

THE LOCALISATION OF THE TEMPERATURE-SENSITIVE DEFECTS IN THE NUCLEOPROTEIN OF TWO INFLUENZA A VIRUS MUTANTS

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Two influenza A virus ts-mutants of strain A/FPV/Rostock/34 (H7N1) were investigated. Both of them have the ts-defect in the nucleoprotein encoded by segment five of the eight negative strand RNA segments.

The phenotype of ts 81 is an extremely lowered synthesis of viral (v) RNA at the nonpermissive temperature. In comparison to the wildtype (FPV-GI) there is a single mutation within the reading-frame causing an amino acid exchange. An alanine at position 332 is replaced by a threonine (FPV-GIA332T). Secondary structure prediction is used to examine conformational changes due to the mutation. The nuclear to cytoplasmic ratio of the ts 81 nucleoprotein was analysed to find out whether the nuclear accumulation is affected by the mutation in the karyophilic region of the ts 81 nucleoprotein.

The second mutant (ts 19) with a defect in virus maturation was analysed in the same way.

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STUDIES OF THE ts LESION OF RNA1 OF THE DONOR VACCINE STRAIN A/ANN/ARBOR/6/60

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Cold Adapted (ca) A/AA/6/60 virus is being used as a donor of attenuation in the development of live influenza virus vaccines for use in man. The formula referred to as the 6/2 gene profile is based on the reassortant vaccine having the six core genes derived from the donor strain (A/AA/6/60-H2N2) and the two surface genes, hemagglutinin and neuraminidase, derived from the circulating wild type (wt) strain. The cold reassortant type A influenza vaccine virus exhibits the phenotypic markers of cold adaptation (ca) and temperature sensitivity (ts) of the donor line. The molecular mechanism(s) which might explain the basis of the attenuation of this vaccine is being pursued by comparing the polymerase genes of the ca ts A/AA/6/60, reassortant non-ts mutants, and various non-ts wild type passages of A/AA/6/60 by sequence analysis with emphasis on RNA1. Ts lesions have been assigned to RNA1 (coding for PB2) and to RNA2 (coding for PB1) of ca A/AA/6/60. Sequence changes in PB2 have occurred between ca A/AA/6/60, the wt A/AA/6/60 from which the ca virus was derived, a wt A/AA/6/60 of later passage, and a reassortant cloned non-ts mutant. The genetic changes will be linked to ts phenotypes and their impact on attenuation.