have the identical *Kk* genotype.

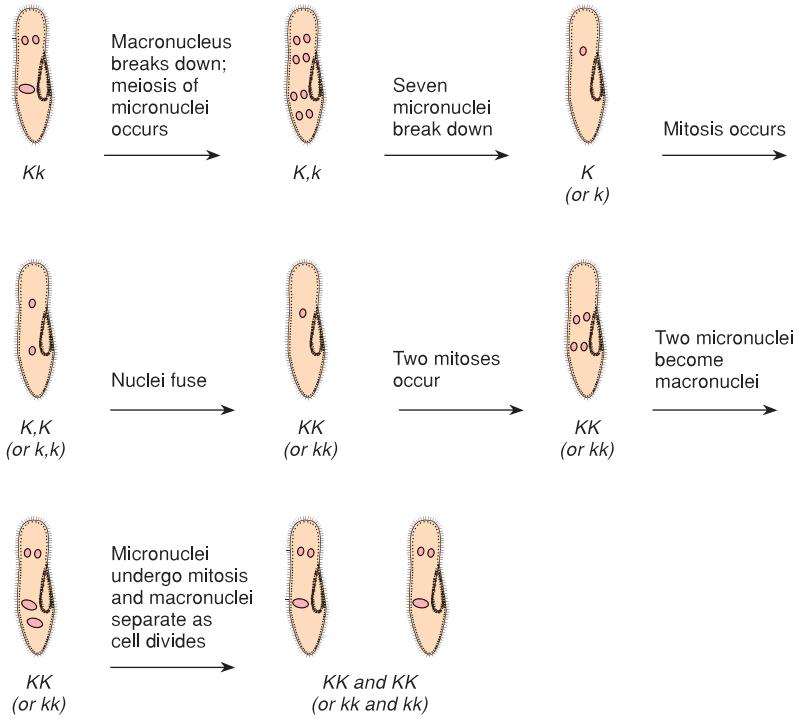


Figure 17.12 Autogamy in *Paramecium.* The letters *K* and *k* represent alleles of a gene in each micronucleus. If a heterozygote undergoes autogamy, it becomes homozygous for one of the alleles (*KK* or *kk*).

Killer Paramecium *and Kappa Particles*

Sonneborn and his colleagues found that when certain stocks of *Paramecium* were mixed together, one stock had the ability to cause the individuals of the other stock to die. Those individuals causing death were called "killers" and those dying were referred to as "sensitives." During conjugation, the sensitives are temporarily resistant to the killers. If cytoplasm is not exchanged during the conjugation, the exconjugants retain their original phenotypes so that killers stay killers and sensitives stay sensitives. When an exchange of cytoplasm occurs between sensitive and killer cells, both exconjugants are killers. The transfer of some cytoplasmic particle seems to be implied. Indeed, Sonneborn observed such particles in the cytoplasm of killers and called them **kappa particles** (fig. 17.13).

Although the occurrence of killer *Paramecium* does not appear to involve chromosomal genes, Sonneborn reported one case in which exconjugant killer paramecia of hybrid origin underwent autogamy. He found that half of the resulting cells had no kappa particles and had become sensitives. He concluded that a gene is required for the presence of kappa particles, which has subsequently been verified by numerous crosses. Figure 17.14 illustrates the sequence of genetic events that would produce a heterozygous killer *Paramecium* that, upon autogamy, would have a 50% chance of becoming sensitive.

Although not yet cultured outside of a *Paramecium,* kappa is presumably a bacterium because it has many bacterial attributes including size, cell wall, presence of DNA, and presence of certain prokaryotic reactions (fig. 17.15). J. Preer and his colleagues, who studied kappa itself, named it *Caedobacter taeniospiralis.* Kappa occurs in at least two forms. The *N* form, the infective form that passes from one *Paramecium* to another, does not confer killer specificity on the host cell. The *N* form is attacked by bacteriophages that induce formation of inclusions, called *R* bodies, inside the kappa particle and thus convert it to the *B* form. These *R* bodies are visible under the light microscope as refractile bodies (fig. 17.15).

