Chapter 13
Transposable Elements of Eukaryotes

- Ac/Ds System of Zea mays
- Retrotransposons
Two different types of transposable elements

A) Transposons with terminal inverted repeats (TIRs)
   transpose by a cut and paste mechanism, via excision and integration

B) Retrotransposons
   share similarities with retroviruses and transpose replicatively
The *Ac/Ds* System of *Zea mays*

Variegated phenotypes
The A1 gene of Z. mays encodes an enzyme for anthocyanin biosynthesis. Integration of a transposon (for example Ac) into this gene results in loss of function of A1. Wild type A1 is converted to a1::Ac (also designated as a1-m).
Excision of $Ac$ from $A1$ can restore the wildtype phenotype, therefore alleles that contain transposons are called mutabel alleles ($a1-m$). These alleles typically exhibit variegated phenotypes, due to somatic reversions.
The *Activator (Ac)* transposable element

The *Ac* element is about 4 kb long and encodes the transposase, that is required for transposition of *Ac*. *Ac* has terminal inverted repeats (11bp) at the ends that are needed for transposition.
The Ac element is called the **autonomous element**, because it encodes all functions for its transposition. There are deletion derivatives of Ac which are called **Ds elements**. Ds are **defective elements** that cannot promote transposition. However, if Ac and Ds are present in one cell, then Ds elements also transpose.
Mechanism of transposition of transposons with TIRs
Some *Ds (Dissociation)* elements not only transpose, but also break chromosomes in the presence of *Ac*. This function was first discovered by Barbara McClintock.
Genetic detection of chromosome breakage

Recessive phenotypes appear

Deleted and lost

Resulting tissue is $c$ (colorless), $sh$ (shrunken), $bz$ (bronze), $wx$ (waxy)
Cross:  $C\, Ds/C\, Ds \times c/c + Ac$ 

- Solid pigment: $\sim 1/2 \quad C\, Ds/c$ 
- Colorless patches: $\sim 1/2 \quad C\, Ds/c; \, Ac$ 
- Unstable colorless: 1 kernel $C-m/c; \, Ac$
Transposition of *Ac* and *Ds*

Stable *Ds*-inactivated allele of gene 1

Reversion in presence of *Ac* only

Transposition to gene 2

Unstable *Ac*-inactivated allele of gene 1

Reversion (and transposition) by *Ac*
Retrotransposons

are derived from retroviruses
The life cycle of a retrovirus
Genes in retroviral DNA and viral retrotransposons

Retroviral DNA

Ty 912 (yeast)

copia (Drosophila)
Viral retrotransposons contain LTRs and behave like retroviruses in the genome
The Ty element of yeast is a retro transposon
Demonstration of a RNA intermediate in transposition.
Message

Retrotransposons are highly repetitive sequences in the genomes. This feature can be explained by the replicative transposition mechanism of retro elements. They can make up 20 - 30% of genomes.
Distribution of retro elements in a human gene
Mobile DNA elements probably had a significant influence on evolution

- Spontaneous mutations may result from the insertion of a mobile DNA element into or near a transcription unit
- Homologous recombination between mobile DNA elements may contribute to gene duplication and other rearrangements, including duplication of introns, recombination of introns to create new genes, and control of gene expression
- Transposons create sequence variation upon excision (footprints)
- Transposons contributed to the evolution of the immune system
Antibody genes are assembled by rearrangements of germ-line DNA

Antibody domain structure
H = Heavy chain
L = Light chain
V = variable domain
C = constant domain
Rearrangement of light-chain DNA

the deleted fragment of genomic DNA is excised like a transposon by RAG1 and RAG2 proteins
Figure 1 Transposition mediated by the RAG1/RAG2 transposase. The excision step is identical to the first step in V(D)J recombination; the second step is now reported by Agrawal et al.\textsuperscript{1} and Hiom et al.\textsuperscript{2}. The combination of excision and integration is a complete transposition reaction, occurring by a similar mechanism to that used by other transposable elements\textsuperscript{13}. After excision, the V and D segments have a hairpin at their ends, and can go on to be joined (‘coding joint’). Owing to the staggered position of the bonds that are attacked in the target DNA, the integrated RAG transposon is initially flanked by five-nucleotide single-strand gaps.
Mechanism of transposition of transposons with TIRs