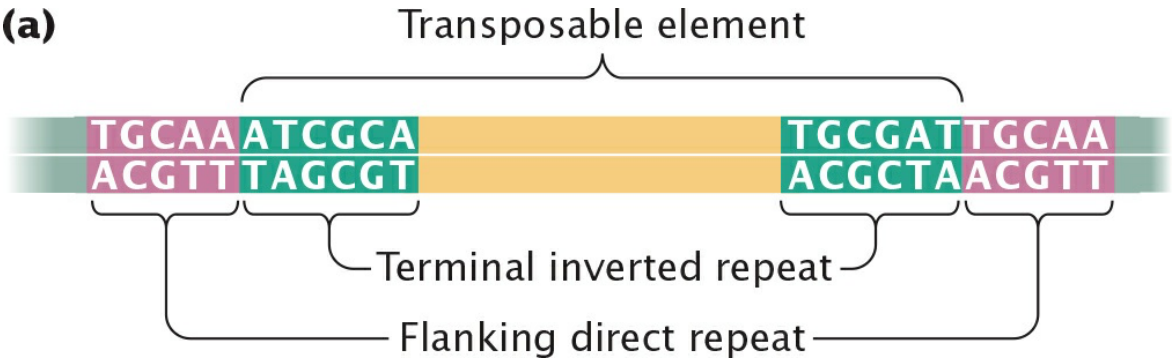
Transposable elements—DNA sequences that can move about in the genome —are often a cause of mutations. These mobile DNA elements have been given a variety of names, including transposons, transposable genetic elements, movable genes, controlling elements, and jumping genes. They are found in the genomes of all organisms and are abundant in many, including our own. Most transposable elements are able to insert themselves at many different locations in the genome, relying on mechanisms that are distinct from homologous recombination. Through their movement (transposition), transposable elements often cause mutations, either by inserting into a gene and disrupting it or by promoting chromosome rearrangements such as deletions, duplications, and inversions