In the *B* form, kappa can no longer replicate; it is often lysed within the cell. It confers killer specificity on the host cell, however. The sensitives are killed by the toxin **paramecin,** which is released by the killer *Paramecium* into the environment. Precisely what steps are involved in its formation are not known, although it is

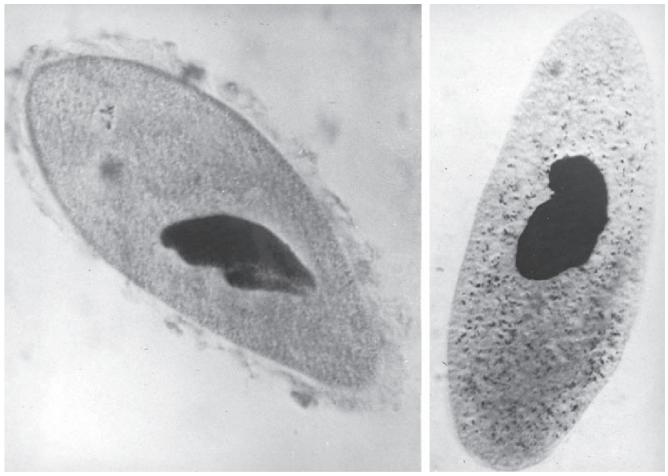


Figure 17.13 (*a*) Normal (sensitive) *Paramecium.* (*b*) Kappa-containing (killer) *Paramecium.* A *Paramecium* is about 200 μm long. (Source: T. M. Sonneborn, figure 29.3, p. 373 in I. H. Herskowitz, *Genetics,* 2nd ed. [Boston: Little, Brown, 1965]. Reproduced by permission.)

plain that the virus plays an integral role. Whether the viral DNA or the kappa DNA codes the toxin is also not known at present.

Mate-Killer Infection and Mu Particles

Kappa is not the only infective agent known in *Paramecium.* Another agent is the **mate-killer** infection. Here again, killer cells have visible, bacterialike particles, called **mu particles,** in the cytoplasm. Preer and his colleagues have named them *Caedobacter conjugatus.* Mate-killers do not release a toxin into the environment, but instead kill their mates during conjugation. One of two unlinked dominant genes, M_1 and M_2, is required for the presence of mu particles. An interesting phenomenon occurs when a mate-killer becomes homozygous m_1m_1 m_2m_2 by autogamy. Although the offspring eventually lose their mu particles, virtually no loss of particles occurs until about the eighth generation, when some offspring lose all their mu. Up to this generation, all the cells maintain a full complement of mu. In the fifteenth generation, only about 7% of the cells still have mu particles.

This phenomenon is explained as the diluting out not of the mu themselves, but of a factor called **metagon,** which is necessary for the maintenance of mu in the cell. Once the cell becomes homozygous recessive, no further metagon production occurs. The verification that metagon is subsequently diluted out is evident in fifteenth-generation cells that still have their mu. We would expect that after fission, one daughter cell would have a metagon and the other would not. What we expect, in fact, happens. The rate of dilution is consistent with an original number of about one thousand metagons per cell. The metagon appears to be

