Presented by: Dr. Asma

Transposons
(Transposable Elements)

A transposable element (**TE**) is a DNA sequence that can change its relative position (self-transpose) within the genome of a single cell.

Recombination allows the movement of transposable elements, or Transposons. These segments of DNA, found virtually all cells, move, or "jump," from one place on a chromosome (the donor site) to another on the same or a different chromosome (the target site).

INTRODUCTION

- Barbara McClintock first discovered transposable elements in corn in the 1940.
- Transposable elements, transposons or even jumping genes are regions of genome that can move from one place to another.
- The first transposable element is discovered in bacteria is called insertion sequences or IS elements. It turns out that these are the simplest transposons.
- Comprises about 45% in human genome.
- Inserts at many different locations.

Discovery of transposable elements

- In 1940s by McClintock Barbara in maize
- Found genetic elements regularly jump to new location affect gene expression
- Maize kernels show variation in colour.
- Later in 1960s bacteria & bacteriophages were shown to posses TE.
- Development of recombinant technology demonstrate TE exist in all organisms.

General characteristics of TE

- They were found to be DNA sequences that code for enzymes, which bring about the insertion of an identical copy of themselves into a new DNA site.
- Transposition events involve both recombination and replication processes which frequently generate two daughter copies of the original transposable elements. One copy remains at the parent site and another appears at the target site.
- A transposable element is not a replicon. Thus, It cannot replicate apart from the host chromosome.

Types of transposable elements

Different types of transposable elements are present in both prokaryotes and eukaryotes.

There 3 types in prokaryotes

a) Insertion sequences

b) Transposons

c) Bacteriophage μ

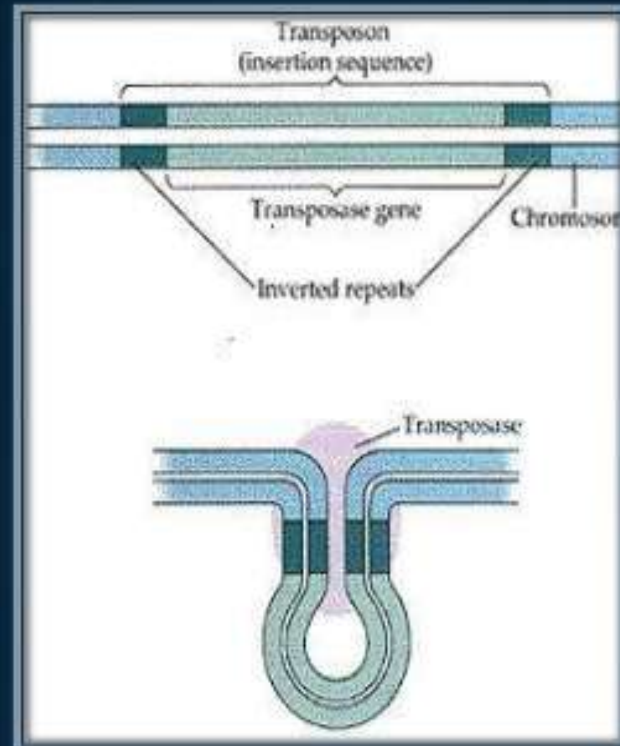
Insertion sequence:

IS were the first transposable elements identified as spontaneous insertion in some bacterial operon.

❖The IS are shorter (800 to 1500 base pairs) and do not code for proteins.

❖In fact, IS carry the genetic information necessary for their transposition (the gene for the enzyme transposase).

❖There are different IS such as IS1, IS2, IS3 and IS4 and so on in *E.coli*.



Transposons:

❖Transposons are similar to IS elements but carry additional genes.

