# Transposons: Prokaryotic

Secondary article

**Rasika M Harshey,** *University of Texas, Austin, Texas, USA*

Transposons are movable genetic elements found ubiquitously in the genomes of living organisms. They generate a variety of DNA rearrangements that have profound consequences for cell survival and evolution.

Article Contents



## Introduction

Elucidation of the complete genome sequence of *Escherichia coli*, the bacterium about which we have the most information, confirmed what geneticists already knew – that its genome is littered with a variety of insertion sequences (IS elements) (Blattner *et al*., 1997). IS elements are a subset of transposable elements, defined as special DNA segments that have the ability to move between unrelated DNA sequences, often accompanied by replication. The existence of movable elements was first deduced in the 1940s (before the discovery of the structure of DNA) by Barbara McClintock while analysing crosses between genetically marked corn plants. In the late 1960s, IS elements were discovered as highly pleiotropic mutations in *E. coli*. There followed the realization that IS-like elements were to be found not only in bacteria, but in virtually all organisms examined. Equally important was the discovery that closely spaced pairs of IS elements ('transposons' or composite elements) can move as units, carrying along the genes lying between them, most commonly those for drug resistance. In this article, all mobile elements will be referred to as transposable elements (TEs).

Most prokaryotic TEs promote transposition and rearrangements at frequencies of $10^{-4}$ to $10^{-7}$ per generation. Rearrangements such as insertions, deletions and inversions occur either as a direct consequence of transposition, or by general recombination between two copies of an element present at different locations. Much has been written about the contribution of these elements to the fitness and survival of their hosts. There is no denying that phenotypic selection pressures such as susceptibility to drugs, viruses and host defence mechanisms provide transpositional regulatory mechanisms that can be maintained through organismal fitness. It has been argued that a second very important function of TEs is the promotion of evolutionary adaptability by increasing the genetic variability of a population through rearrangements or through increased DNA content. Another view is that TEs represent 'selfish' DNA sequences, which, by enabling their own perpetuation ensure their preservation within genomes without operating through phenotypes (Sapienza and Dolittle, 1980). In this scenario, the limits to their propagation are imposed by organismal physiology, such as, for example, the energetic burden of excess DNA replication. This view is not inconsistent with the proposition that the increased genetic variability produced by TEs offers a long-term advantage for the evolution of their hosts. No doubt all of these mechanisms are responsible, in one degree or another, to the omnipresence of TEs.

## Transposition Mechanisms and DNA Rearrangements

The basic steps of transposition involve an initial severance of TE sequences from flanking host DNA (DNA cleavage), followed by joining of TE ends to new sequences in target DNA (strand transfer). Studies on the well-known TEs (discussed individually below) have shown that the initial DNA cleavage event occurs either on only one DNA strand at each end of the TE, or on both strands at both ends (**Figure 1**). In either case, the uncovered 3′ ends participate in the subsequent strand transfer event. In the first case, a branched intermediate is formed which, upon replication of the element using primers provided by the broken target DNA ends, generates a 'cointegrate' or a 'replicon fusion' where directly repeated copies of the TE bridge the donor and target DNA. Some TEs (e.g. Tn*3* family) encode a site-specific recombinase called resolvase, which acts on the cointegrate to resolve it into its original replicons, the target replicon now having acquired a copy or 'simple insertion' of the TE originally present on the donor replicon. Homologous recombination between the TEs will also lead to cointegrate resolution.

Another way to obtain a simple insertion in the cointegrate mode of transposition is by alternate processing of the branched intermediate. The broken donor DNA generated in such a scheme can, in principle, invade a homologous sister genome and restore its original configuration by replication repair.