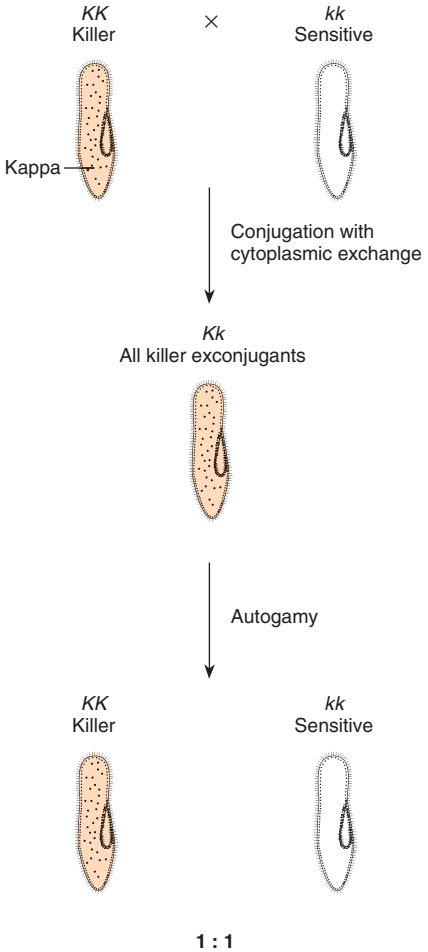


Figure 17.14 Autogamy in a heterozygous (*Kk*) killer *Paramecium* (formed by conjugation, with cytoplasmic exchange, of a *KK* killer and a *kk* sensitive cell). Upon autogamy, the heterozygote has a 50% chance of becoming a homozygous (*KK*) killer or a homozygous (*kk*) sensitive cell that loses its kappa particles.

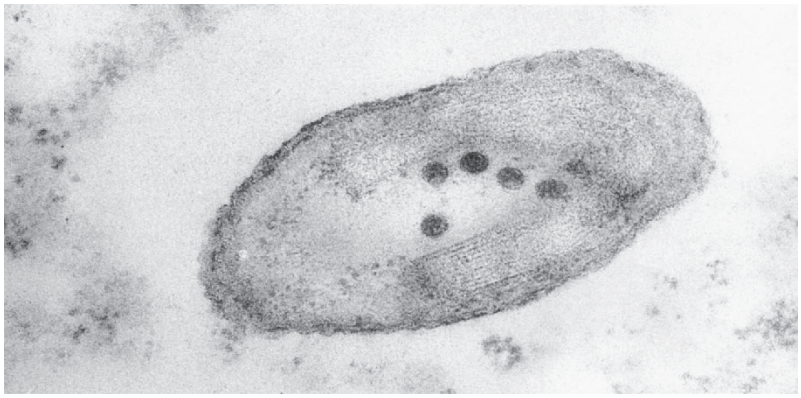


Figure 17.15 Electron micrograph of a sectioned kappa particle (*Caedobacter taeniospiralis*). Phage particles appear as dark inclusions. The plane of the section cuts through a rolled-up *R* body. Magnification 61,200×. (Reproduced by permission of J. R. Preer, Jr.)

messenger RNA because it is destroyed by RNase. Its protein product is presently unknown.

We thus see several instances of infective particles that interact with the *Paramecium* genome to produce interesting phenotypic results. Similar interactions are known in other organisms—for example, the killer trait in yeast.

Drosophila

Several infective particles mimic patterns of inheritance in insects. In *Drosophila,* we find forms of the **sex-ratio phenotype** in which females produce mostly, if not exclusively, daughters. One form is inherited as a chromosomal gene; another form, however, is not chromosomal. In the nonchromosomal form, females usually produce a few sons. These sons do not pass on the sex-ratio trait, but the daughters of sex-ratio females do. Because the trait persisted even after all the chromosomes had been substituted out of the stock by appropriate crosses, it was proven to be extrachromosomal.

In addition, about half the eggs of a sex-ratio female fail to develop. Cytoplasm can be withdrawn from the undeveloped eggs and used to infect other females. The trait, then, is caused by some cytoplasmic factor that could infect other females and is not passed on by sperm. Detailed cytological examination of the cytoplasm of sex-ratio females has revealed a spirochete (fig. 17.16) that has been isolated and used to infect other female *Drosophila* with the sex-ratio trait; it is, therefore, the causal agent of this phenotype.