❖Tn are several thousands base pair long and have genes coding for one or more proteins

❖On either side of a transposon is a short direct repeat. The sequence into which the transposable element insert is called target sequence

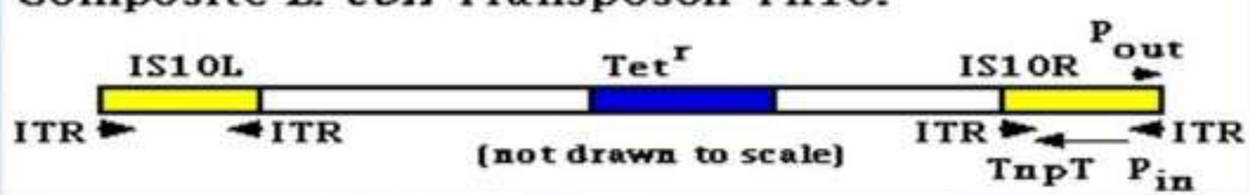
Two types of transposon

a) Composite transposon
b) Noncomposite transposon

Composite transposon:

- Any segment of DNA that flanked by two copies of an IS and central coding region with antibiotic resistant gene and no marker gene.
- Designated by the Tn.

Composite *E. coli* Transposon Tn10:



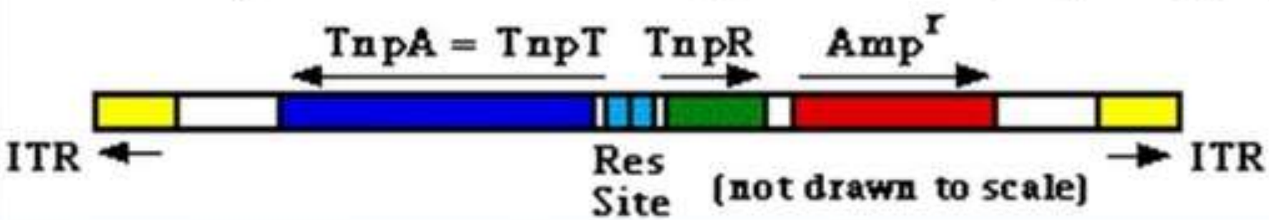
Noncomposite transposon:

Do not terminate with IS elements but contain terminal inverted repeats.

Has three genes at central region

- 1.bla-beta-lactamase-breaks amphicilin
- 2.tnpA-Transposase-for insertion
- 3.tnpB-resolvase-recombinational events

Non-composite *E. coli* Transposon Tn3 (TnpA type):



<u>Bacteriophage Mu</u>

- ✓The longest transposon knows so far.
- ✓Caries numerous genes for viral head and tail formation.
- ✓The vegetative replication of mu produces about 100 viral chromosomes in a cell arises from the transposition of Mu to about 100 different target sites.
- ✓Therefore considered as giant mutator transposon.

Mechanism of transposition

Movement of transposon occurs only when enzyme transposase recognizes and cleaves at either 5′ or 3′ of both ends of transposon and catalysis at either 5′ or 3′ of both the ends of transposon and catalysis staggered cut at the target site

Depending on transposon, a duplication of 3 to 12 bases of target DNA occurs at the site where insertion is to be done. One copy remains at each end of the transposon sequence.

After attachment of both ends of transposon to the target site, two replication forks are immediately formed. This stage there starts two paths for carrying out onward.

Transposition

- ✓Mechanism of movement of TE from one location to another.
- ✓In the process staggered cuts are made in the target DNA.
- ✓The TE is joined to single stranded ends of the target DNA
- ✓Finally DNA is replicated in the single stranded gap.

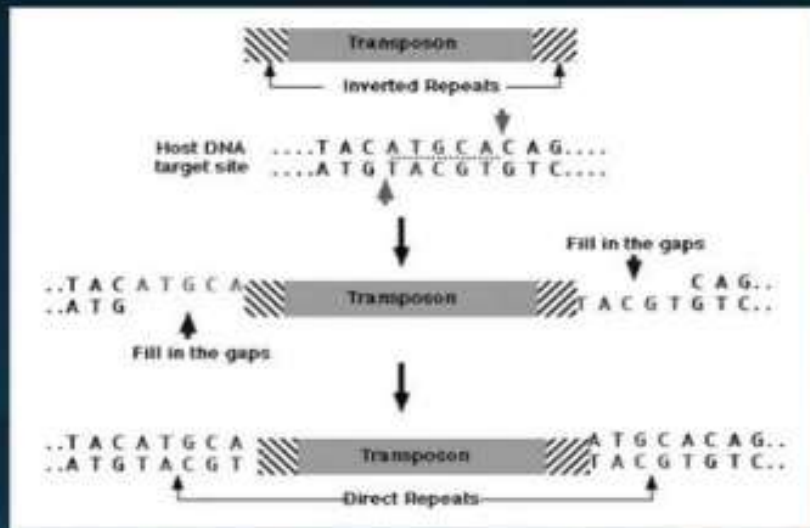
Transposable elements in Bacteria

There are three main types:

