# Sequence homologies between a viroid and a small nuclear RNA (snRNA) species of mammalian origin

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## 1. INTRODUCTION

Viroids are small, covalently closed circular single-stranded RNA molecules [1] with a length of ~250–370 nucleotide residues and a highly base-paired rod-like secondary structure [2–6]. They are pathogenic to higher plants and seem to replicate the nuclei of their hosts [7,8]. Despite a firm knowledge of the primary and secondary structure of some of them, and rapidly accumulating information about their mode of replication [9–12], practically nothing is known about the mechanism by which they induce disease symptoms. To support the idea that viroids may interfere with host gene expression, the hypothesis was advanced that the viroid RNA could qualify as a class of small nuclear RNA (snRNA) both in terms of its locus and metabolic stability [13]. At that time no allusion to a possible similarity in primary structure between these 2 molecular entities was made. A more precise picture emerged when it was shown [14], by comparing published sequences, that potato spindle tuber viroid (PSTV) contains a stretch of 23 nucleotides that shows homology with the 5′-end of mammalian U1 RNA, which is a member of the snRNA series (U1–U6) and believed to play a vital role in the splicing of mRNA [15]. Thus, it has been proposed that viroids may interfere with the splicing of host pre-mRNA, mediated by the plant equivalent of U1 RNA. It was expected [14] that all viroids should have in common a sequence homologous with the 5′-end region of this snRNA species. Indeed, the same homology region was later found [5] in 2 additional viroids, chrysanthemum stunt viroid (CSV) and citrus exocortis viroid (CEV). In this paper we show that:

(i) A similar homology region exists in another viroid, avocado sunblotch viroid (ASBV) as well;

(ii) This particular viroid contains >60% of the sequence of U5A RNA from Novikoff hepatoma cells;

(iii) Sequence homologies between viroids and mammalian snRNAs are more general than has been anticipated.

## 2. APPROACH AND RESULTS

The complete primary and secondary structure of ASBV has been established [3]. Strangely enough, for this particular viroid no sequence homology with the 5′-end of chicken U1 snRNA was noticed [3]. However, a closer, computer-aided inspection of the primary structures of Novikoff hepatoma U1 RNA and ASBV revealed to us that sequence homology with the 5′-end of U1 RNA does exist in ASBV and that it even extends over a stretch of ~40 nucleotide residues (fig.1). This finding prompted us to look for further possible sequence homologies between ASBV and snRNAs other than U1. We have found a striking homology (fig.2) between stretches of ASBV and stretches of U5A RNA from Novikoff hepatoma cells.

It became apparent that >60% of the sequence of U5A RNA from Novikoff hepatoma cells is contained in the ASBV molecule. The sequence between nucleotide residues 13–21 of U5A is also present in the form of an uninterrupted stretch of 9



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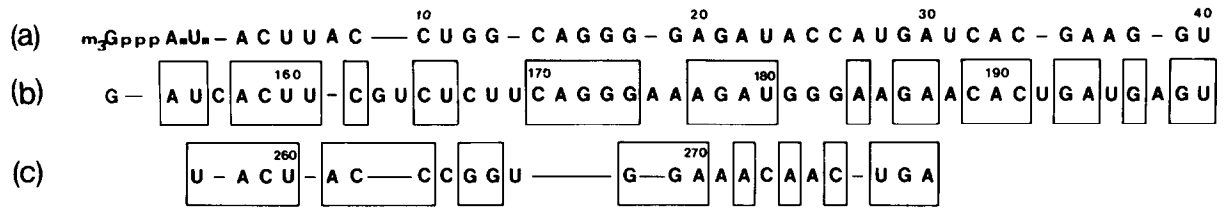

Fig.1. Sequence homology between the 5′-end of Novikoff hepatoma U1A RNA (a) and a stretch of the ASBV molecule (b). For comparison, the region of PSTV (c), found in [5,14] to be homologous with the 5′-end of mammalian and chicken U1 RNA, respectively, is also included. The sequences were aligned for maximum homology. The boxed areas in (b) and (c) contain the residues homologous with (a). The figures above the letters refer to the positions of nucleotide residues in the linear U1 RNA (fig.2(a) in [16]) or to those in the circular viroids (fig.1 in [3] for (b) and fig.3 in [5] for (c)).