Figure 17.16 Electron micrograph of the spirochete associated with the extrachromosomal sex-ratio trait in *Drosophila.* Magnification 22,700×. (K. Oishi and D. F. Poulson, "A virus associated with SR-spirochetes of *Drosophila nebulosa,*" *Proceedings of The National Academy of Sciences, USA,* 67 [1970]:1565–72. Reproduced by permission of the authors.)

Prokaryotic Plasmids

In chapters 7 and 13, we discussed the role of plasmids in the study of prokaryotic genetics and in recombinant DNA work. They are mentioned again here because they represent extrachromosomal genetic systems, primarily in prokaryotes. The autonomous segments of DNA known as plasmids are, for the most part, known from bacteria, in which they occur as circles of DNA within the host cell (noncircular DNA is soon degraded). When plasmids become integrated into the chromosomes, they become indistinguishable from chromosomal material.

R *and* Col Plasmids

In addition to the F factor found frequently in bacteria, a variety of other plasmids occur, including the R and Col plasmids. The **R plasmids** carry genes for resistance to various antibiotics, and the **Col plasmids** have genes that are responsible for producing proteins called *colicins,* which are toxic to strains of *E. coli* (fig. 17.17). Plasmids containing genes for Col-like toxins specific for other bacterial species are also known. Col and R plasmids can exist in two states. In one state, the plasmid has

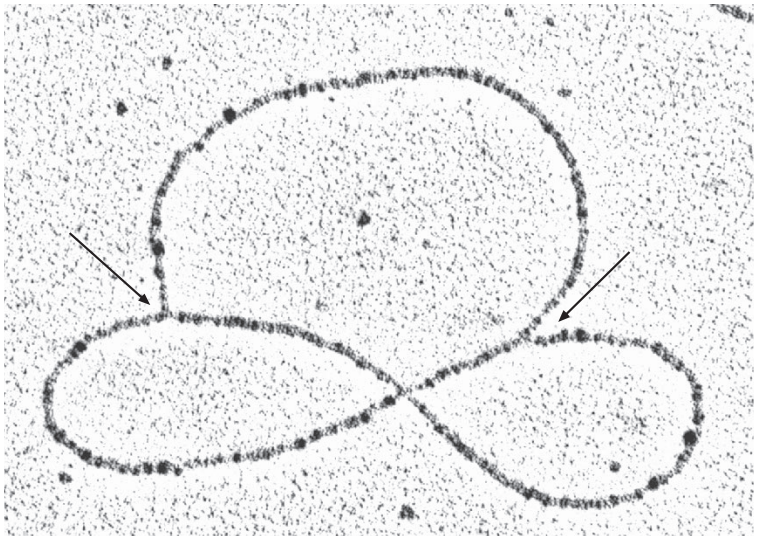


Figure 17.17 Electron micrograph of replication of Col E1 circular plasmid. The *arrows* mark the branch points of the theta structure. Magnification 90,000×. (Source: J. I. Tomizawa, Y. Sakakibara, and T. Kakefuda, "Replication of Colicin E1 plasmid DNA in cell extracts: Origin and direction of replication," *Proceedings of The National Academy of Sciences, USA,* 71 [1974]:2260–64.)

a sequence of genes called the **transfer operon *(tra)***, which makes the plasmids similar to F factors in that they can transfer their genes from one bacterium to the next. In the other state, the plasmids lack this operon and cannot transfer their loci to another cell. Thus, Col and R plasmids are actually made of two parts: the loci for antibiotic resistance or colicin production and the part responsible for infectious transfer. In R plasmids, the infectious transfer part is called the **resistance transfer factor** (RTF).

The occurrence of resistance plasmids was observed in Japan in the late 1950s, when it was discovered that bacteria were simultaneously acquiring resistance to several antibacterial agents. When cultures of *Shigella,* a dysentery-causing bacterium, were exposed to streptomycin, sulfonamide, chloramphenicol, or tetracycline, the bacteria exhibited resistance not only to the one particular agent they were exposed to but to one or more of the others as well. The plasmid responsible for this multiple resistance was named R222.