In the second mode of transposition, where DNA cleavage occurs on both strands at both ends of the TE, a 'simple insertion' (without immediate replication) of the element is obtained (**Figure 1b**). This scheme is also referred to as the 'cut-and-paste' mechanism. Although both

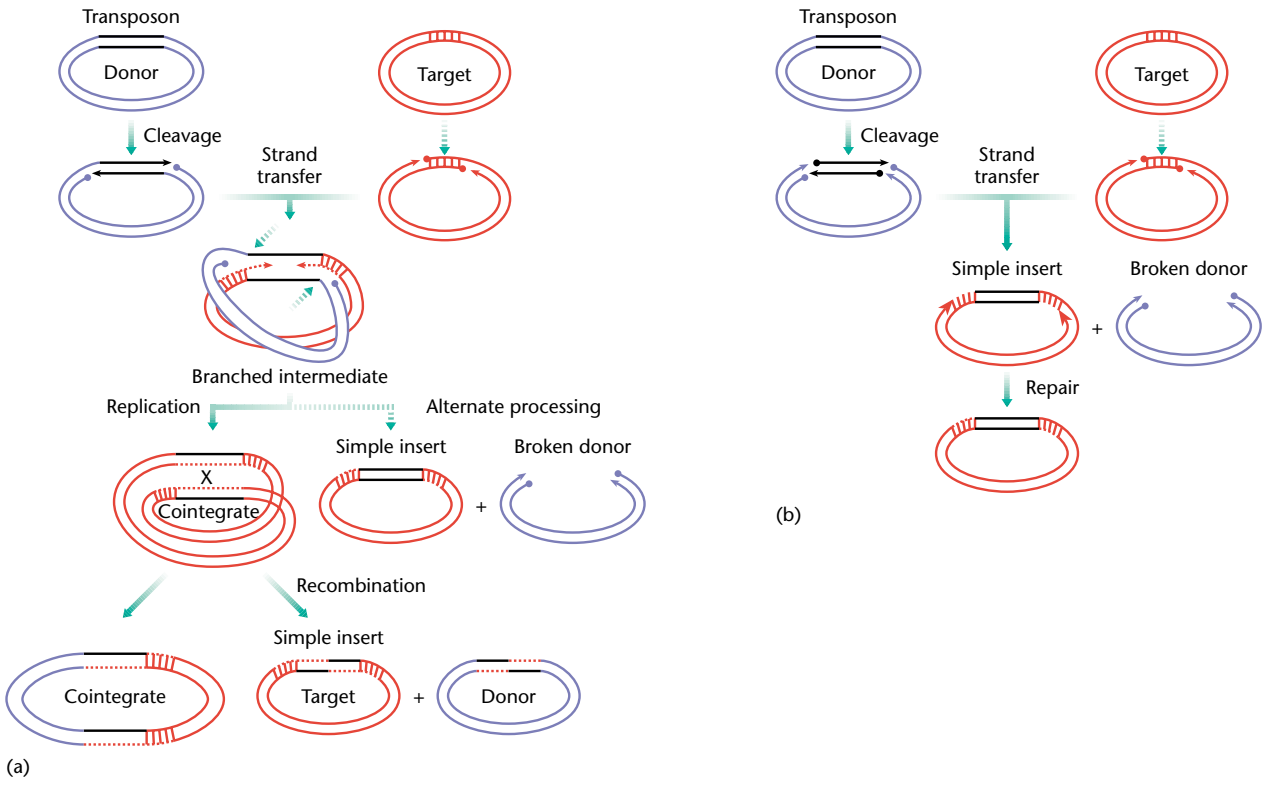


**Figure 1** Two transposition pathways. (a) Replicative 'cointegrate' pathway. 3′-OH groups are denoted by arrowheads, and 5′ phosphate groups by filled circles. The two target DNA phosphodiesters that will be attacked by transposon ends during strand transfer are shown already cleaved, for clarity. The short lines connecting the two DNA chains in the target represent the characteristic sequence duplicated after transposition. Wavy arrows denote alternative processing of the branched intermediate. Recombination between duplicated TEs in the cointegrate is signified by a cross. (b) Conservative 'cut-and-paste' pathway. All symbols as in (a).

strands are cleaved at each end, only the 3′ ends participate in subsequent strand transfer. The unjoined 5′ ends are probably repaired by replication. The severed donor sequences flanking the original TE can encounter the same fate (i.e. degradation or repair) as described above for the broken donor generated in the cointegrate mechanism. Note the important role played by DNA replication in both transposition pathways.

