The 3' Terminal RNA Sequences of Bunyaviruses and Nairoviruses (Bunyaviridae): Evidence of End Sequence Generic Differences within the Virus Family

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SUMMARY

The 3' terminal nucleotide sequences of the three virus RNA species of viruses representing eight serogroups of bunyaviruses (genus Bunyavirus, Bunyaviridae) and six serogroups of nairoviruses (genus Nairovirus, Bunyaviridae) have been characterized. Members of the Bunyavirus genus have conserved 3' end sequences (generally, 3' UCAUCACAUGA...) that differ from the conserved 3' end sequences of members of the Nairovirus genus (generally, 3' AGAGUUUCU...).

Four genera of Bunyaviridae have been recognized: Bunyavirus, Nairovirus, Phlebovirus and Uukuvirus (Bishop et al., 1980). Members of each of these genera have been shown to have a genome consisting of three segments of single-stranded RNA, designated L (large), M (medium) and S (small) (Bishop & Shope, 1979; Robeson et al., 1979; Ushijima et al., 1980; Cash et al., 1981; Clerx et al., 1981). Most of the viruses belonging to the Bunyavirus and Nairovirus genera have been assigned to serogroups by the results of various serological tests (neutralization of infectivity, complement fixation, haemagglutination inhibition). Currently, some 15 serogroups of bunyavirus and six serogroups of nairoviruses are recognized (Bishop et al., 1980; Clerx et al., 1981; Klimas et al., 1981). In the present study we have analysed the 3' end sequences of the virus RNA species of 11 bunyaviruses and seven nairoviruses in order to determine to what extent such sequences are characteristic of members of those genera.

Included for comparison are previously reported data (Clerx-van Haaster & Bishop, 1980; Clerx-van Haaster et al., 1982; Obijeski et al., 1980) for the California serogroup bunyaviruses snowshoe hare (SSH), La Crosse (LAC) and an alternate LAC isolate (L74). The other bunyaviruses that have been analysed in the present study include Oriboca virus (ORI, group C), Capim virus (CAP, Capim serogroup), Main Drain virus (MD, Bunyamwera serogroup), Pahayokee virus (PAH, Patois serogroup), Aino and Mermet viruses (AINO, MER, Simbu serogroup), Boraceia virus (BOR, Anopheles B serogroup) and Turlock virus (TUR, Turlock serogroup). The nairoviruses that have been analysed include Qalyub (QYB) and Bandia (BDA) viruses (Qalyub serogroup), Hughes virus (HUG, Hughes serogroup), Avalon virus (AVA, Sakhalin serogroup), Hazara virus (HAZ, Crimean-Congo haemorrhagic fever serogroup), Dugbe virus (DUG, Nairobi sheep disease serogroup) and Abu Mina virus (AM, Dera Ghazi Khan serogroup).

Virus origins (Clerx et al., 1981; Klimas et al., 1981; Ushijima et al., 1980, 1981) and the procedures employed for virus growth, purification, extraction of nucleic acids and 3' end-labelling of RNA species by radiolabelled pCp (Clerx-van Haaster & Bishop, 1980; Clerx-van Haaster et al., 1982) have been described. The end-labelled viral L, M and S RNA species were separated by electrophoresis and recovered from low-temperature-gelling agarose gels (Wieslander, 1979). Nucleotide sequences were deduced after either enzymic or chemical digestion of labelled RNAs as described elsewhere (Clerx-van Haaster & Bishop, 1980). In some cases, insufficient labelled RNA was obtained for analyses of all three virus
Fig. 1. The 3' end sequence analysis of large (L), medium (M) and small (S) RNA species of Bunyavirus genus members. Identical nucleotides (by reference to the LAC sequence) are indicated by filled circles in the sequence; unknown nucleotides are indicated by an N.