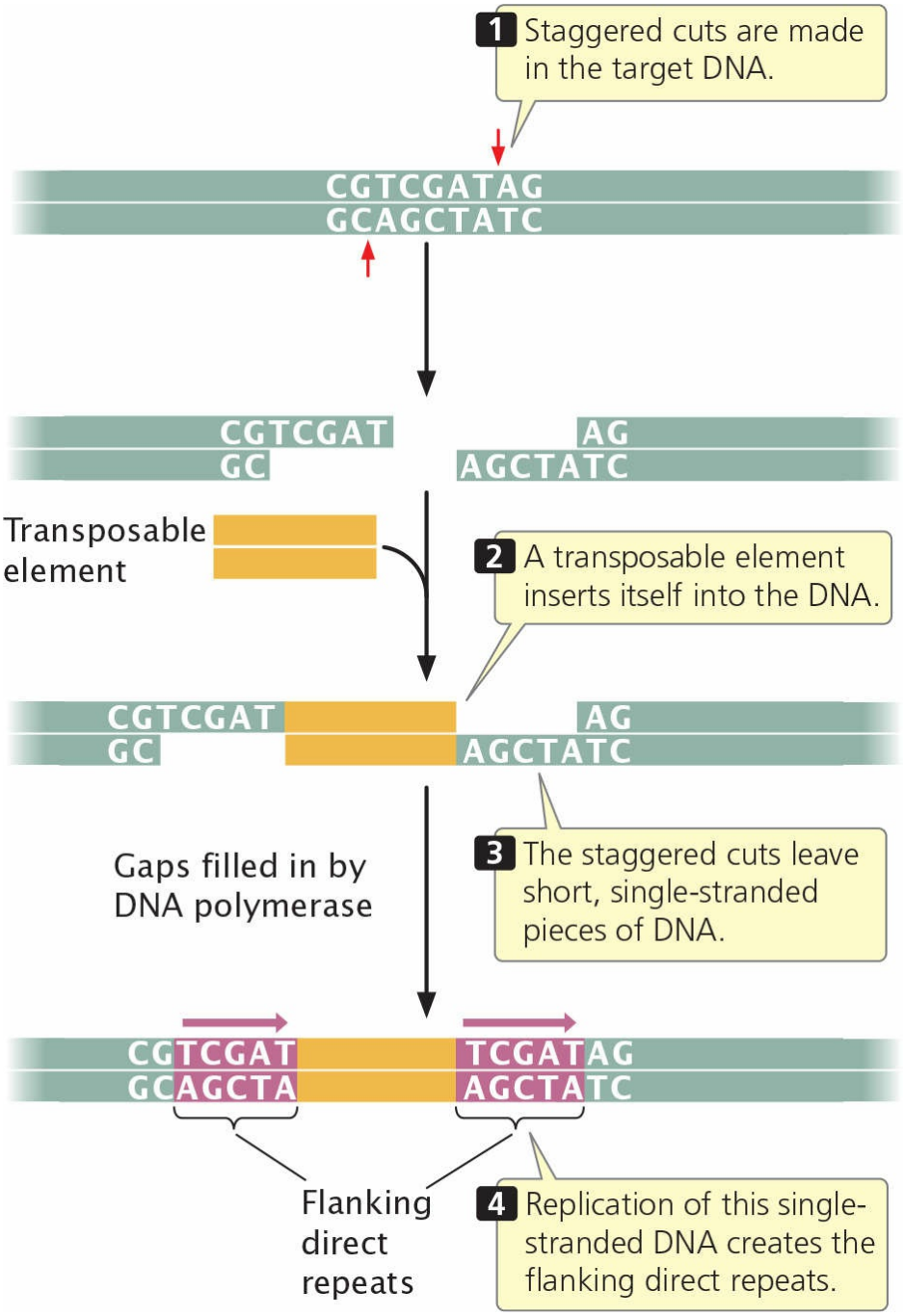
Short ***flanking direct repeats*** from 3 to 12 bp long are present on both sides of most transposable elements. The sequences of these repeats vary, but their length is constant for each type of transposable element. These repeats are not a part of the transposable element and do not travel with it. Rather, they are generated in the process of transposition at the point of insertion. Flanking direct repeats are created when staggered cuts are made in the target DNA. These staggered cuts leave short single-stranded pieces of DNA on either side of the transposable element. Replication of these single-stranded pieces creates the flanking direct repeats.

At the ends of many, but not all, transposable elements are ***terminal inverted repeats***—sequences from 9 to 40 bp in length that are inverted complements of each other.



The Process of Transposition

Transposition is the movement of a transposable element from one location to another. Several different mechanisms are used for transposition in both prokaryotic and eukaryotic cells. Nevertheless, all types of transposition share several steps: (1) staggered breaks are made in the target DNA (2) the transposable element is joined to single-stranded ends of the target DNA; and (3) DNA is replicated at the single-strand gaps. A ***transposase*** enzyme, often encoded by the transposable element, is used to make the staggered breaks in DNA and to integrate the transposable element into a new site.



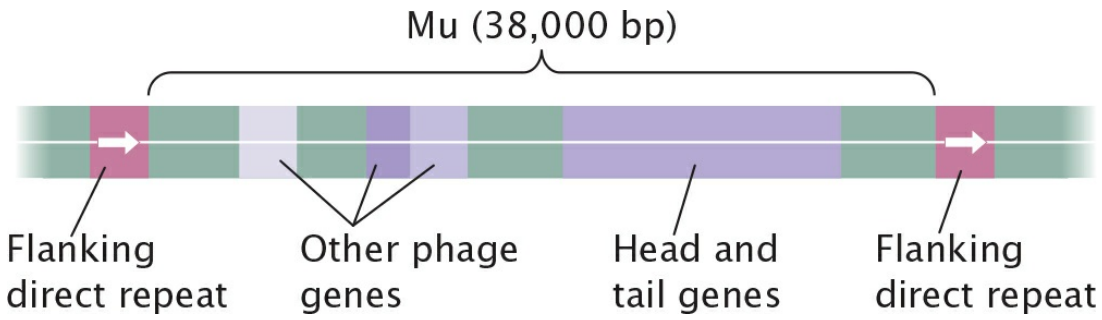
Among DNA transposons, transposition may be replicative or nonreplicative. In ***replicative transposition*** (also called *copy-and-paste transposition*), a new copy of the transposable element is introduced at a new site while the old copy remains behind at the original site, so the number of copies of the transposable element increases as a result of transposition. In ***nonreplicative transposition*** (*cut-and-paste transposition*), the transposable element is excised from the old site and inserted at a new site without any increase in the number of its copies. Nonreplicative transposition requires the replication of only the few nucleotides that constitute the flanking direct repeats. Retrotransposons use replicative transposition only.

