Transposing elements

Transposable elements (TEs) are defined as DNA sequences that are able to move from one location to another in the genome. TEs have been identified in all organisms, prokaryotic and eukaryotic, and can occupy a high proportion of a species genome.The mobilization of TEs is termed **transposition or retrotransposition,** depending on the nature of the intermediate used for mobilization.

Transposons fall into two categories: (1) those that transpose directly as **DNA**(2) those that transpose via an **RNA intermediate** transcribed from the mobile element by an RNA polymerase and then converted back into double-stranded DNA by a **Reverse transcriptase**. Mobile elements that transpose through a DNA intermediate are generally referred to as **Transposons** and other mobile elements ,transposing to new sites in the genome via an RNA intermediate are called **retrotransposon,** because their movement is analogous to the infectious process of retroviruses.

(figure 1)

Most mobile elements in bacteria transpose directly as DNA. In contrast, most mobile elements in eukaryotes are retrotransposons.TE mobilization can promote gene inactivation, modulate gene expression or induce illegitimate recombination.TEs can be considered as *selfish* DNA or *junk* DNA.

The first molecular understanding of mobile elements came from the study of certain *E. coli* mutations resulting from the spontaneous insertion of a DNA sequence (approximately 1 – 2 kb long) in a gene . The inserted piece of DNA is called ***insertion sequences (I S)***. An ***inverted repeat*** of about 50 base pairs is invariably found at each end of an insertion sequence. The protein coding region is found between the inverted repeats ,which encodes one or two enzymes required for transposition of an IS element to a new site.The IS encoded proteins are expressed at a very low rate and having low frequency of transposition. The IS elements have at their end ***direct repeats*** of 5 to 11 base pairs. The *length* of the direct repeat is characteristic of each type of IS element, but its *sequence* depends on the target site where a particular copy of the IS element is inserted.The enzyme that catalyzes transposition of an IS element is called a ***transposase.***

Figure 2

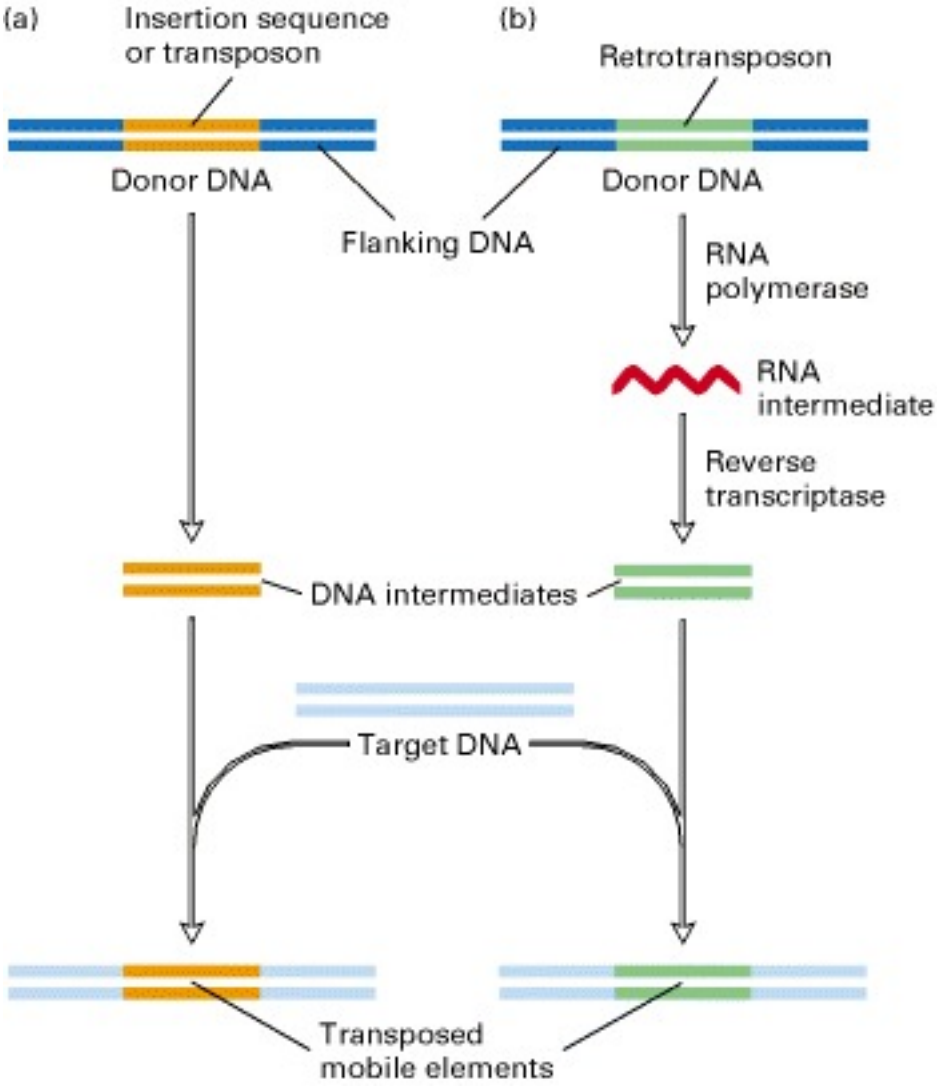
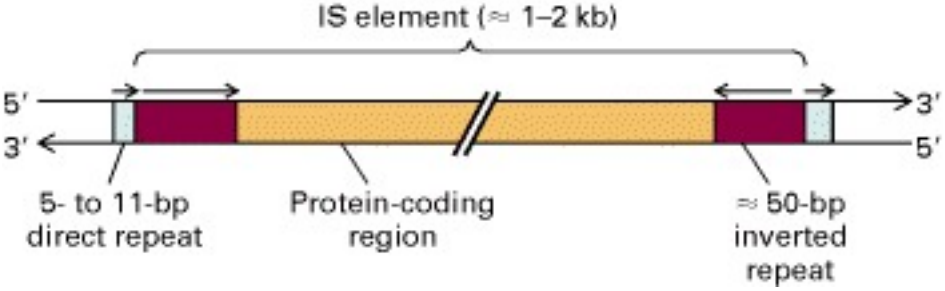