Fig. 2. The 3' end sequence analysis of L, M and S RNA species of Nairovirus genus members. For details see text and the legend to Fig. 1.
RNA species (MD, MER, PAH). Ambiguities in a nucleotide sequence that could not be resolved due to limited amounts of available RNA are represented by an N in the deduced sequences. In each case, the principal factor that prevented our obtaining the missing data was the difficulty encountered in growing and purifying an adequate quantity of virus. A preliminary review of some of the data reported below was given in the 1980 Negative Strand Virus meeting (Bishop et al., 1981).

Fig. 1 presents the results obtained from analyses of 11 virus isolates representing eight bunyavirus serogroups. More extensive sequence data for the L, M and S RNA species of LAC, L74 and SSH viruses are reported elsewhere, in addition to deduced coding information of the virus complementary mRNA species (Clerx-van Haaster & Bishop, 1980; Clerx-van Haaster et al., 1982; Obijeski et al., 1980). The L, M and S RNA species of the 10 bunyaviruses all share a common 3′ nucleotide sequence of six nucleotides (3′, UCAUCA) and, depending on the virus and the particular RNA species, a very similar nucleotide sequence for another five residues (Fig. 1). Thereafter, other than for viruses which are, by serological criteria, closely related, e.g. LAC, L74 and SSH, the sequences diverge. Inkoo virus (another member of the California serogroup of bunyaviruses) has recently been shown by Parker & Hewlett (1981) to have similar 3′ end sequences to those given in Fig. 1, i.e. (3′) UCAUCACAGGUGAAGUUAU (S), (3′) UCAUCACAGUGAUGGAUUU (M) and (3′) UCAUCAGAGGUGAAUGU (L).

The 3′ terminal sequences of seven viruses representing six nairovirus serogroups are shown in Fig. 2. In general, the nairoviruses have a common 3′ terminal sequence of (3′) AGAGUUUCU. Variations for particular RNA species and particular viruses from this common sequence are shown in Fig. 2.

The data presented here suggest that the Bunyaviridae viruses have conserved sequences at the 3′ termini of the L, M and S virion RNA species. The end sequence is equivalent for each RNA species of viruses belonging to the same genus, but different for viruses representing the Nairovirus or Bunyavirus genera. The 3′ terminal sequences of picornaviruses also show significant homologies for viruses belonging to a particular genus, whereas viruses representing different Picornaviridae genera have little 3′ terminal sequence similarities (Porter et al., 1978). The 3′ terminal sequences of the L, M and S RNA species of Uukuniemi virus, prototype virus of the Uukuvirus genus (Bunyaviridae), have been reported by Parker & Hewlett (1981) to be (3′) UGUGUUUUCUGGAG. Again, this sequence is different from that of bunyaviruses or nairoviruses. Preliminary sequence data for all three virus RNA species of Punta Toro and Buenaventura phleboviruses (Phlebovirus genus, Bunyaviridae) indicate that they have a common 3′ terminal sequence of nine nucleotides, i.e. (3′) UGUGUUUCG. This sequence is similar to the Uukuniemi virus RNA 3′ sequences, and represents an attribute that, in addition to the comparable sizes of their virion polypeptides and RNA species, relates these viruses.

Presumably, the similar 3′ end sequences of different virus serotypes of a particular Bunyaviridae genus represent conserved enzyme recognition sites for transcription and/or RNA replication. To what extent viruses with similar RNA termini are genetically compatible (e.g. able to form reassortment viruses) remains to be elucidated.

From radioimmune and molecular analyses, it has been proposed that the Anopheles B and Turlock serogroup viruses be placed in the Bunyavirus genus (Klimas et al., 1981). The similar 3′ end sequences of BOR (Anopheles B serogroup) and TUR viruses, by comparison with those of other members of the Bunyavirus genus, substantiate those placements. RNA end sequence analyses may well prove to be a useful additional tool for categorizing viruses (such as those described as possible or probable members of the Bunyaviridae; Bishop et al., 1980). This may be particularly useful for viruses that are only distantly related by antigenic analyses to other members of the family.
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REFERENCES


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