The following other rearrangements are also associated with transposition. (1) Duplication of 2–13 bp (characteristic of the element) of target DNA, with one copy of the duplication flanking each TE end (see **Figure 1**). The duplication is a result of a staggered attack of the TE ends on relevant phosphates of the target DNA, presumably filled-in by host repair functions. (2) Adjacent deletions, produced as a result of intramolecular transposition that follows the cointegrate pathway (**Figure 2a**). Such deletions are also generated by inverse transposition of composite IS elements, when transposition is initiated at the inside ends of the IS elements. Aberrant single-ended transposition events can also lead to adjacent deletions. (3) Adjacent inversions, produced by intramolecular transposition via the cointegrate pathway (**Figure 2b**). These are also generated by inverse transposition of composite IS elements. Deletions, inversions and duplications can in addition be produced by homologous recombination between copies of TEs present as direct or inverted repeats on the same molecule, or between TEs on different molecules. (4) Precise and imprecise excisions of TEs, which occur at a low frequency ($10^{-9}$ to $10^{-10}$). The molecular details of the excision reaction are not known. Imprecise events generally leave several nucleotides of the transposon sequences at the site of insertion. These can be processed further to yield precise events with restoration of the original donor sequence. In some elements, like Mu, excision requires the transposase as well as the homologous recombination function (an intact *recA* gene) of the host, while in most other elements excision is not dependent on either.

All of the rearrangements associated with transposition have been exploited as tools for gene mapping, cloning and analysis of gene structure, function and regulation. The inherent potential for genetic havoc accompanying transposition is probably responsible for the low frequencies of

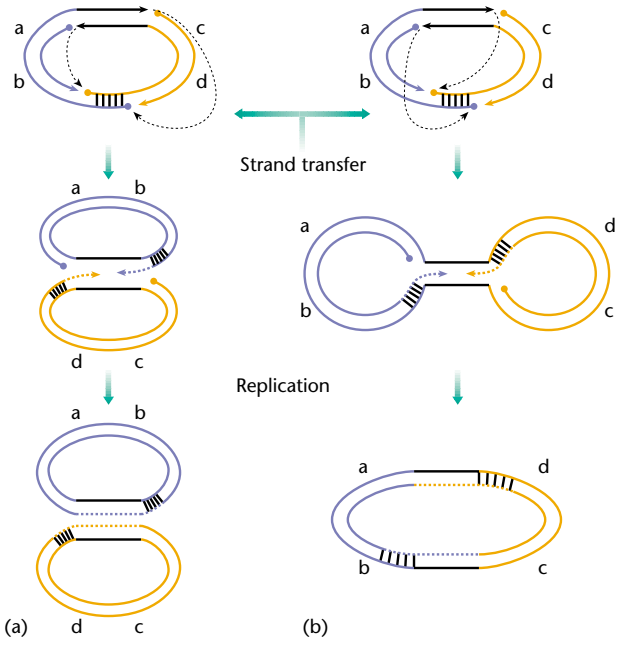


**Figure 2** Adjacent deletions and inversions produced as a consequence of intramolecular 'cointegrate' events. (a) Deletions; a–d represent genetic markers in the donor replicon. Following cleavage and strand transfer, replication of the branched intermediate produces two replicons, one deleted for markers c–d and the other for markers a–b flanking the original transposon. (b) Inversions; as in (a), except that opposite DNA strands are used as target in the strand transfer step. Replication of the branched intermediate produces inversion of markers a–b with respect to c–d. Symbols as in **Figure 1**.

transposition observed with most TEs. A variety of regulatory mechanisms (described below) have evolved for controlling transposition.

In considering the molecular mechanism of transposition, knowledge obtained from studies on Mu will be discussed in some depth, while that from three other transposons (Tn*10*, Tn*7*, and Tn*5*) will be compared and contrasted with Mu. Novel insights provided by work from other transposons will be described where appropriate.

# Mu

Mu is a temperate bacteriophage, which uses transposition to both lysogenize its host (*E. coli* and several Gram-negative bacteria), as well as to amplify its genome during the lytic cycle. It has the highest frequency of transposition among known TEs ($\sim 10^2$ events per cell per infectious cycle), facilitating establishment of the first *in vitro* system for studying molecular details of the process.

