I. Barbara McClintock and Ds/Ac in maize

Ds (*Dissociation*) factor causes tendency toward chromosome breakage, but only if the individual also has *Ac* (*Activator*).

Ds could not be mapped – it seemed to occur in different places in the genome in different lines, and could move to a new place in different progeny; she called this **transposition**.

Ds can cause **unstable** mutations, that frequently revert back to wild-type, but only if *Ac* is present.

Ds is a **transposable element**; it is **non-autonomous**, because it requires *Ac* to be present. *Ac* encodes the **transposase**, the enzyme that catalyzes transposition.

II. Transposable elements

Transposable elements (TEs): segments of DNA that can move (**transpose**) in the genome.

Many different types; each can be present in a few copies to hundreds of thousands of copies per genome. 45% of human DNA is derived from TE sequences.

TEs can cause mutations by inserting into genes; subsequent excision of the TE leads to reversion back to wild-type. TEs can also damage DNA by creating breaks when they excise.

TEs can mediate some aspects of evolution, by creating duplications, and by **horizontal** transmission across species.

III. Retrotransposons

In eukaryotes, many TEs transpose via an RNA intermediate:

1) The TE is transcribed by RNA polymerase
2) A DNA copy is made from the RNA by the enzyme **reverse transcriptase** (RT)
3) The DNA copy gets integrated into a new site in the genome by an integrase

Transposition via RNA intermediate was shown by putting an artificial intron into the yeast *Ty1* element; the intron was lost during transposition.

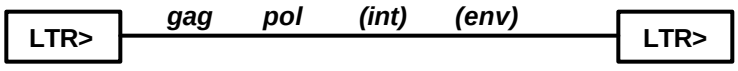
RT is encoded by the retrotransposon, not the host genome.

RT is an RNA-dependent DNA polymerase; it is very useful in genetic engineering.

RT can sometimes make a copy of an RNA from a host gene, which can then integrate back into the genome. This is called a **pseudogene**; it lacks introns (because it was made from mRNA) and has a poly-A region at the 3' end; pseudogenes usually lack promoters, so they are not transcribed. About 1/3 of the 1000 tRNA genes in the human genome are pseudogenes.

Viral retrotransposons are similar in structure and action to retroviruses, but never leave cell.

Structure (see p. 97 also)



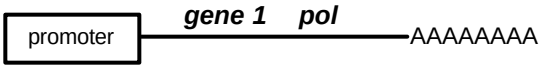
LTR = **long terminal repeat**; transcription starts within 5' LTR, goes into 3' LTR

may include genes for protease (*gag*), reverse transcriptase (*pol*), integrase (*int*), and viral coat (envelope) protein (*env*)

Examples: *copia* and *gypsy* in Drosophila (about 10-50 copies of each), *Ty* in yeast (60-70 copies).

Non-viral retrotransposons do not have LTRs; most common TE in human genome (most are inactive and cannot move)

LINE = **l**ong **in**terspersed **e**lement



nick genomic DNA, and use DNA end to prime RT, which is often incomplete
autonomous elements have both genes and promoter

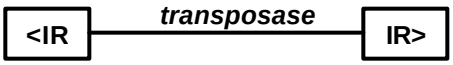
Example: human L1, present in 100,000 copies per genome

SINE = **s**hort **in**terspersed **e**lement
promoter derived from tRNA or another RNA gene
no genes encoded; uses LINE machinery to move, therefore **non-autonomous**

Example: human Alu element, present in >10^6 copies (5% of our DNA)

IV. DNA transposons

Structure:



"Cut-and-paste" mechanism of transposition:

1) DNA segment directly excised from surrounding DNA by **transposase**
2) Transposase carries the TE elsewhere and integrates it into a new site
3) Original site has a DNA break, which gets repaired by the cell. This often involves copying from the sister chromatid. Since the sister still has the TE, the result is that a copy of the TE is placed back into the original position, yielding in a net gain of one copy in the genome.

Copies that have a deletion or mutation in the transposase gene are non-autonomous – they can still transpose if transposase is provided by an intact copy of the same TE.

Examples: Maize *Ac* (*Ds*) Drosophila *P* and *hobo* elements (0-50 per genome), *Mariner* and *PiggyBac* (widespread species distribution)