

LECTURE 27

TRANSPOSABLE GENETIC ELEMENTS

A. There are three types of transposable elements described in prokaryotes.

Insertion Sequences (IS elements)

Composite transposons

Tn3 elements

1. IS elements:

- a) IS elements are relatively small transposable elements that range in size from 760 to less than 2,500 base pairs (bp). They can insert at many different sites in bacterial and viral chromosomes and plasmids and episomes, and they contain genes whose products are involved in promoting and regulating transposition. One of the genes is a *transposase* that functions in excision of the element from a chromosome, plasmid, or episome.
- b) IS elements typically generate unstable mutants that revert to wild-type at a detectable frequency. For that reason, IS elements originally were called "mutable" genes.
- c) All IS elements contain *inverted terminal repeats* that range in size (length) from 9 to 40 base pairs. At the site of integration there invariably is a *target site duplication* of from 2-13 base pairs.

Note: Inverted terminal repeats are characteristic of most (but not all) transposons, whereas target site duplications are found in nearly all "integrated" molecules (e.g., prophages).

- d) Plasmids harbor IS elements, and when a plasmid and chromosome harbor the same IS elements there can be homologous recombination between chromosome and plasmid. By definition, this makes the plasmid an episome that can promote high frequency exchange or recombination (e.g., Hfrs).

2. Composite transposons (denoted by symbol *Tn*):

- a) *Tn* elements stem from two IS elements that insert near one other. The regions (sequences) between the two elements can be "mobilized" by the joint action of the two IS elements. This is of significance in that many *Tn* elements possess genes that confer resistance to antibiotics between the two IS elements.
- b) *Tn* transposition is regulated by a "repressor" that appears to exist to keep the elements somewhat quiescent.

3. *Tn3* elements are simply large transposable elements that are not generated by flanking IS elements (as in *Tn* elements). They are generally ~5,000 bp, have ~386 bp inverted repeats at both ends, and carry antibiotic resistant genes.

4. Medical significance:

- a) Many bacterial transposons carry genes for generic antibiotic resistance. These genes typically produce enzymes that cleave and render antibiotics non-functional. Resistance is to several antibiotics within a class of antibiotic compounds, and differs from resistance conferred when cell metabolites affected by antibiotics are altered (e.g., streptomycin resistance in *E. coli*).
- b) Resistance of this sort when transposed to a plasmid/episome [*conjugative R plasmids*] can then be transferred horizontally as well as vertically.
- c) Species pathogenic to humans and that harbor such plasmids include *Staphylococcus*, *Neisseria*, *Shigella*, and *Salmonella*.

B. Transposable elements in eukaryotes are of two types: those that have DNA as their genetic material, and those that have RNA as their genetic material.

1. DNA transposable elements are exemplified by the P elements in *Drosophila*.

- a) P elements were discovered when it was found that certain strains of *Drosophila* exhibited an assortment of aberrant phenotypes, including elevated mutation (and reversion), chromosome breakage, and sterility. This phenomenon was termed “hybrid dysgenesis” and turned out to be situations where transposable P elements had been induced to “jump.” The phenomenon was termed “hybrid dysgenesis” because normally (within populations) the P elements are quiescent and do not “jump.” When “hybrids” were made between individuals from different geographic populations, the elements “moved” and promoted the dysgenic phenotypes.
- b) P elements vary in size (the largest are nearly 3,000 base pairs in length). Complete (intact) P elements possess a gene for a transposase. The number of P elements per individual varies from a few to up to 50.
- c) P elements characteristically have a 31 bp inverted repeat at both ends and an 8 bp target-site duplication.
- d) There are two experimental uses of P elements.
 - (i) *Transposon tagging*, where genes mutated by P element insertion can be isolated and “discovered” by using the P element sequence as a “tag”; and
 - (ii) *Transformation vectoring*, where genes or sequences of interest are “vectored” into a chromosomal location by putting the gene/sequence of interest into an incomplete P element (no transposase) and carrying out a mixed infection (transformation or electroporation) with a complete P element.

- e) Another group of transposable elements, initially discovered in *Drosophila* are the *mariner* elements. Mariner elements appear to be a fairly widespread transposon of roughly 1,200 base pairs.
 - (i) Mariner elements initially were found in arthropods, but now have been identified (by sequence similarity) in humans and in plants
 - f) Interestingly, mariner elements are found in distantly related species, suggesting the possibility that mariner elements may be horizontally transferred, perhaps by a virus that has a wide range of host species.
2. Retrotransposons are transposable elements that have RNA as their genetic material. There are two types: retrovirus-like elements and retroposons.
- a) Retrovirus-like elements:
 - (i) The basic structure of retrovirus-like elements is a central coding region of two genes flanked by *long terminal repeats* [LTRs] that are oriented in the *same* direction and bounded by short inverted repeats. THE LTRs play a role in integration of the element into the host genome. The two genes are homologous to two genes in retroviruses and encode a structural protein of the virus capsule and a reverse transcriptase/integrase enzyme.
 - (a) Minimal (active) retroviruses carry a third gene that codes for a protein of the virus envelope. Active retroviruses are capable of exiting cells and infecting other cells.
 - (ii) Transposition involves transcription (RNA synthesis) of the DNA sequence integrated in the chromosome, reverse transcription of the RNA, synthesis of a double-stranded DNA from the RNA, and insertion into a new chromosomal location.
 - b) Retroposons:
 - (i) These are elements that move through an RNA intermediary but do *not* possess direct or inverted repeats at their termini. They possess instead a string of A=T base pairs at one end (of the DNA), and presumably represent a copy from reverse transcription of the poly-A tail of the mature RNA transcript.
 - (ii) Several retroposons are known in *Drosophila*. They appear to occur non-randomly at the ends of chromosomes and to function in replicating telomeres.
 - (iii) Some LINE sequences in mammals are retroposons, and the LINE-1 retroposon is the only transposable element thus far documented in humans.