The Col plasmids contain loci that produce proteins that are toxic, for various reasons, to strains of bacteria not carrying the plasmids. Colicins attack sensitive bacterial cells at bacterial surface receptors. They have been classified into twenty or more categories according to the types of receptors they attack. Some colicins may enter the cell directly, but others do not. For example, colicin K appears to kill sensitive cells by inhibiting DNA, RNA, and protein synthesis, although not directly entering the cell. Colicin E3, however, acts as an intracellular ribonuclease that cleaves off about fifty nucleotides from the 3′ end of the 16S ribosomal RNA within the ribosome. The cleavage inactivates the sensitive cell's ribosomes and is, of course, lethal.

Since many R plasmids, Col plasmids, and F factors, as well as host chromosomes, have insertion sequences (chapter 14), a good deal of exchange occurs among the plasmids, and many are able to integrate into the host chromosome. Although their mobility makes it easier to map and study plasmids, it also poses a human health problem. Resistance to various antibacterial agents is easily transferred among enterobacteria worldwide. This can even occur outside of host organisms (people) where pollution or sewage is found. In addition, resistance found in relatively harmless enterobacteria, such as *E. coli,* can easily pass to more pathogenic bacteria, such as *Shigella* and *Salmonella.* Since we are selecting for resistance every time we use antibacterial drugs, we should not use these drugs indiscriminately. For some time, health workers have been concerned about excessive medical use of antibacterial drugs as well as about the large quantities of antibiotics used in animal feed.

Uncovering Plasmids

How do we know when the phenotype is controlled by a plasmid rather than by the chromosomal genes of a bacterium? Plasmids can be seen with an electron microscope or by density-gradient centrifugation of the cell's DNA. But several less direct lines of evidence also supply the answer. To begin with, multiple aspects of the phenotype (e.g., resistance to several antibacterial agents) change simultaneously, as with plasmid R222. Another clue is that the phenotypic change is infectious: Japanese workers found that with R222, resistant cells converted nonresistant cells. As B. Lewin stated, "Resistance is infectious."

Several other clues point to the presence of a plasmid. In linkage studies, using transduction for example,

plasmid loci show no linkage to host loci; plasmids themselves can be mapped because their loci are linked to each other. Since the plasmid DNA replicates at its own speed, it can miss being incorporated into a daughter cell. Thus, many spontaneous losses of the plasmid occur. And finally, certain treatments—with acridine dyes, for example—have little effect on the replication of the host chromosome, but selectively prevent the plasmid from replicating; thus the plasmid can be eliminated from the cell population. The existence of plasmids in a bacterial population can, therefore, be verified with morphological, physiological, and analytical evidence.

IMPRINTING

Although sex linkage alters inheritance patterns, we do not expect different inheritance patterns, dependent on the parent of origin, from genes located on autosomal chromosomes. That is, the genotype of an offspring should be predicted by its alleles regardless of which parent donated which allele. That understanding has now been shown to be incorrect for a group of genes whose phenotypic effects are determined by the parent that donated a particular allele. This phenomenon is called *imprinting* (or *molecular imprinting* or *parental imprinting*). It falls under the general classification of an **epigenetic effect**, a term that has come to mean an effect due to an environmentally induced change in the genetic material but not causing a change in base pairs. It is a phenomenon of differential expression of the alleles at a locus depending on which parent the gene originated with.

