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In vivo Estimation of Mutation Rate of the Aleutian Mink Disease Virus

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Abstract : The Aleutian mink disease virus (AMDV, Carnivore amdoparvovirus 1) causes persistent infection, plasmacytosis, and formation and deposition of immune complexes in various organs in adult mink, leading to glomerulonephritis, arteritis and sometimes death. The disease has no cure nor an effective vaccine, and identification and culling of mink positive for anti-AMDV antibodies have not been successful in controlling the infection in many countries. The failure to eradicate the virus from infected farms may be caused by keeping false-negative individuals on the farm, virus transmission from wild animals, or neighboring farms. The identification of sources of infection, which can be performed by comparing viral sequences, is important in the success of viral eradication programs. High mutation rates could cause inaccuracies when viral sequences are used to trace back an infection to its origin. There is no published information on the mutation rate of AMDV either in vivo or in vitro. The in vivo estimation is the most accurate method, but it is difficult to perform because of the inherent technical complexities, namely infecting live animals, the unknown numbers of viral generations (i.e., infection cycles), the removal of deleterious mutations over time and genetic drift. The objective of this study was to determine the mutation rate of AMDV on which no information was available. A homogenate was prepared from the spleen of one naturally infected American mink (Neovison vison) from Nova Scotia, Canada (parental template). The near full-length genome of this isolate (91.6%, 4,143 bp) was bidirectionally sequenced. A group of black mink was inoculated with this homogenate (descendant mink). Spleen sampled were collected from 10 descendant mink after 16 weeks post-inoculation (wpi) and from anther 10 mink after 176 wpi, and their near-full length genomes were bi-directionally sequenced. Sequences of these mink were compared with each other and with the sequence of the parental template. The number of nucleotide substitutions at 176 wpi was 3.1 times greater than that at 16 wpi (113 vs 36) whereas the estimates of mutation rate at 176 wpi was 3.1 times lower than that at 176 wpi (2.85×10-3 vs 9.13×10-4 substitutions/ site/ year), showing a decreasing trend in the mutation rate per unit of time. Although there is no report on in vivo estimate of the mutation rate of DNA viruses in animals using the same method which was used in the current study, these estimates are at the higher range of reported values for DNA viruses determined by various techniques. These high estimates are logical based on the wide range of diversity and pathogenicity of AMDV isolates. The results suggest that increases in the number of nucleotide substitutions over time and subsequent divergence make it difficult to accurately trace back AMDV isolates to their origin when several years elapsed between the two samplings.

Keywords : Aleutian mink disease virus, American mink, mutation rate, nucleotide substitution
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