## Transposition *in vivo*

The Mu virion genome is linear, approximately 37 kb long, with variable lengths of host DNA attached at each end. Supercoiled circular DNA has been recovered after Mu infection, where the ends of the linear genome are held together by a coinjected phage protein. This DNA is thought to serve as the donor substrate for transposition. The first integration event after infection is not accompanied by replication of Mu DNA, and results in a simple insertion of Mu at virtually any site in the *E. coli* genome (hence Mu, for mutator). No evidence as yet exists to suggest a cut-and-paste mechanism for generating the simple insert. It is possible that this event proceeds through alternate processing of the branched intermediate generated by the cointegrate mode of transposition (**Figure 1a**). During the lytic cycle, transposition occurs by the replicative cointegrate mode. Five base pairs of target DNA are duplicated during integration/transposition, and a target site consensus of NYG/CRN has been derived (N is any nucleotide, Y is a pyrimidine, R is a purine). Mu transposition is accompanied by adjacent deletions and inversions (**Figure 2**), as well as precise and imprecise excision events.

## Transposition *in vitro*

For transposition to occur *in vitro*, sequences spanning *att*L, *att*R, and the enhancer are required (each composed of three sites: L1–L3, R1–R3 and O1–O3, respectively; **Figure 3a**). The distance of the enhancer from the two ends can be varied, but its orientation with respect to the ends is specific. Negative supercoiling in the donor substrate is essential for the initial steps of the reaction, where it plays

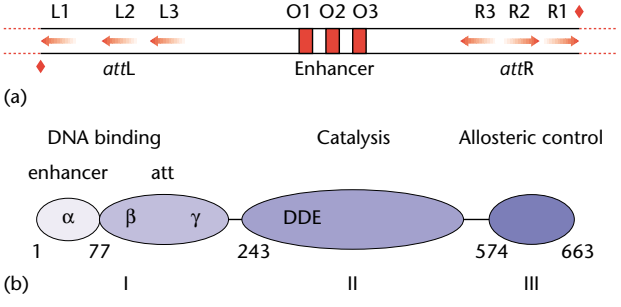


**Figure 3** Essential DNA and protein components of Mu transposition. (a) *Att*L, *att*R and enhancer regions encompass multiple DNA sites essential for transposition. Cleavage and strand transfer occurs at specific nucleotides (diamonds) outside L1 and R1, at the junction of Mu and non-Mu DNA. (b) Domain structure of transposase MuA. Of the three major proteolytic fragments or domains, Iα binds to sites in the enhancer and Iβγ to sites in *att*L and *att*R. Domain II has the catalytic DDE residues. Domain III is essential for assembly of the transpososome, as well as for interaction with the allosteric regulator MuB. Amino acid numbers are indicated below the protein structure.

several roles. Two phage proteins (MuA and MuB) and one host protein (HU) are required, as are divalent metal ions ($Mg^{2+}$). Metal ions are essential for both assembly of the active complex ('transpososome'), as well as for catalysis. HU is thought to play a role in closing the gap between L1 and L2 sites (**Figure 3a**) by wrapping the DNA between them, a process likely to be facilitated by DNA supercoiling. HU may also be involved in stabilizing an altered DNA conformation detected near the Mu ends in the assembled complex. MuA is the transposase (described in some detail below), which is catalytically inactive in its monomeric form in solution, and active only upon assembly into a tetramic nucleoprotein complex. MuB is an ATP-dependent DNA-binding protein, that allosterically regulates the activity of MuA, captures target DNA, as well as prevents Mu from integrating into itself.

The transposase MuA is a 75-kDa protein (663 amino acids in length), composed of three major globular domains (**Figure 3b**). The N-terminal domain encodes separate regions for interaction with the enhancer and the *att* sequences. Variations of the helix-turn-helix secondary structure motif are used to contact both families of DNA sites. The central MuA domain (DDE domain) contains a triad of DDE residues (Asp, Asp35Glu motif) essential for both DNA cleavage and strand transfer. The DDE motif is found in transposases from both prokaryotic as well as eukaryotic TEs. These residues are thought to coordinate the binding of divalent metal ions that are required for generating the nucleophiles for catalysis (OH of water for cleavage, and 3′-OH of cleaved DNA for strand transfer). The crystal structure of the DDE domain reveals a remarkable similarity in the overall topology of this domain to DDE domains from two retroviral integrases, in spite of little or no similarity in their primary sequences. The C-terminal domain of MuA interacts with MuB protein.