- **The insertion sequences or IS elements**
- **Composite transposons**
- **The Tn3 elements.**

IS Elements

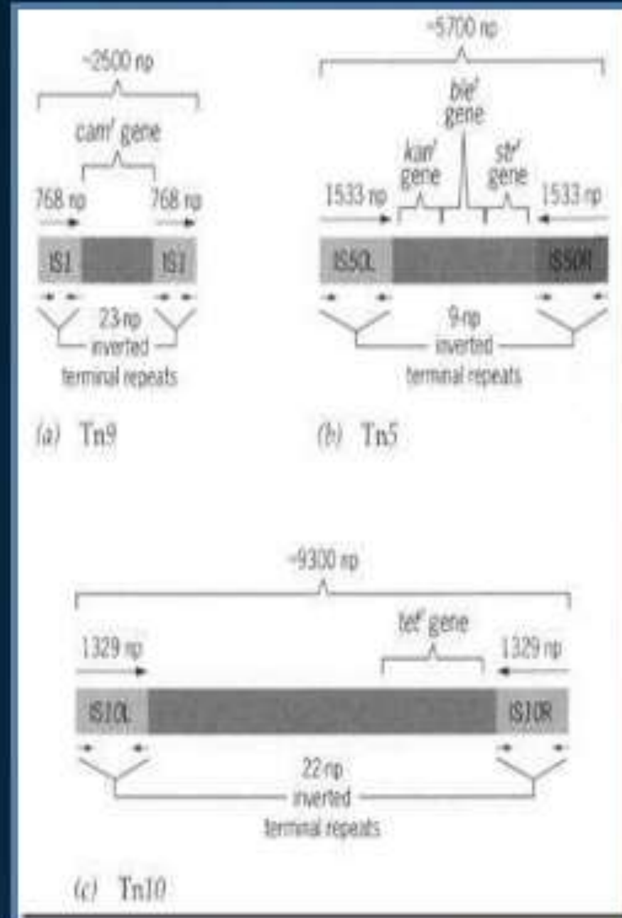
IS elements are compactly organised. Typically, they consist of fewer than 2500 nucleotide pairs and contain only genes whose product is involved in promoting or regulating transposition



At least some IS elements encode a protein that is needed for transposition. This protein, called transposase, seems to bind at or near the ends of the element, where it cuts both strands of the DNA. Cleavage of DNA at these sites excises the element from the chromosome or plasmid, so that it can be inserted at a new position in the same or a different DNA molecule. IS elements are therefore cut –and – paste mechanism.