Figure 1: classification of transposons

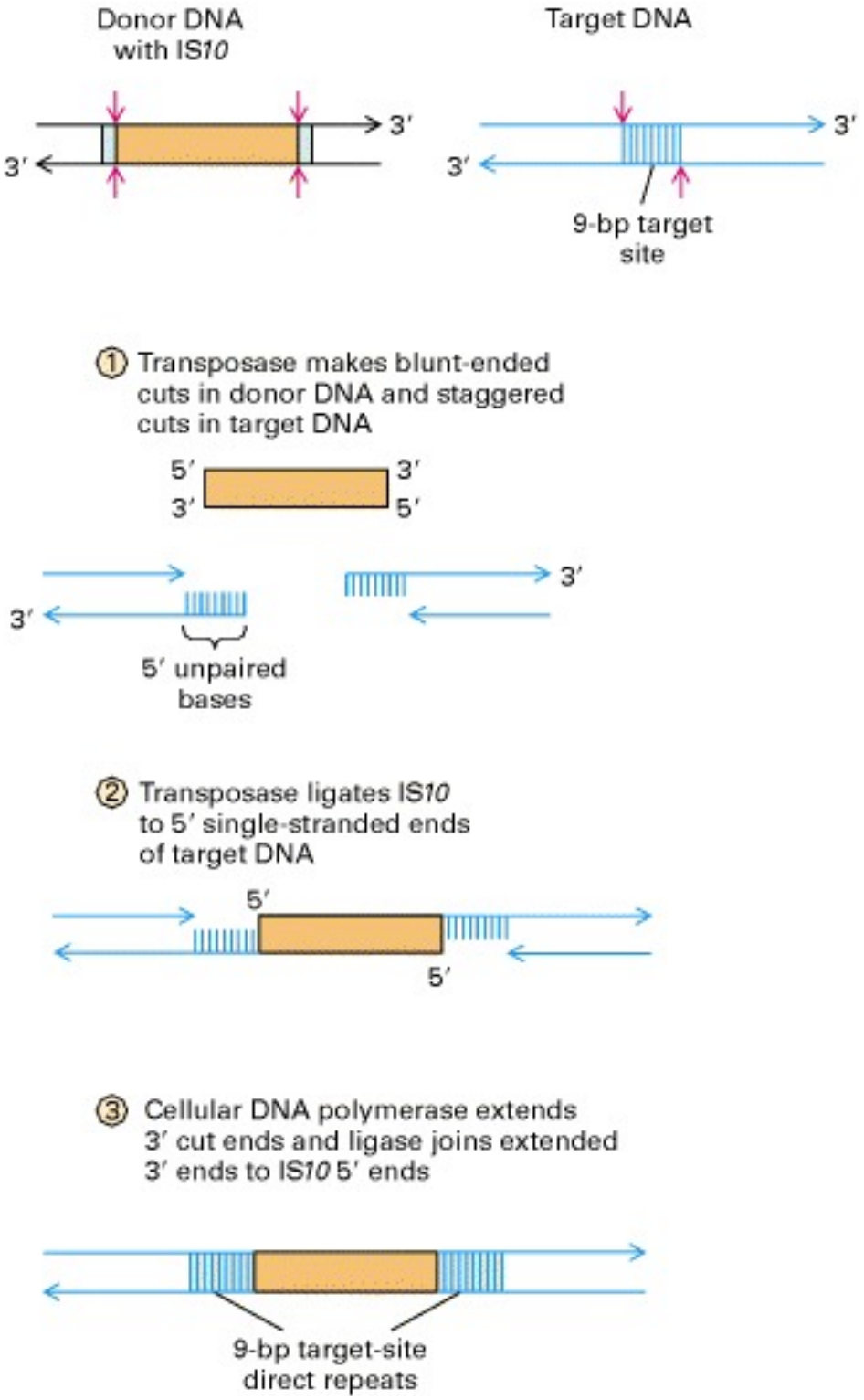
Figure 2 Insertion sequence element



There are two types of transpositions 1. **Conservative transposition** or **cut and paste** 2 **Replicative transposition or Replicate and Paste**

In **conservative transposition(cut and paste transposition) ,** the **transposon** is completely removed from the genome and reintegrated into a new, non-homologous locus, the same genetic sequence is conserved throughout the entire process. This is a non-**replicative** mode of **transposition**. Figure3

Figure 3



In conservative or cut ans paste transposition ,the transposase molecules bind to the inverted-repeat sequences present at each end of the IS element in the donor DNA and cleave the DNA, precisely excising the element. Transposase molecules also bind to and make staggered cuts in a short