Several nucleoprotein complexes have been isolated throughout the process of Mu transposition (**Figure 4**). A short-lived LER complex is the first synaptic complex identified, where a three-site interaction occurs between the *att*L and *att*R ends and the enhancer. The topology of DNA supercoiling is likely to be important for this interaction. The LER converts to a stable type 0 complex (which can be trapped in the presence of $Ca^{2+}$, a divalent metal that supports assembly but not cleavage), wherein MuA has assumed its active tetrameric configuration, and a single-stranded character can be detected in the DNA around and outside the cleavage sites. A large activation barrier is associated with this step, probably due to the DNA and protein conformational changes accompanying type 0 formation. The free energy of supercoiling in the DNA outside Mu ends is thought to be utilized for promoting this rate-limiting step of the cleavage reaction. Neither DNA supercoiling, HU, nor the enhancer are required after type 0 assembly. Addition of $Mg^{2+}$ to the type 0 complex promotes single-strand cleavage of specific phosphodiester bonds at the 3′ end of each DNA chain (next to *att* sites L1 and R1, **Figure 3a**), revealing 3′-OH groups (see **Figure 1a**). The MuA subunits at L1 and R1 contribute their DDE domains in *trans* for both cleavage and strand transfer.

The cleaved complex (type I) is more stable than type 0. The cleaved ends in type I directly attack specific phosphodiesters in target DNA to produce an even more stable strand-transferred complex type II. Target capture is promoted by MuB, which can bring DNA into the MuA complex at any stage of the reaction (Naigamwalla and Chaconas, 1997). Besides capturing target DNA, MuB also allosterically regulates the activity of MuA all along the reaction pathway. The MuA–MuB interaction is responsible for a phenomenon called 'target immunity', defined as the capacity of one copy of a TE in a target DNA to substantially reduce the frequency of subsequent insertions elsewhere in the same target of another copy of the TE, thus preventing genocide as well as suicide. The molecular basis underlying this phenomenon is the ability of *att* end-bound MuA to stimulate hydrolysis of ATP by MuB, followed by dissociation of MuB from DNA. Thus, MuB preferentially distributes itself to non-Mu DNA, capturing it as a target for Mu integration.

Thus far, catalytic function has been assigned to only the two MuA subunits located at L1 and R1 in the tetrameric complex (Namgoong and Harshey, 1998). While it is possible that the other two subunits are responsible for a hitherto unknown function, it is equally likely that a tetrameric form of MuA provides the structural integrity necessary for precisely choreographing each step along the transposition pathway.

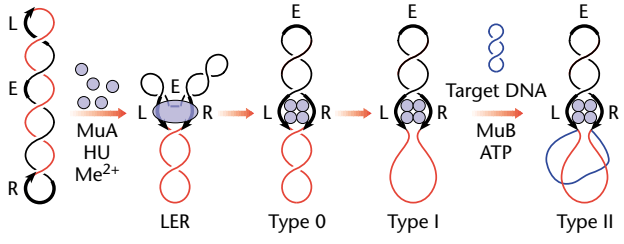


**Figure 4** Nucleoprotein complexes in the Mu transposition pathway. *Att*L, *att*R and the enhancer sequences are designated L, R and E, respectively.

## Replication

The stability of the type II complex poses an impediment to the entry of the replication machinery upon completion of strand transfer. ClpX, a molecular chaperone which is a heat-shock protein and the ATPase regulatory subunit of the Clp protease, is required for Mu replication *in vivo* and has been found to destabilize and eventually dislodge the

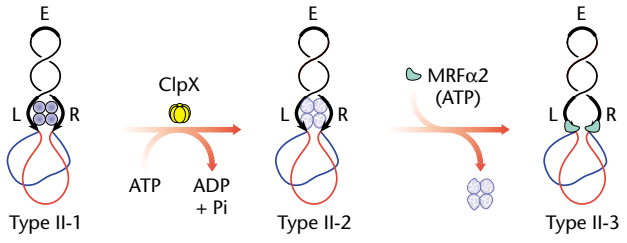


**Figure 5** Remodelling transposition complexes for Mu replication. The stable strand transfer complex (type II-1; see **Figure 4**) is first destabilized by ClpX (type II-2), allowing displacement and exchange of MuA with a host factor MRFα2 (type II-3), prior to entry of PolIII holoenzyme for Mu replication.