A striking example of imprinting in human beings involves two medical syndromes, both resulting in mental retardation. In Prader-Willi syndrome, affected persons are extremely obese; in Angelman syndrome, those affected are thin and sometimes referred to as "happy puppets," because they exhibit a happy facial expression and erratic, jerky movements. It turns out that both syndromes are associated with deletions in the long arm of chromosome 15, in bands 15q11–q13. The effect is seen in an individual arising from a gamete missing a 15q11–q13 region. If the remaining region is of paternal origin, due to a deletion of the maternal gene, the offspring will have Angelman syndrome; if the remaining region is of maternal origin, the offspring will have Prader-Willi syndrome. This unusual situation indicates that the phenotype is dependent on the parent from which the region comes. Recently, this region of chromosome 15 has come under intense scrutiny. In males, from five to seven genes are expressed from this area, and in females, one gene has been identified as the cause of Angelman syndrome, *UBE3A* (E3 ubiquitin protein ligase). It has been hypothesized that there is an **imprinting center (IC),** a region responsible for the control of imprinting. The imprinting mark is almost certainly DNA methylation, which has the property of turning off gene transcription. Stretches of CG repeats (called **CpG islands,** in which CpG indicates sequential bases on the same strand of DNA rather than a C-G base pair) have been found in these imprinting centers. The imprinting center would be the site of the erasure of past imprinting and the initiation of new imprinting during gametogenesis. Over twenty genes exhibit imprinting, and the epigenetic phenomenon also appears in proteins, with differential acetylation of proteins as the imprinting mark.

The question arises as to how imprinting evolved; that is, what evolutionary advantages come from silencing an allele from one of the parents? Although we don't really know at this point, several hypotheses have been suggested, including competition among maternal and paternal alleles for expression (see chapter 21). For example, the *Igf-2* gene (insulin-like growth factor) places demands on pregnant females to produce larger fetuses. This is advantageous to the father (assuming that the female will have offspring from several fathers), but not the mother. So, the mother's gene is usually methylated and therefore inactive. It is as if the genes are in competition with each other, with the father's gene promoting the formation of a large fetus and the mother's gene promoting the formation of a smaller fetus. Currently, the phenomenon of imprinting is under active study.

SUMMARY

STUDY OBJECTIVE 1: To analyze the inheritance patterns of maternal effects 509–510

Patterns of non-Mendelian inheritance fall into two categories: maternal effects and cytoplasmic inheritance. Maternal effects are illustrated by snail-shell coiling. The direction of coiling is determined by the genotype of the maternal parent, with dextral coiling dominant to sinistral coiling.

STUDY OBJECTIVE 2: To analyze the patterns of cytoplasmic inheritance 511–524

Cytoplasmic inheritance is usually seen in organelles, sym-

bionts, or parasites that have their own genetic material. Chloroplasts and mitochondria have relatively small, circular chromosomes with prokaryotic affinities. An interaction exists between organelles and nuclei; the organelles do not encode all their own proteins and enzymes. Mitochondrial defects can be inherited through nuclear genes or through the mitochondrion itself. A similar pattern is seen in chloroplasts. The processes of cytoplasmic inheritance are exemplified by symbiotic bacteria in *Paramecium.*

Plasmids are autonomous segments of DNA. In prokaryotes, R and Col plasmids, as well as the F factor, have been well studied. Plasmids usually carry an operon for transfer and insertion sequences for attachment to cell chromosomes and to each other. Hence, they represent highly mobile segments of genetic material.

STUDY OBJECTIVE 3: To analyze the patterns of imprinting 524

Imprinting is a phenomenon of gene activity affected by the parent of origin. Due to a pattern of gene methylation that differs in male and female parents, a gene may show differential activity depending on the parent from which it came. More than twenty genes exhibiting this epigenetic phenomenon are known.

SOLVED PROBLEMS

PROBLEM 1: What possible phenotypes and genotypes could the female parent of a sinistrally coiled snail have?

Answer: If a snail is sinistrally coiled, its mother must have had the *dd* genotype, since sinistrality is recessive. If the female parent is a recessive homozygote, its mother must have contributed a recessive *d* allele. Therefore *its* mother (the grandmother) could have had either a *Dd* or *dd* genotype. Its daughter could therefore be either dextrally or sinistrally coiled (respectively). Thus, to answer the question, a sinistrally coiled snail could have had a mother that was either dextrally or sinistrally coiled, but only of the *dd* genotype.