Transposable Elements in Bacteria

The DNA transposons found in bacteria constitute two major groups: (1) simple transposable elements, called insertion sequences, that carry only the information required for movement, and (2) more complex transposable elements that contain DNA sequences not directly related to transposition.

INSERTION SEQUENCES The simplest type of transposable element in bacterial chromosomes and plasmids is an ***insertion sequence (IS)***. This type of element carries only the genetic information necessary for its movement. A number of different insertion sequences have been found in bacteria. They are typically from 800 to 2000 bp in length.

TRANSPOSING BACTERIOPHAGES A few bacteriophage genomes reproduce by transposition and use transposition to insert themselves into a bacterial chromosome in their lysogenic cycle. The best-studied transposing bacteriophage is Mu. Although Mu does not possess terminal inverted repeats, it does generate short (5-bp) flanking direct repeats when it inserts randomly into bacterial DNA. Mu replicates through transposition and causes mutations at the site of insertion, properties characteristic of transposable elements.



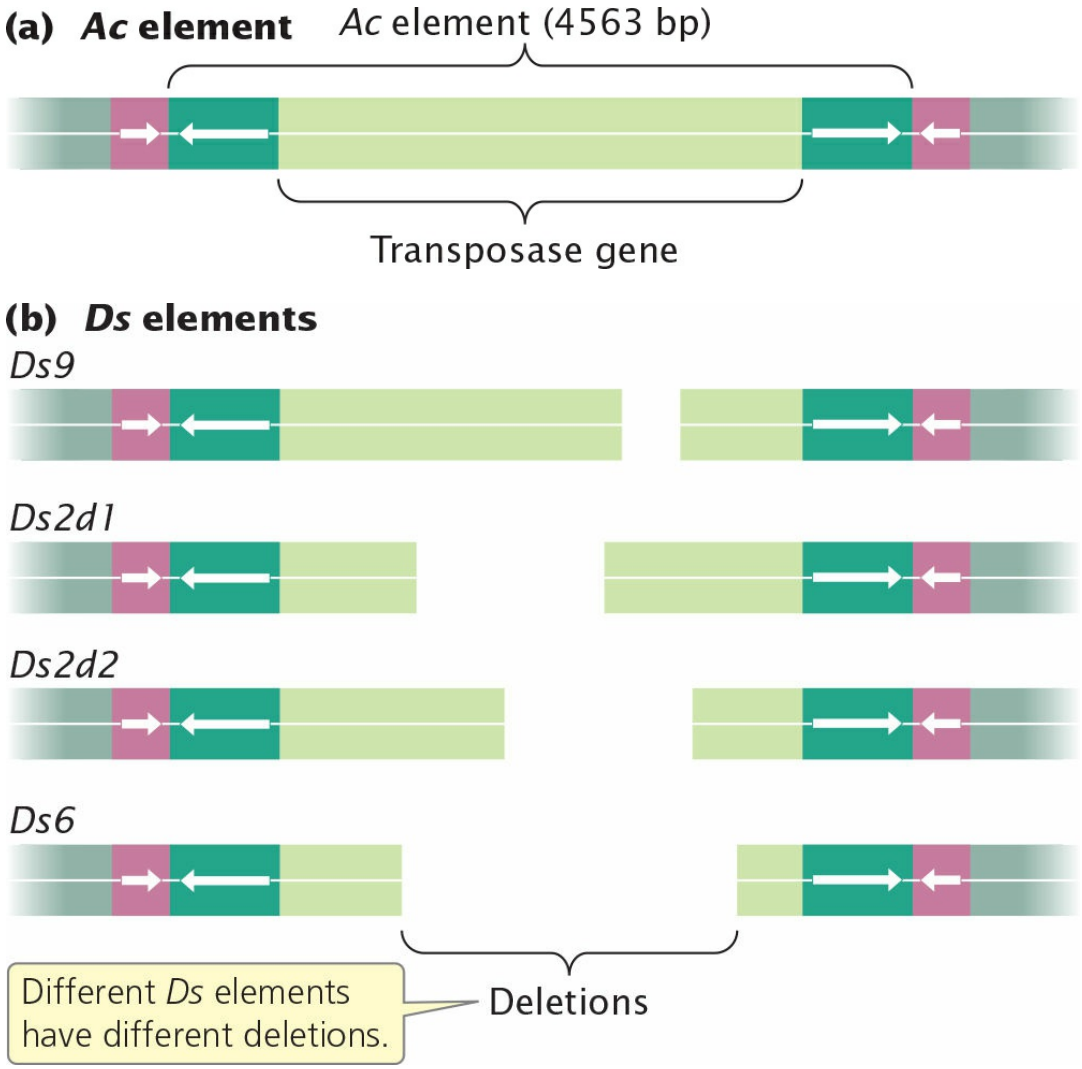
Transposable Elements in Eukaryotes

Eukaryotic transposable elements can be divided into two groups. One group is structurally similar to transposable elements in bacteria, typically ending in short inverted repeats and transposing as DNA; examples include the *P* elements in *Drosophila* and the *Ac* and *Ds* elements in corn (maize). The other group comprises retrotransposons: these elements use RNA intermediates, and many are similar in structure and movement to retroviruses.

Ac AND Ds ELEMENTS IN CORN Transposable elements were first identified in corn more than 50 years ago by Barbara McClintock. The significance of McClintock's early discoveries was finally recognized in 1983, when she was awarded the Nobel Prize in physiology or medicine.

McClintock's discovery of transposable elements had its genesis in the early work of Rollins A. Emerson on the corn genes that caused variegated (multicolored) kernels. Most corn kernels are either wholly pigmented or colorless (yellow), but Emerson noted that some yellow kernels

had spots or streaks of color. He proposed that these kernels resulted from an unstable mutation. McClintock discovered that the cause of the unstable mutation was a gene that moved. She noticed that chromosome breakage in corn often occurred at a gene that she called *Dissociation* (*Ds*), but only if another gene, the *Activator* (*Ac*), was also present. Occasionally, the genes moved together to a different chromosomal location. McClintock called these moving genes ***controlling elements*** because they controlled the expression of other genes.