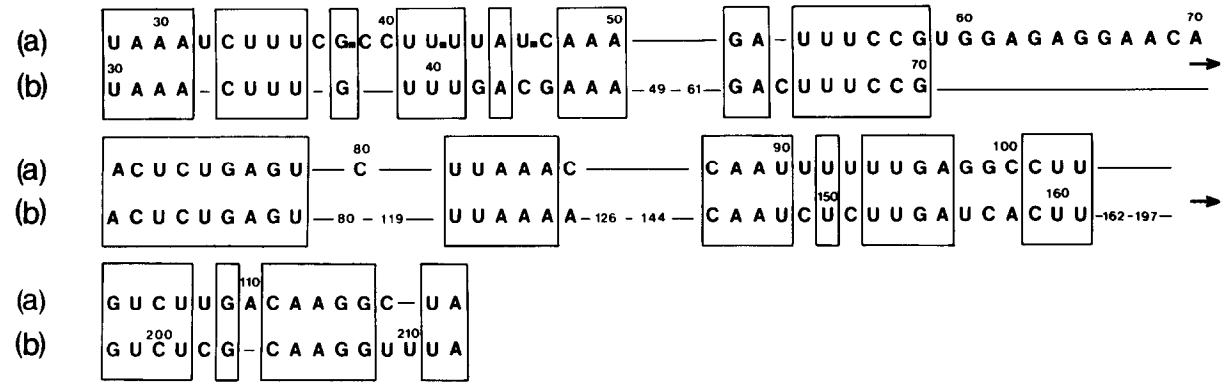

Fig.2. Sequence homologies (boxed areas) between stretches of the 118 nucleotide residue-long Novikoff hepatoma U5A RNA (a) and those of ASBV (b). Sequences are aligned for maximum homology. The figures above the letters refer to the positions of nucleotide residues in the linear U5A RNA (fig.2 (e) in [16] for (a)) or to those in ASBV (fig.1 in [3] for (b)).

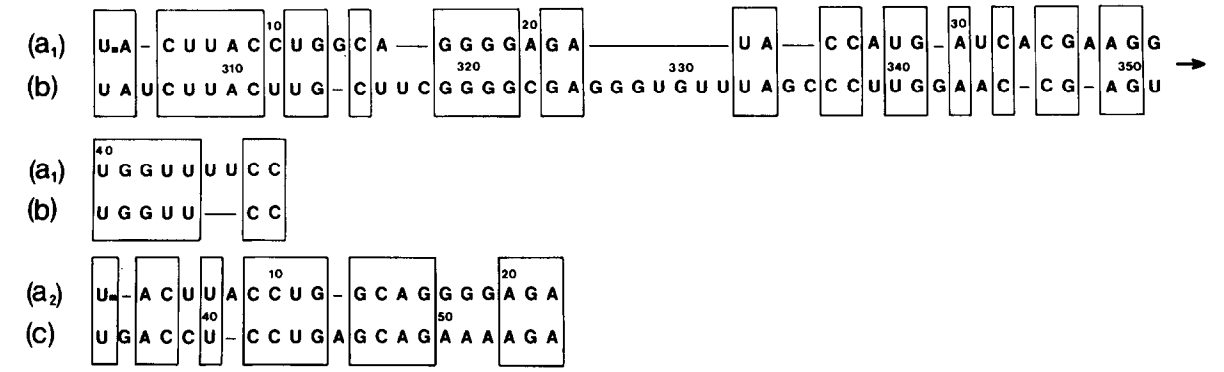

Fig.3. Sequence homologies (boxed areas) between Novikoff hepatoma U1 RNA stretches of different lengths ($a_1$, $a_2$), both comprising the 5′-end region, and various regions of the PSTV molecule (b,c). Sequences are aligned for maximum homology. The figures above the letters refer to the positions of nucleotide residues in the linear Novikoff hepatoma U1 RNA (fig.2(a) in [16] for ($a_1$–$a_3$)) or to those in the circular PSTV molecule (fig.3 in [5] for (b) and (c)).

nucleotide residues between residues 164–172 of ASBV (not shown). Furthermore, a number of additional homology sequences were detected (not shown).

Such a pronounced homology between a plant viroid and mammalian snRNA does not seem to be restricted to this particular viroid–snRNA combination. PSTV, for example, contains 2 more notable sequences, in addition to that in [5,14] which, if aligned for maximum homology, will match U1A stretches of different lengths, both comprising the 5′-end region of U1A RNA (fig.3), claimed to be active in splicing.

## 3. CONCLUSIONS

The striking sequence homology between ASBV and U5A RNA from Novikoff hepatoma cells, as shown here, as well as a number of sequence homologies between viroids and mammalian snRNAs in general (unpublished) strongly suggest that there is a phylogenetic, and most probably also a functional, relationship between plant pathogenic viroids and mammalian snRNAs.

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