PROBLEM 2: You have just noticed a petite yeast colony growing in a petri plate under aerobic conditions. What type of petite is it?

Answer: The simplest way to determine the nature of the lesion resulting in the petite phenotype is to make a cross of the petite strain with a wild-type strain. After meiosis, isolate the four products (spores) and allow them to grow separately under normal, aerobic conditions. If the ratio of petite to wild-type is 1:1, the mutation is of a nuclear gene. If progeny are wild-type, the mutation is in the mitochondrial genome and is of the neutral type. If progeny are mostly petites, the mutation is also in the mitochondrial genome, but it is of the suppressive type.

PROBLEM 3: Killer *Paramecium* with the genotype *KK* are mated with *kk* cells under a situation that allows cytoplasmic exchange. If the exconjugants undergo autogamy, what types of progeny would you expect?

Answer: Both exconjugants will be *Kk,* and since cytoplasmic exchange occurred, both cytoplasms will contain kappa. Autogamy will produce either *KK* or *kk* cells. Since at least one *K* gene is needed for the maintenance of kappa, the *kk* cells eventually lose the kappas and become sensitive. Thus, we expect 1/2 sensitive:1/2 killers.

EXERCISES AND PROBLEMS*

DETERMINING NON-MENDELIAN INHERITANCE

1. J. Christian and C. Lemunyan have shown that mice raised under crowded conditions produce two generations with reduced growth rates. What sort of genetic control might exist, and how could this control be demonstrated?
2. Describe the types of evidence that could be gathered to determine whether a trait in *E. coli* is controlled by chromosomal or plasmid genes. (*See also* CYTOPLASMIC INHERITANCE)
3. The maroon-like (*ma-l*) locus in *Drosophila* is inherited in an X-linked recessive fashion. If you cross a heterozygous female with a maroon-like male, all the progeny are wild-type. If the female progeny from this cross are mated again with maroon-like males, half of the females produce all maroon-like progeny, and the other half produce all wild-type progeny. Explain these results. (*See also* MATERNAL EFFECTS)

*Answers to selected exercises and problems are on page A-20.

MATERNAL EFFECTS

4. Snail coiling is called a maternal trait. Is it possible that it is caused by an allele at a sex-linked locus?

5. How would you rule out a viral origin for snail-shell coiling?

6. Give the genotypes involved when a sinistral female snail produces dextral offspring. What genotypes could the male parent of the sinistral female have?

7. A dextral snail is self-fertilized and produces only sinistral progeny. What is the probable genotype of this snail and its parents?

8. In corn, male sterility is controlled by a maternal cytoplasmic element. A dominant nuclear gene, Restorer (*Rf*), restores fertility to male sterile lines. If pollen from a homozygous *RfRf* plant is used to pollinate a male sterile plant, what genotypes and phenotypes would you expect in the progeny?

CYTOPLASMIC INHERITANCE

9. What evidence indicates that it is not absolutely essential, in an evolutionary sense, for mitochondria to have genes for specific components of oxidative phosphorylation?

10. How would you determine that a segregative petite mutant in yeast is controlled by a chromosomal gene?

11. What results would you obtain by making all possible pairwise crosses of the three types of yeast petites?

12. An ornamental spider plant has green and white striped leaves. How can you determine whether cytoplasmic inheritance is responsible for the striping and whether there is interaction with an *iojap*-type chromosomal gene?

13. In *Chlamydomonas,* 0.02% of the meiotic products are of the mt^- parental type. How can you use this information in mapping? (Use streptomycin sensitivity, str^s, and resistance, str^r, as an example.)