MuA tetramer by promoting its exchange with a specific ATP-requiring host factor (MRFα2), which in turn interacts with the PolIII holoenzyme (**Figure 5**). Replication then proceeds unidirectionally, starting from the left end of Mu (Jones and Nakai, 1997).

## Regulation

Why is the activity of MuA manifested only within a tetrameric assembly? It appears that the complexity of the assembly process can be exploited at various stages to regulate transposition. For example, tetramerization of MuA can be achieved only after interaction of monomeric MuA with the multiple *att* and enhancer elements during LER formation. Although it is likely that each *att*–enhancer site interaction is highly ordered, inducing specific and incremental conformational changes in MuA such that assembly occurs only along specific protein interfaces, it is virtually certain that interaction with the enhancer has been built into the system to ensure regulation. The enhancer plays a critical role in the decision between lysis and lysogeny during the life cycle of Mu, by binding to the lysogenic repressor and controlling transcription of Mu*A* and Mu*B* genes.

Participation of the enhancer in Mu transposition therefore not only assures that conformational changes needed for activating MuA in the assembled transpososome do not occur until the *att*L and *att*R ends are correctly synapsed, but also provides a mechanism to divine the presence of the lysogenic repressor and hence the physiological state of the cell. The latter can also be gauged by the level of DNA supercoiling and accessory proteins like HU and integration host factor (IHF) (IHF can substitute for HU as well as participate in enhancer function when the superhelical density of DNA is low), which vary depending upon growth conditions and cell cycle.

In the assembled tetrameric complex, evidence suggests that MuA activity requires a reciprocal sharing of catalytic/structural residues between different subunits. Thus, active sites are assembled only concomitant with tetramer assembly, ensuring coordination of the reaction at both ends, and avoiding wasteful partial transposition. Additional checkpoints for avoiding incomplete transposition include a *trans* configuration of the DDE domains during cleavage and strand transfer (i.e. the DDE domain of the MuA subunit at the left L1 site transposes the right end, and that of the subunit at the right R1 site transposes the left end), and an inhibition of single-end strand transfer when only one of the two ends is cleaved (Namgoong and Harshey, 1998). Thus, Mu appears to have harnessed its considerable powers, evolving appropriate measures to 'look before it leaps'.

## Tn*10*

Tn*10* is a 9.3-kb composite tetracycline resistance transposon having inverted repeats of the 1329-bp insertion sequence IS*10* at its ends. Tetracycline resistance is specified by proteins encoded in the DNA between the IS elements. IS*10*-right(R) is a fully functional transposition module; IS*10*-left(L) has a defective transposase. While transposition of the composite element using the outside ends (outer 25 bp are essential) of each IS*10* occurs at the rate of $10^{-7}$ per element per generation, the IS*10* elements can transpose independently at a much higher rate ($10^{-4}$ per element per generation; IS*10*-L needs the transposase made by IS*10*-R). The inside ends of the IS*10* elements can also be used to give inverse transposition. Although Tn*10* inserts into a large number of different sites in the bacterial genome, it does exhibit 'hot spots' whose consensus is a 3-bp palindrome flanking a central base pair in the middle of the 9-bp target site duplicated by the insertion. Tn*10* insertion can turn downstream genes either on or off, depending on the orientation of the transposon. IS*10*-R carries a fairly strong outward promoter (pOUT), that can direct downstream transcription. Tn*10* transposition can generate all of the rearrangements described above.