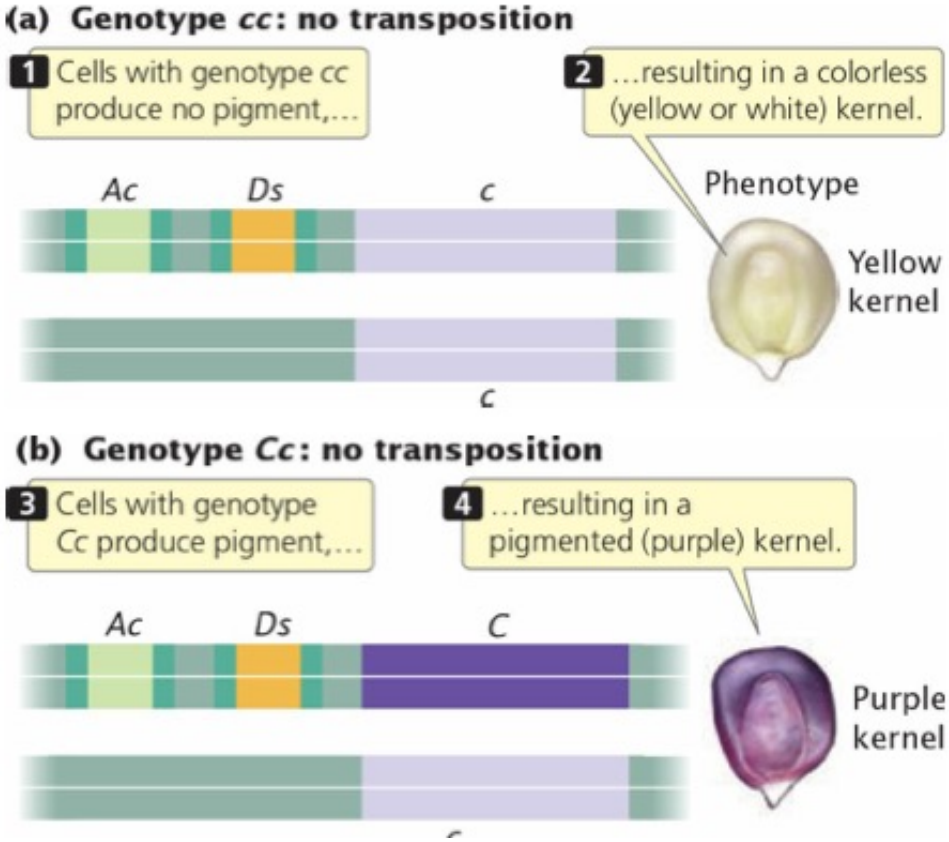


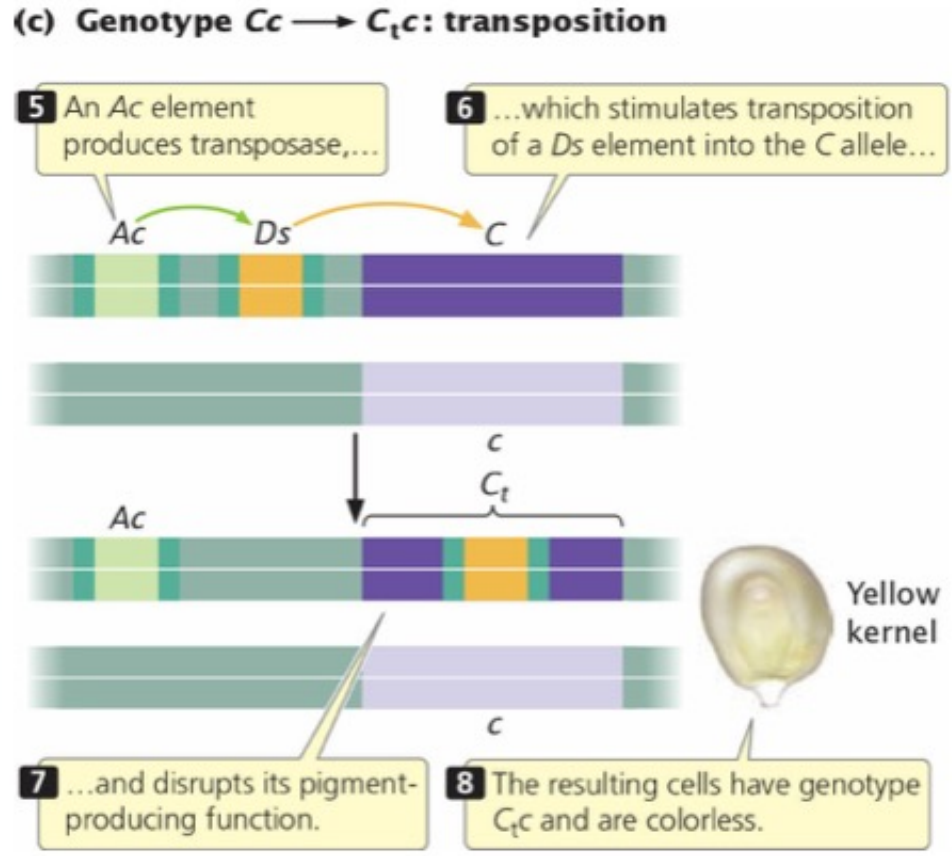
Ac and *Ds* elements are DNA transposons that possess terminal inverted repeats and generate flanking direct repeats at the points of insertion. Each *Ac* element contains a single gene that encodes a transposase enzyme. Thus, *Ac* elements are *autonomous*— able to transpose. *Ds* elements are *Ac* elements containing one or more deletions that have inactivated the transposase. Unable to transpose on their own (*nonautonomous*), *Ds* elements can transpose in the presence of *Ac* elements because they still possess terminal inverted repeats recognized by Ac transposase.