14. What similarities do mitochondria and plastids share?

15. What evidence is there that mitochondria and chloroplasts originated from prokaryotes?

16. Individuals from killer and nonkiller strains of *Paramecium* are mixed together. Cytoplasmic exchange occurs during conjugation. Approximately 25% of the exconjugants are sensitive, and the remaining 75% are killers. What are the genotypes of the individuals of the two strains, and what ratios of sensitives and killers would result if the various exconjugants underwent autogamy?

17. What genetic tests could you conduct to show that the mate-killer phenotype in *Paramecium* requires a dominant allele at any one of *two* loci?

18. Resistant and sensitive strains of *Drosophila melanogaster* differ in their ability to tolerate CO_2—anesthetization with it kills sensitive flies. What genetic experiments would you perform to determine whether the trait is caused by a virus? How would you rule out chromosomal genes?

19. Suppose you have identified a person who has introns in his or her mitochondrial DNA. What would you deduce about the origin of this DNA?

20. A mutation in the mitochondrial genome in people causes blindness. If reciprocal matings between affected and normal individuals occur in a family pedigree, what types of children would you expect from each cross?

21. When chloroplast DNA from *Chlamydomonas* is digested with a particular restriction enzyme and then hybridized with a particular probe, two bands are detected. Some strains (type 1) yield bands of 1.5 and 3.7 kilobases; other strains (type 2) yield bands of 2.5 and 6.0 kilobases. For the following crosses, predict the progeny:
a. mt^+, strain 1 × mt^-, strain 2
b. mt^+, strain 2 × mt^-, strain 1

22. What type of asci do you expect if you cross a yeast strain carrying an antibiotic resistance gene in its mitochondria with a strain that has normal (sensitive) mitochondria?

23. In *Paramecium,* the maintenance of kappa particles requires the dominant nuclear gene *K.* A *Kk* killer cell conjugates with a sensitive cell of the same genotype without cytoplasmic exchange. Predict the genotypes and phenotypes that result if each exconjugant then undergoes autogamy.

24. In *Neurospora,* the slow-growing trait *poky* is inherited maternally and is due to an abnormal respiratory protein. A nuclear gene *F* makes *poky* individuals grow faster, even though the protein is still defective. Such strains are called *fast-poky* (*F′* is normal *poky*). *Poky* cytoplasm is not altered by *F* in a zygote, and *F* has no effect on normal cytoplasm. What genotypes and phenotypes do you expect if the maternal parent is *fast-poky* and the paternal parent is normal?

25. In corn, two independent, recessive nuclear genes, *japonica (j)* and *iojap (ij),* produce variegation (green and white striped leaves). Matings between individuals heterozygous for *japonica* always produce 3 green:1 striped individuals regardless of how the cross is performed. The behavior of *iojap* was described in figure 17.9. You have a variegated plant that could be either *jj* or *ijij.* What cross can you make to determine the genotype of this plant, and what results do you expect in the F_1 generation in each case?

26. If *Paramecium* cells heterozygous for both genes involved in the maintenance of the mate-killer trait are forced to undergo autogamy, what phenotypic ratios do you expect?

27. A petite yeast strain is crossed with a wild-type strain. What phenotypic ratio do you expect after meiosis if the petite is
a. nuclear?
b. suppressive?
c. neutral?

CRITICAL THINKING QUESTIONS

1. When a eukaryotic cell divides, cell organelles such as mitochondria and chloroplasts are distributed to the daughter cells. What mechanisms might exist to ensure an even distribution of these organelles?

2. Lamarckian inheritance, the inheritance of acquired characteristics, is generally discounted as a major evolutionary mechanism (chapter 21). (For example, Lamarck suggested that the long neck of the giraffe came about by as giraffes stretched for food, followed by the inheritance of this longer, stretched neck.) Is the progression of the lysogenic state of *E. coli* from one generation to the next an example of Lamarckian inheritance? Why or why not?

Suggested Readings for chapter 17 are on page B-18.