

Transposition

Evidence

Mechanisms:

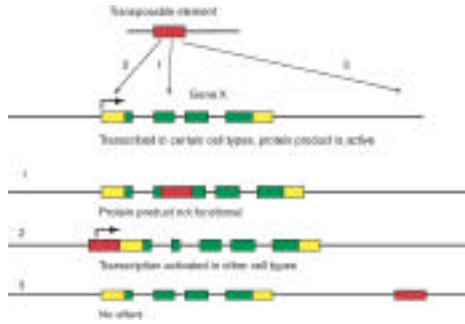
DNA-mediated

RNA-mediated

Transposable elements

- Mobile genetic elements - they move from one location in the genome to another
- Found in all organisms (so far studied)
- Effects:
 - Insertion near or within a gene can inactivate or activate the target gene.
 - Cause deletions, inversions, and translocations of DNA
 - Lead to chromosome breaks

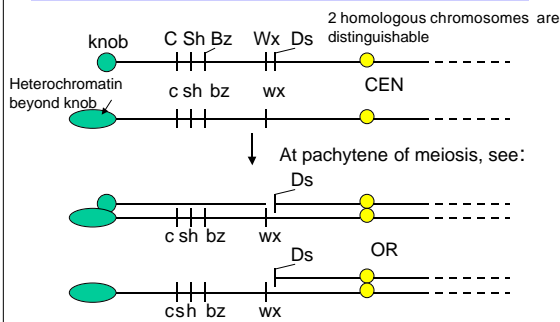
Effects of transposable elements depends on their location



Observations of B. McClintock (1930's-1950's)

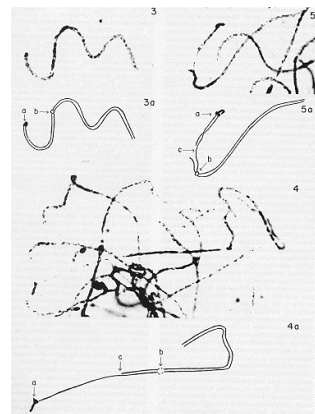
- Certain crosses in maize resulted in large numbers of *mutable* loci.
 - The frequency of change at those loci is much higher than normally observed.
- Studies of these plants revealed a genetic element called "Dissociation" or *Ds* on the short arm of chromosome 9.
- Chromosome breaks occurred at the *Ds* locus, which could be observed cytologically
 - i.e. by looking at chromosome spreads from individual cells, e.g. sporocytes.
- Frequency and timing of these breaks is controlled by another locus, called "Activator" or *Ac*.

Breaks are visible cytologically on morphologically marked chromosome 9

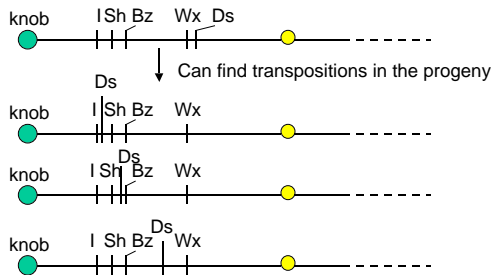


McClintock's chromosome breaks, 1952 CSHSQB

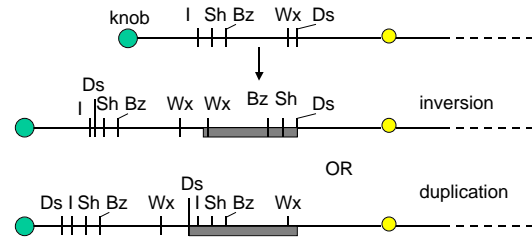
Chromosome 9, short arm, pachytene phase of meiosis



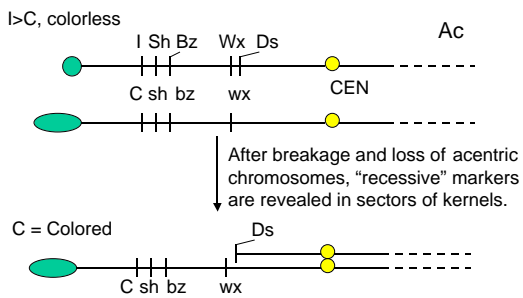
Ds activity can appear at new locations on chromosome 9



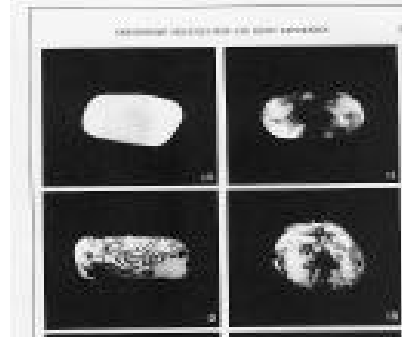
Appearance of Ds at a new location is associated with breaks: e.g. Duplications and Inversions