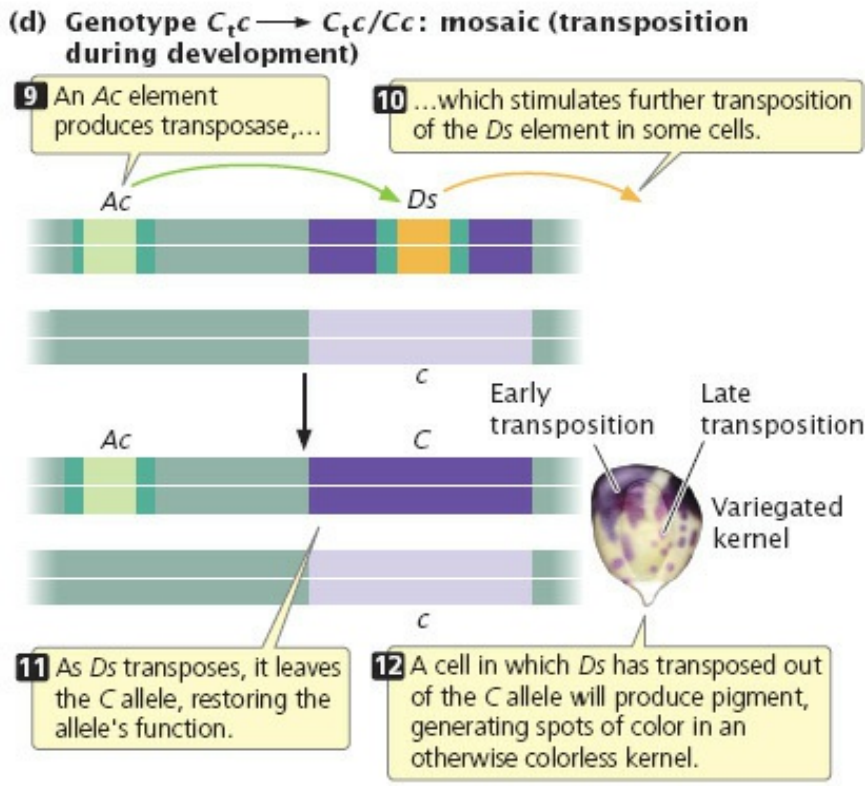
Each kernel in an ear of corn is an individual offspring, originating as an ovule fertilized by a pollen grain. A kernel's pigment pattern is determined by several loci. A pigment-encoding

allele at one of these loci can be designated *C*, and an allele at the same locus that does not produce pigment can be designated *c*. A kernel with genotype *cc* will be colorless—that is, yellow or white; a kernel with genotype *CC* or *Cc* will produce pigment and be purple.