Composite Transposons

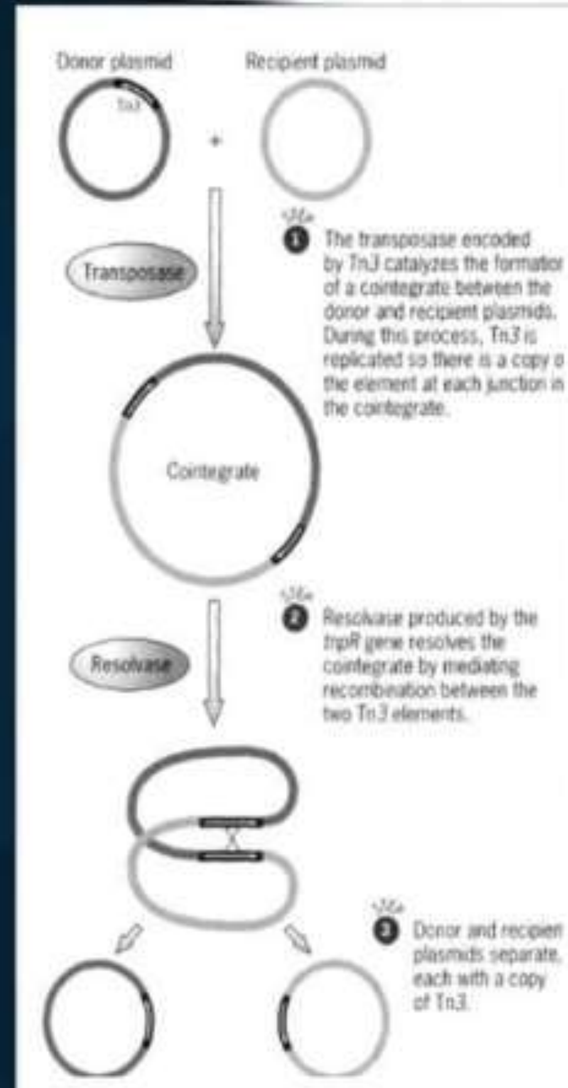
Composite transposons, which are bacterial cut-and-paste transposons denoted by the symbol Tn, are created when two IS elements insert near each other. In Tn9, the flanking IS elements are in the same orientation with respect to each other, whereas in Tn5 and Tn10, the orientation is inverted. The region between the IS elements in each case of these transposons contains gene that have nothing to do with transposition.



Tn3 Elements:

❖The elements in this group of transposons are larger than the IS elements and usually contain genes that are not necessary for transposition.

❖The transposition of Tn3 occurs in two stages. First, the transposase mediates the fusion of two circular molecules, one carrying Tn3 and other not. The resulting structure is called a Cointegrate. During this process, the transposon is replicated, and one copy is inserted at each junction in the cointegrate are oriented in the same direction. In the second stage tnpR encoded resolvase generates two molecules, each with a copy of the transposon.



Transposable elements in eukaryotes:

- In eukaryotes TE can be divided into 2 groups
- One group is structurally similar to TE found in bacteria.
- Other is retrotransposon, they use RNA intermediates.
- These include the Ty elements in yeast, copia elements in Drosophila, Alu sequences in humans.

Transposons in maize

The bacterial transposons were discovered in 1940s by Barbara McClintock who worked with maize. She found that they were responsible for a variety of types of gene mutation, usually

- ✓ Insertion
- ✓ Deletion
- ✓ Translocation

Transposons in *Drosophila*

P elements are class II transposons found in drosophila's they do little harm because expression of their transposase gene is usually repressed. However, when male flies with p elements mate female flies lacking them, the transposase becomes active in the germ line producing so many mutations that their offspring are sterile. P elements seem to have first appeared I drosophila melanogaster about 50 years a

Elements in Humans

- About 45% of human genome consists of sequence derived from TE.
- Common TE in human genome is Alu transposed through an RNA intermediate.
- Alu belongs to repetitive sequences are collectively called as SINE's constitute 11% of human genome.
- It also has LINE's usually about 6000bp constitute 21% of human genome.
- These two are identified as cause of mutations in 20 cases of genetic diseases

Effects caused by Transposons

I. Transposons are mutagens. They can cause mutations in several ways.

II. A transposons inserts itself into a functional gene, it will probably damage it. Insertion into exons, introns, and even into DNA flanking the genes can destroys or alter the genes activity.

Mutations responsible for some human genetic diseased, including,

a. Hemophilia A, Hemophilia B.
b. X-linked severe combined immunodeficiency
c. Porphyria
d. Cancer , etc,.

Uses of Transposons.

- As cloning vehicles
- Transformation vectors for transferring genes between organisms.
- Also drug resistance genes encoded by many transposons are useful in the development of plasmids as cloning vehicles.
- Transposons mutagenesis:
- Use of transposons to increase rate of mutation due to insertional inactivation

Conclusion:

- Transposons are present in the genomes of all organisms, where they can constitute a huge fraction of the total DNA sequence. They are a major cause of mutations and genome rearrangement.
- The ability of transposable elements to insert and to generate deletions and inversions accounts for much of the macromolecular rearrangement.
- They cause mutation which is used in the production of different colour of grapes, corn and other fruits.
- As a result they are used in the genetic studies.