In the presence of Ac, Ds events lead to variegation in sectors of kernels

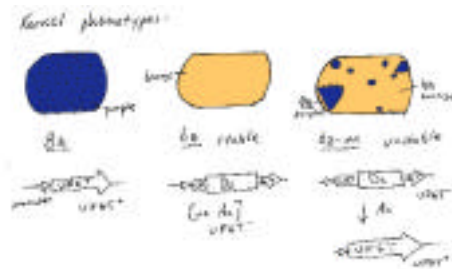


Variegation in sectors of kernels



Ac need not remain at any one location in the genome

Transposition of Ds can lead to formation of mutable loci, controlled by Ac

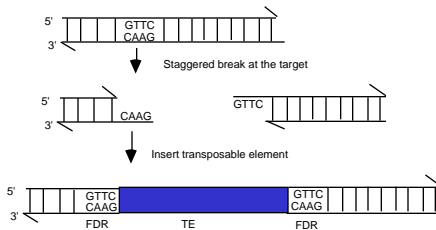


Variegation in wild flox



Mechanisms of Transposition

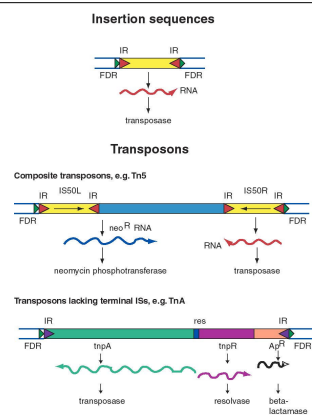
Flanking direct repeats are generated by insertions at staggered breaks



Transposable elements that move via DNA intermediates

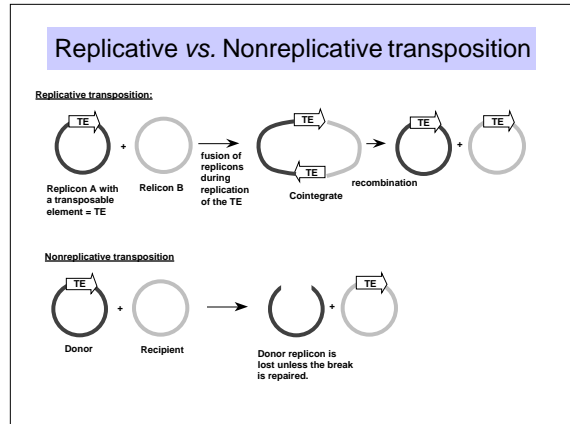
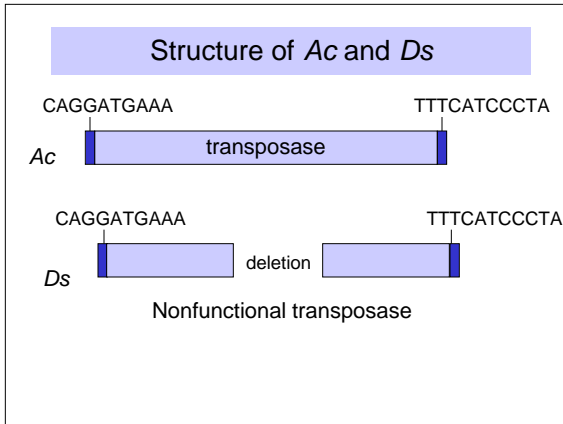
- Bacterial insertion sequences
 - Inverted repeat at ends
 - Encode a transposase
- Bacterial transposons:
 - Inverted repeat at ends
 - Encode a transposase
 - Encode a drug resistance marker or other marker
 - TnA family: transposase plus resolvase

IS elements and transposons



Ac/Ds transposons in maize

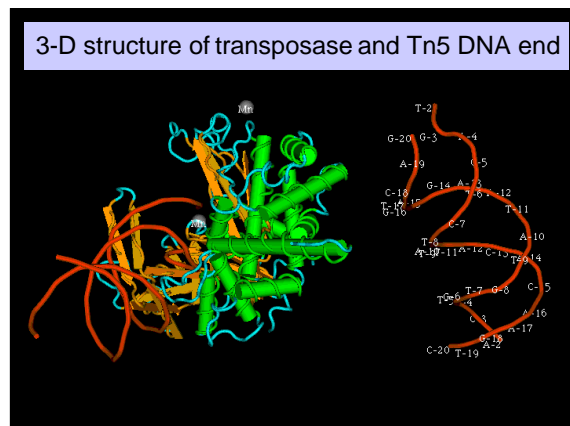
- *Ac* is autonomous
 - Inverted repeats
 - Encodes a transposase
- *Ds* is nonautonomous
 - Inverted repeats
 - Transposase gene is defective because of deletions in coding region