In some kernels, a *Ds* element, transposing under the influence of a nearby *Ac* element, may insert into the *C* allele, destroying its ability to produce pigment. An allele inactivated by a transposable element is designated by a subscript t; in this case, the allele would be C_t. If a kernel is initially heterozygous with genotype *Cc*, then after the transposition of *Ds* into the *C* allele, the kernel will have genotype C_t *c*. This kernel will be colorless (white or yellow) because neither the C_t allele nor the *c* allele produces pigment. As the original one-celled corn embryo develops and divides by mitosis, additional transpositions may take place in some cells. In any cell in which the transposable element excises from the C_t allele and moves to a new location, the *C* allele may be rendered functional again: all cells derived from those in which this event has taken place will have the genotype *Cc* and be purple. The presence of these pigmented cells, surrounded by the colorless (C_tc) cells, produces a purple spot or streak (called a sector) in the otherwise yellow kernel. The size of the sector varies depending on when the excision of the transposable element from the C_t allele takes place. If excision is early in development, then many cells will contain the functional *C* allele, and the pigmented sector will be large; if excision is late in development, few cells will have the functional *C* allele, and the pigmented sector will be small.

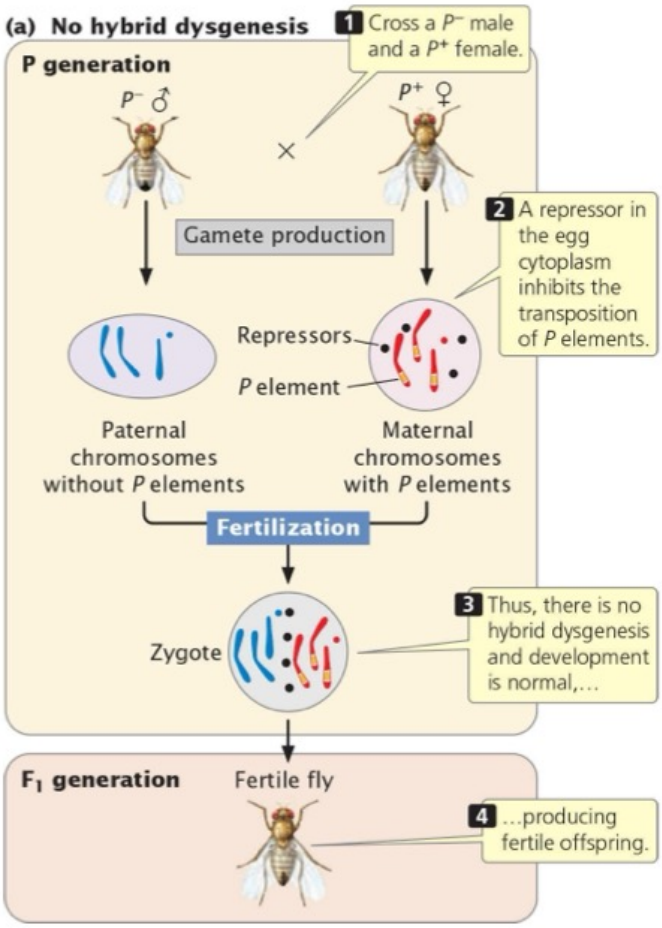


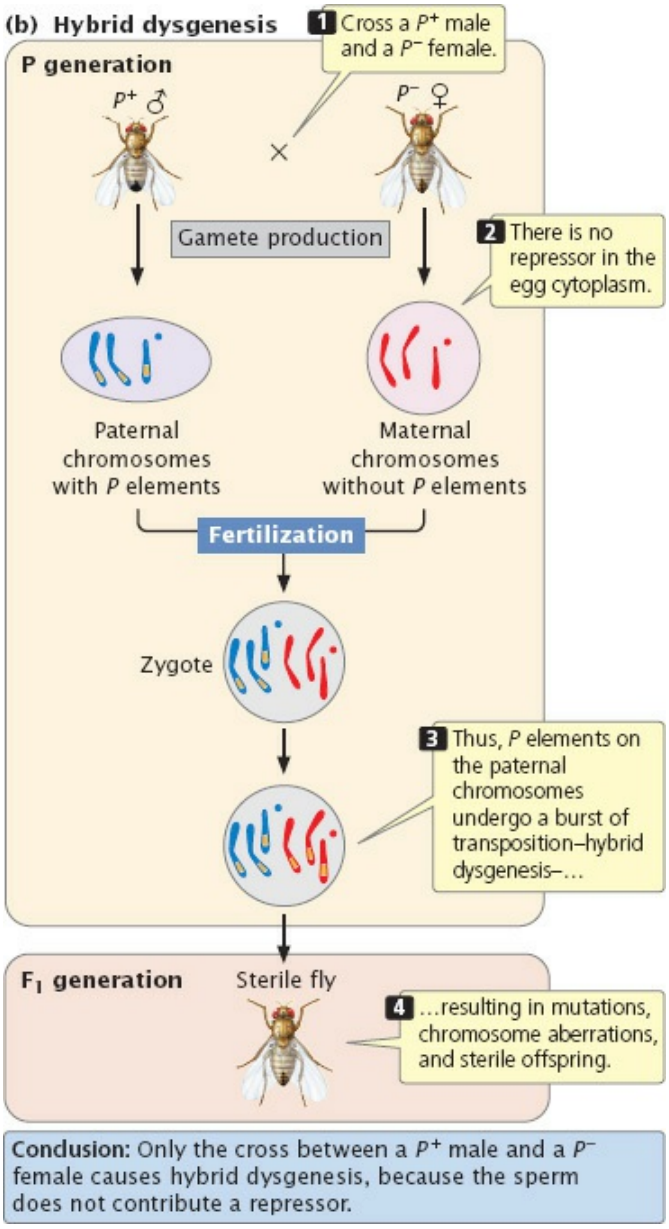




TRANSPOSABLE ELEMENTS IN DROSOPHILA A number of different transposable elements are found in *Drosophila*. One family of *Drosophila* transposable elements comprises