sequence in the target DNA, generating single-stranded tails.The transposase enzyme then ligates the 3′ termini of the IS element to the 5′ ends of the cut donor DNA. A DNA polymerase encoded by the host cell then extends the 3′ ends of the target site, filling in the single-stranded gaps and generating a short repeat of the target-site sequence at either end of the newly inserted IS element. This is the origin of the short direct repeats that flank IS elements.

2. Replicative transposition

In replicative transposition , a copy of the original IS element is generated in the target DNA and the original copy is retained in the donor DNA.

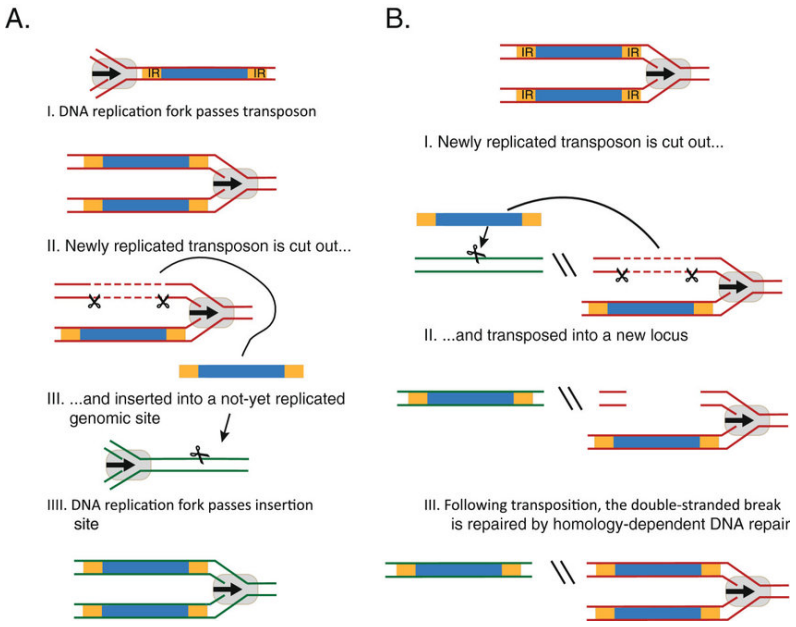


Figure 4 : Models of replicative transposition.

(A)After replication, the transposon is excised and integrated into a yet unreplicated genomic site thus duplicating the newly inserted transposon.

