Reverse Transcriptase-containing DNA Viruses and Plasmids Lack Integrase

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125. *Reverse Transcriptase-containing DNA Viruses and Plasmids Lack Integrase*

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The transfer of genetic information from RNA into DNA was thought to be a unique feature of retroviruses, but there is a growing evidence that it may be a more general strategy.[1] Both DNA viruses, hepatitis B virus (HBV)[2] and cauliflower mosaic virus (CaMV)[3] as well as eukaryotic transposons, *Drosophila copia*[4] and yeast Tyl[5] elements were found to have RNA intermediates that are reverse transcribed into DNA. Furthermore, these DNA viruses and a *Drosophila copia*-like element 17.6 have polymerases which share striking sequence homologies with retroviral *pol* gene products for a region (RT domain) that is thought to carry reverse transcriptase activity.[6),7]

Another line of evidence for the possibility of nonretroviral reverse transcriptase came from a recent report by Michel and Lang.[8] Following the suggestion for the possibility of a Neurospora mitochondrial plasmid being related to transposon,[8] they compared amino acid sequences predicted from the ORFs (open reading frames) of fungal mitochondrial class II introns together with a mitochondrial plasmid with those of polymerases of retroviruses, CaMV, HBV and a *Drosophila* transposon 17.6 and found remarkable homologies within the RT domain. This finding added further evidence for the view that the RT-like sequence can now be recognized as a ubiquitous one distributed over many genetic elements of such a wide evolutionary distance. In addition, such a widespread occurrence of similar sequences suggests that these homologies were derived by divergence, but not by convergence.

Apart from the RT-like sequence, the ORF product of *copia*-like element 17.6 contains another sequence related to the DNA endonuclease (EN) of retroviral *pol* gene products,[10] thought to be important in integration of viral DNA into host DNA. This strongly suggests that the transposition mechanism of the *copia*-like element is retrovirus-like. Interestingly CaMV polymerase exhibits a striking homology with ORF2 product of the 17.6 over its entire region, but is completely lacking the EN-like sequence.[10] Also no EN-like sequence presents in HBV.[10] The *Drosophila copia* is distantly related to retroviruses and its putative polymerase shares less extensive homology with retroviral *pol* gene products,[11] but has both highly conserved stretches of amino acids -YXDD- (X, any one of amino acids) flanked by three hydrophobic residues and -GXXERXN- which are diagnostic of the RT and EN domains, respectively. Similar searches revealed the presence of both sequences in ORFs of mitochondrial introns but the mitochondrial plasmid lacks the latter sequence (Fig. 1). Interestingly the RT and EN domains present in reverse order in the *copia* and mitochondrial introns.

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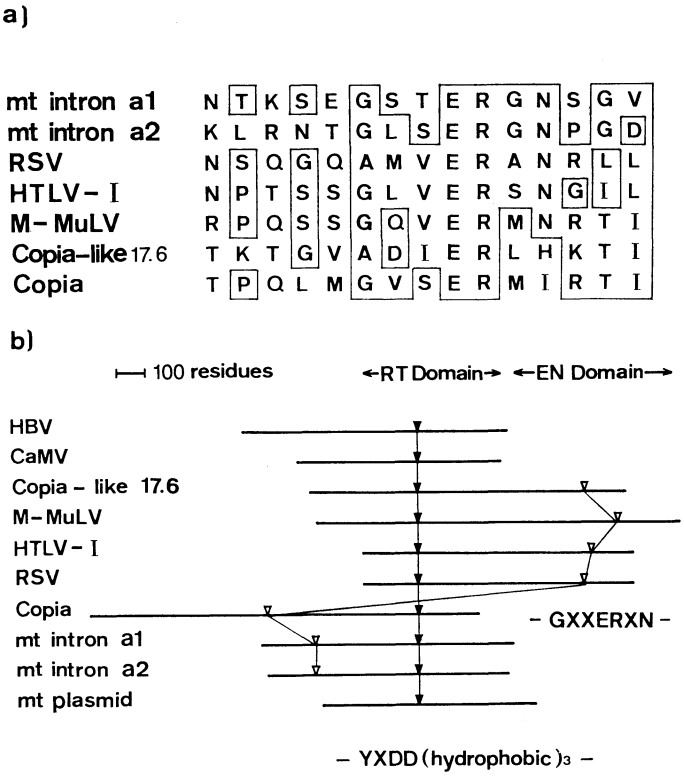

Fig. 1. Alignment of amino acid sequences of viral and transposon polymerases. a: Alignment for a highly conserved segment of the DNA endonuclease (EN) domain. Mt introns a1 and a2, amino acid sequences predicted from ORFs in introns a1 and a2 of yeast mtDNA-coded cytochrome oxidase subunit I gene. Mt plasmid, the sequence predicted from ORF in *Mauriceville* mitochondrial plasmid. Most common amino acids (identical or chemically similar amino acids) were boxed. b: Homology map. Positions of highly conserved stretches of amino acids in the RT (reverse transcriptase) and EN domains were indicated by ▼ and ▽, respectively. Their consensus sequences were also shown.

In conclusion, of all the reverse transcriptase-containing viruses and transposons examined so far, DNA viruses and plasmids lack endonuclease-related domain, which is in sharp contrast to retroviruses and transposons involving the endonuclease and intrachromosomal phase, thought to be important in their life cycle. Although HBV is known to have an intrachromosomal phase,[12] the mechanism of integration into host DNA possibly differs from that of retroviruses. Mitochondrial plasmids could be transposons that lack an intrachromosomal phase. It may be of interest to know whether or not the relationship between the presence of DNA endonuclease and the chromosomal form (RNA or DNA) could be extended to most reverse transcriptase-containing viruses. Further data will clarify this point.

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