the *P* elements. Most functional *P* elements are about 2900 bp long. Each *P* element possesses terminal inverted repeats and generates flanking direct repeats at the site of insertion. Like transposable elements in bacteria, *P* elements are DNA transposons. Each *P* element encodes both a transposase and a repressor of transposition. The role of the repressor in controlling transposition is demonstrated dramatically in ***hybrid dysgenesis***, which is the sudden appearance of numerous mutations, chromosome aberrations, and sterility in the offspring of a cross between a P^+ male fly (*with P* elements) and a P^- female fly (*without* them). The reciprocal cross between a P^+ female and a P^- male produces normal offspring. Hybrid dysgenesis arises from a burst of transposition when *P* elements are introduced into a cell that does not possess them. In a cell that contains *P* elements, a repressor protein in the cytoplasm inhibits transposition. When a P^+ female produces eggs, the repressor protein is incorporated into the egg cytoplasm, which prevents further transposition in the embryo and thus prevents mutations from arising. The resulting offspring are fertile as adults. However, a P^- female does not produce the repressor protein, so none is stored in the cytoplasm of her eggs. Sperm contain little or no cytoplasm, so a P^+ male does not contribute the repressor protein to his offspring. When eggs from a P^- female are fertilized by sperm from a P^+ male, the absence of repression allows the *P* elements contributed by the sperm to undergo rapid transposition in the embryo, causing hybrid dysgenesis.




(b) Hybrid dysgenesis
P generation
1 Cross a P+ male and a P− female.
P+ ♂
P− ♀
Gamete production
2 There is no repressor in the egg cytoplasm.
Paternal chromosomes with P elements
Maternal chromosomes without P elements
Fertilization
Zygote
3 Thus, P elements on the paternal chromosomes undergo a burst of transposition–hybrid dysgenesis–…
F1 generation
Sterile fly
4 …resulting in mutations, chromosome aberrations, and sterile offspring.
Conclusion: Only the cross between a P+ male and a P− female causes hybrid dysgenesis, because the sperm does not contribute a repressor.