Both genetic and biochemical evidence have shown that Tn*10* transposes by a nonreplicative cut-and-paste mechanism (see **Figure 1b**). *In vitro*, the 46-kDa transposase and a host protein (HU or IHF), along with divalent metal ions are sufficient to promote transposition of two IS*10* ends from a negatively supercoiled donor substrate. Like Mu transpososomes, all nucleoprotein complexes are stable. Formation of a precleavage synaptic complex is followed by cleavage of 3′ ends (like in Mu) to generate 3′-OH groups, which, prior to strand transfer, attack the nontransferred strand to form hairpins at the transposon ends (unlike Mu), releasing the flanking donor DNA as double-stranded ends (Kennedy *et al.*, 1998; **Figure 6**). The hairpins are hydrolysed again to regenerate 3′-OH groups at the transferred strands. Once double-strand cleavage has occurred at both ends of the element, only then is the synaptic complex capable of capturing target DNA for

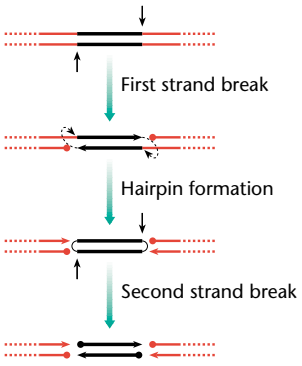


**Figure 6** Formation of a hairpin intermediate during the cut-and-paste pathway of Tn*10* transposition. Symbols as in **Figure 1**.

strand transfer, unlike Mu transposition where target DNA can be captured at any stage in the reaction pathway. As with MuA, DDE residues of the Tn*10* transposase are essential for catalysis, and the same 'active site' is involved in all chemical reactions (Bolland and Kleckner, 1996). A variation of the hairpin mechanism has also been found in IS*911* and IS*2*. Another example of a system that uses a hairpin mechanism to make a double-strand break in DNA is provided by V(D)J recombination, the process that generates immunoglobulin diversity in vertebrates. It is speculated that this system may have evolved from a transposon.

The rate of transposition of IS*10* is limited by several factors *in vivo*. These include low expression levels of the transposase, and its preferential action in *cis* (i.e. site of synthesis). Both transcription of the transposase, as well as its ability to bind the ends are regulated by methylation of DNA specified by the host *dam* gene. The hemimethylated state of IS*10* DNA is the most active, thus coupling transposition to DNA replication. This feature may be important for replication-repair of the broken host DNA ends after IS*10* transposition (**Figure 1b**). An 'antisense' regulation plays a role in decreasing the rate of Tn*10* transposition as its copy number increases. This is achieved by pairing of the transcript made from pOUT with the 5′ end of the transposase mRNA, inhibiting transposase gene translation. Thus, IS*10* has evolved several mechanisms to live in harmony with its host.

## Tn*7*

Tn*7* is a 14-kb transposon that contains several antibiotic-resistance (trimethoprim, streptomycin, spectinomycin) and transposition genes. Unlike Tn*10*, it is not flanked by IS modules, but has about 30 bp of highly related inverted repeats. In contrast to Mu and Tn*10*, Tn*7* transposes at a high frequency to only one specific site in *E. coli* (*att*Tn*7*). If the specific site is unavailable, Tn*7* will transpose to other sites at 100-fold lower frequency. Some of these sites resemble *att*Tn*7* and others do not. Five transposition genes (*tnsABCDE*) mediate two distinct but overlapping pathways. *tnsABC* genes are essential for both pathways, but *tnsD* or *tnsE* is required in addition. The *tnsABC* + *D* pathway mediates transposition to *att*Tn*7* as well as to the pseudo-*att*Tn*7* sites, while the *tnsABC* + *E* pathway mediates transposition to sites unrelated to *att*Tn*7*. Bacterial plasmids that can conjugate between cells appear to be preferential targets for Tn*7*. IS*903* also integrates into conjugating plasmids. The molecular details of this process are not known.