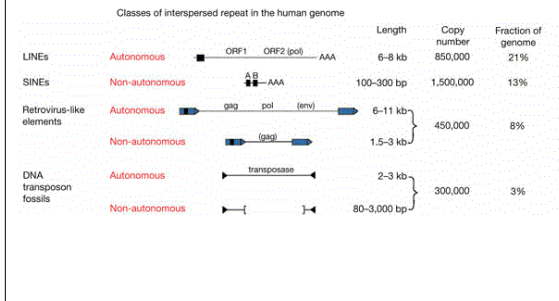
- ### Mechanism for DNA-mediated transposition
- Transposase nicks at ends of transposon (note cleavage is at the same sequence, since the ends are inverted repeats).
 - Transposase also cuts the target to generate 5' overhangs
 - The 3' end of each strand of the transposon is ligated to the 5' overhang of the target site, forming a **crossover structure**.

- ### Replicative transposition from the crossover structure
- The 3' ends of each strand from the staggered break (at the target) serve as primers for repair synthesis.
 - Copying through the transposon followed by ligation leads to formation of a **cointegrate structure**.
 - Copying also generates the flanking direct repeats.
 - The cointegrate is resolved by recombination.

- ### Nonreplicative transposition from the crossover structure
- Crossover structure is released by nicking at the other ends of the transposon (i.e. the ones not initially nicked).
 - The gap at the target (now containing the transposon) is repaired to generate flanking direct repeats.



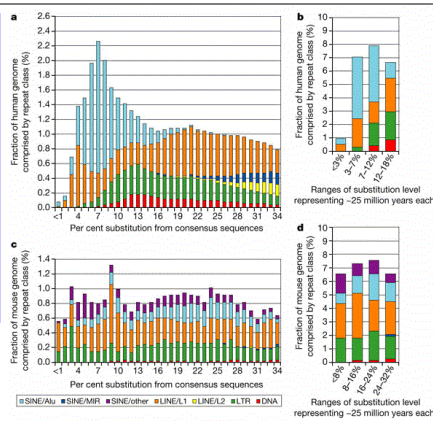
Almost all transposable elements in mammals fall into one of four classes



Transposable elements that move by RNA intermediates

- Called **retrotransposons**
- Common in eukaryotic organisms
 - Some have long terminal repeats (LTRs) that regulate expression
 - Yeast *Ty-1*
 - Retroviral proviruses in vertebrates
 - Non-LTR retrotransposons
 - Mammalian LINE repeats (long interspersed repetitive elements, L1s)
 - Similar elements are found even in fungi
 - Mammalian SINE repeats (short interspersed repetitive elements, e.g. human *Alu* repeats)
 - *Drosophila jockey* repeats
 - Processed genes (have lost their introns). Many are pseudogenes.

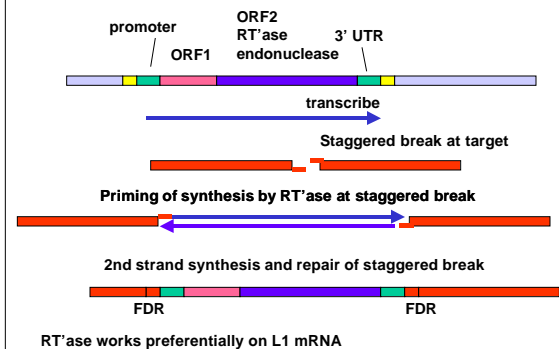
Age distribution of repeats in human and mouse



Mechanism of retrotransposition

- The RNA encoded by the retrotransposon is copied by reverse transcriptase into DNA
- Primer for this synthesis can be generated by endonucleolytic cleavage at the target
- Both reverse transcriptase and endonuclease are encoded by SOME (not all) retrotransposons
- The 3' end of the DNA strand at the target that is not used for priming reverse transcriptase can be used to prime 2nd strand synthesis

Events in L1 transposition



Recombination between two nearly identical sequences (e.g. transposons) will lead to rearrangements

- Deletion if the repeats are in the same orientation
- Inversion if the repeats are in the opposite orientation

Consequences
of
recombination
between two
transposons

