Structure and Function of Viroids

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Viroids are an independent class of plant phatogens which are distinguished from viruses by the absence of a protein coat and by their unusually small size. They have been characterized as circular chains composed of about 360 nucleotide residues (1).

Sequence analysis of the potato spindle tuber viroid (2) and physicochemical studies of 5 different viroid species (3-5) have shown that, as a result of intra molecular base pairing, viroids form a unique rod-like secondary structure *in vitro*, which is characterized by a serial arrangement of double-helical sections and internal loops. There is no indication for an additional tertiary structure because all parts of the molecule are freely accessible to ligand interaction. During the denaturation all of the native base pairs of viroids are dissociated in one highly co-operative transition, and in the same process very stable hairpins are formed that are not present in the native structure. The circularity of the molecule is needed to guarantee the extraordinary high co-operativity. In specifically nicked molecules the left and the right half of the molecule are thermodynamically uncoupled.

The common principle of the structure and the structural transitions in viroids can now be interpreted by comparing three different viroid species the sequences of which have been determined recently (6). The close similarity between these viroid is more expressed in the overall structure and in thermodynamic and functional domains than in the primary sequence. Characteristically, regions of premelting, regions of stable hairpins, and the sequence UACUACCCGGUGG which is opposite to one of the stable hairpins, are the most conservative sequences in the molecules (6).

From the uniform features mentioned above a hypothesis for the origin and the pathogenic action of viroids could be deduced (7). The conservative sequence UACUACCCGGUGG corresponds very closely to a segment in the small nuclear RNA U1 which has been found identical in isolates from several organisms and was considered to support mRNA splicing by aligning intron-exon junctions (8). A model is discussed in which viroids may have originated as escaped introns and may act today as pathogens by strong interference with the splicing process. The thermodynamic properties of the complexes of viroids with RNA U1 and mRNA are estimated showing that these complexes were only possible by simultaneous formation of one or two of the stable hairpins which had been detected in the earlier experiments.

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