The products of Tn*7* insertion are simple insertions. These are very stable, and no other rearrangements have been reported. *In vitro*, the reaction proceeds by a cut-and-paste mechanism (**Figure 1b**), but a hairpin intermediate (like that observed for Tn*10*; **Figure 6**) has not been reported. Cleavage occurs by staggered double-strand breaks that leave 5′ overhanging ends. Strand transfer involves an attack of the 3′ ends on target DNA to give a 5-bp target duplication. TnsB binds to the ends specifically, and is thought to recruit TnsA to the ends. Both TnsA and B have a DDE motif. TnsA cleaves 5′ ends of Tn*7*, while TnsB cleaves the 3′ ends. TnsC has an ATPase activity, and is involved in target binding, the recognition and capture of which precedes donor cleavage. Two host proteins, the ribosomal protein L29 and the acyl carrier protein (ACP), together stimulate the binding of TnsD to *att*Tn*7*, as well as stimulate Tn*7* transposition. ACP also promotes cleavage *in vitro* of the 3′ ends of Tn*3* by its transposase (Sharpe and Craig, 1998).

Tn*7* displays transposition immunity. Tn*7* derivatives containing only the terminal ends, and TnsB and C proteins are sufficient to confer immunity. A mechanism similar to that found in the Mu system might operate here, given that TnsB triggers the dissociation of TnsC from the Tn*7* end-containing target DNA, accompanied by hydrolysis of ATP (Stellwagen and Craig, 1997).

## Tn*5*

Tn*5* is a 5.8-kb composite transposon, flanked by 1533-bp IS*50* modules. The central segment encodes resistance to kanamycin, bleomycin and streptomycin. Tn*5* exhibits a striking similarity to Tn*10* in the mechanism of transposition and its regulation. For example, each IS*50* module (L and R) is capable of independent transposition, and depending on whether the outside or inside ends of these elements are used, they generate direct or inverse transposition respectively. The spectrum of resulting DNA rearrangements are similar for both transposons. Although Tn*5* has a low specificity for insertion (target consensus is GNTYWRANC), some 'hotspots' exist, characterized by a GC-rich sequence, although not all

GC-rich sequences are hotspots. Tn*5* insertions in an operon are generally 'polar' in that they block the transcription of distal genes from the normal operon promoter, independent of transposon orientation.

Like Tn*10*, only one IS*50* module (IS*50*-R) produces functional transposase. This module encodes two proteins, the transposase and a related protein, the transposition inhibitor, from the same open reading frame. The synthesis of these proteins is influenced by host DNA methylation function, Dam, which inhibits transposase promoter recognition and competitively enhances the transposition inhibitor promoter. The inhibitor lacks the N-terminal 55 amino acids of the transposase (which encodes binding to the 19-bp end DNA sequences), and decreases transposition rates via the formation of nonproductive complexes with transposase. Transposase-end DNA interaction is itself regulated by several host proteins: DnaA, Dam and Fis. The lower frequencies of transposition of incoming Tn*5* in a cell already containing Tn*5*, as well as in a cell with multiple copies of Tn*5*, is explained by the *trans* activity of the inhibitor, but only *cis* activity of the transposase.

*Cis* activity is common to a large number of transposases. While the mechanisms for *cis* action can be many, the *cis* preference of Tn*5* transposase may be attributable to nonproductive transposase-inhibitor multimerization. In contrast, the *cis* preference of IS*10* appears to depend on the rate at which transcripts are released from their templates and/or the half-life of the transposase message. In IS*903*, the *cis* preference of the transposase is mediated by a combination of instability and inefficient translation (Derbyshire and Grindley, 1996).

Like Tn*10*, Tn*5* transposes by the simple insert pathway (Goryshin and Reznikoff, 1998). A hairpin intermediate has been identified *in vitro*, catalysed by the 46-kDa transposase that belongs to the DDE family of proteins (Davies *et al*., 1999).

## Summary

Transposable elements move either by a replicative cointegrate mechanism or a nonreplicative cut-and-paste mechanism. While the transposases they encode are responsible for the cleavage and strand transfer steps of transposition, they are dependent on their hosts for the posttransposition steps of replication, repair and recombination. The transposases all belong to the DDE superfamily of proteins, which use metal ions to generate nucleophiles for the cleaving and joining reactions. Transposition generates a plethora of DNA rearrangments in its wake. The activity of the transposases is regulated in a myriad ways, lowering the frequency of transposition and assuring a peaceful coexistence of TEs with their hosts.

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