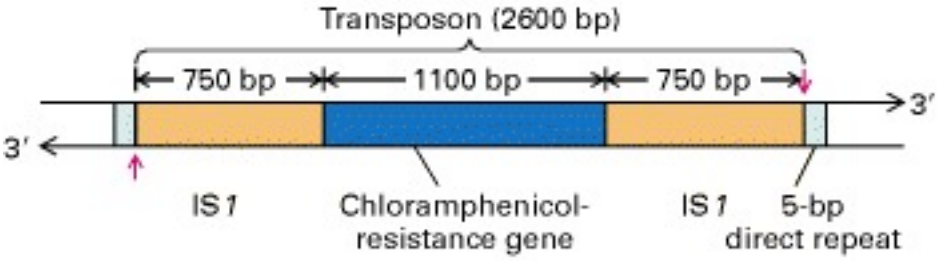
(B) The double-stranded break created by transposition at newly replicated DNA is repaired using the sister chromatid as a template for homology-directed DNA repair, leading to reconstitution of the excised transposon. IR, terminal inverted repeat.

The major distinguishing feature between the two pathways is whether a double-strand break or a single-strand nick occurs at the ends of the transposon before integration . A double-strand break effectively removes all connections with the donor DNA and thus precludes co-integrate formation in conservative transposition . In contrast, a nick allows maintenance of connections to both donor and target replicons after integration, and, following replication, results in formation of a co-integrate in replicative transposition.

The initial step of both transposition pathways involves the generation of a 3′ OH at the transposon termini . In the simple insertion pathway, subsequent cleavage of the 5′-flanking DNA generates an excised transposon.The 3′ OH ends of the excised transposon then act as nucleophiles in a concerted strand transfer reaction that results in integration of the transposon into a target. The target DNA is cleaved in a staggered manner and the short single-stranded regions that flank the newly inserted transposon are repaired by the host replication apparatus to generate short direct repeats, a signature of the transposition reaction.

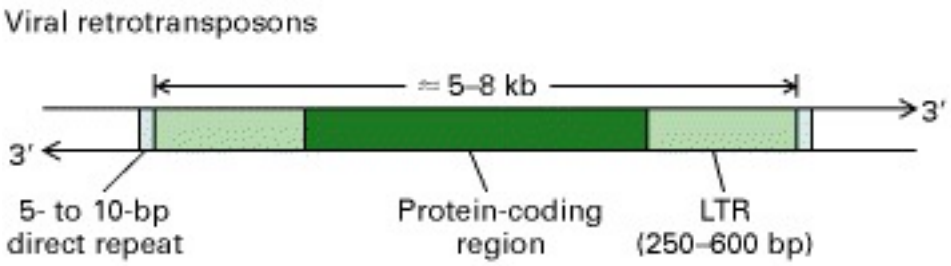
Bacterial transpositions , in addition to IS elements, contain composite mobile genetic elements that are larger than IS elements and contain one or more protein coding genes in addition to those required for transposition. Bacterial transposons are composed of an antibiotic-resistance gene flanked by two copies of the same type of IS element . Insertion of a transposons into plasmid or chromosomal DNA is readily detectable because of the acquired resistance to an antibiotic. Transposition produces a short direct repeat of the target site on either side of the newly integrated transposon, just as for IS elements. Figure 5

Figure 5 Bacterial Transposons



The **eukaryotic elements** are similar to bacterial IS elements but they move by the nonreplicative mechanism . Majorly eukaryotes have retrotransposons. These retro transposons may be divided into two major categories, ***viral*** (e.g.Ty elements in yeasts and copia elements in drosophila) **and *nonviral* retrotransposons (e.g . Mammalas)**

Figure 6



The central protein coding region is flanked by two long terminal repeats (LTRs), which are element-specific direct repeats. LTRs, the hallmark of these mobile elements, also are present in retroviral DNA . Like other mobile elements, integrated retrotransposons have short target-site direct repeats at their 3′ and 5′ ends.

The leftward LTR functions as a promotor for RNA polymerase II transcription .After the entire retroviral DNA has been transcribed, the RNA sequence corresponding to the rightward LTR directs host-cell RNAprocessing enzymes to cleave the primary transcript and add a poly(A) tail at the 3′ end of the R sequence. The resulting retroviral RNA genome lacks complete LTRs. However, after a virus infects a cell, reverse transcriptase yields a double-stranded DNA containing LTRs *Integrase,* other enzyme ,encoded by retroviruses, then inserts the double-stranded retroviral DNA into the host-cell genome; in this process, short direct repeats of the target-site sequence are generated at either end of the inserted viral DNA sequence. Like retroviral DNA, Ty elements and *copia* encode reverse transcriptase and integrase; these enzymes are thought to function in transposition by converting the RNA intermediate into DNA and inserting the DNA into the target site in a manner similar to retroviruses.