GENOMICS OF LOUPING ILL VIRUS

Background

Louping ill virus (LIV), first isolated in the early 1930s, which is closely related to TBE virus, is endemic to the British Isles and spread by the hard tick *Ixodes ricinus*. LIV can cause mortalities in sheep and red grouse, while it only occasionally infects humans. It has also been reported from Ireland, Southern Norway, the Danish island of Bornholm, Far Eastern Russia, and Turkmenistan. Only very little is known about the phylogeography of LIV, its phylogenetic relationship to TBE virus and the evolutionary rate and divergence time of LIV and TBE virus.

Results

New complete genome sequences of 22 LIV isolates, sampled over a period of 80 years, were obtained and aligned with 4 already known LIV genomes, as well as 36 TBE-EU virus genomes, 4 TBE-Sib virus genomes, 21 TBE-FE virus genomes, one Spanish sheep encephalitis virus genome, one Spanish goat encephalitis (SGE) virus genome, one Greek goat encephalitis virus genome and one Turkish sheep encephalitis virus genome. The 26 LIV isolates shared a mean nucleotide identity of about 96% across the entire genome and a mean amino acid identity of 98.6 %. The NS2A gene was the most variable gene (88.4% identity). The genetic diversity within the LIV dataset was found to be similar for the TBE-Eu virus with the exception of the 3' untranslated region (3' UTR), which was approximately 96% identical between the LIV isolates, but is highly variable between TBE-EU virus isolates, sharing only 78% identity.

A Bayesian phylogenetic tree of TBE virus genomes placed all LIV isolates into a single monophyletic clade, with SGEV being the closest relative. Most splits in the LIV phylogeny took place hundreds of years ago, with a few nodes having estimated ages within the past century. A reliable molecular clock rate for LIV could not be estimated. No evidence for a recombination event between LIV and TBE virus has been found. The recombination signal detected and published earlier was found to be an artefact.

Discussion

Genetic diversity within the LIV dataset was found low. Compared to the dataset of TBE-Eu virus genomes, LIV appears to exhibit less genetic variability. While LIV only occasionally infects humans, the TBE virus is an important human pathogen, therefore a potential LIV/TBE-Eu virus recombinant may exhibit altered pathogenicity and present a public health risk. The length of the 3' UTR can modulate the virulence in some TBE virus subtypes, and therefore, a LIV/TBE virus recombinant possessing the shorter LIV 3' UTR may possess increased virulence. The 3' UTR of the LIV and TBE virus genomes share a mean identity of 77.5%. Considering the emergence of TBE virus in the UK, the dataset presented by the authors could support the development of tools for differential diagnosis between the LIV and TBE virus.

The most extreme cases of long-distance dispersal are the strains isolated in Far East Russia and Turkmenistan. The cluster of these viruses is nested within the UK isolates, indicating that they are direct descendants of the latter. LIV may have been introduced to FE Russia by animal trade following World War 1 or 2 or earlier after the construction of the trans-Siberian railway. Alternatively, LIV may have been introduced via transport of ticks by migratory birds, however, there are no direct migratory links between northeast Eurasia and the UK. A stop-over in Norway and/or Denmark might have contributed to the tick transport by migratory birds. In Russia, LIV has been isolated from I. persulcatus. As these vectors have also been found in the Baltic countries and parts of Scandinavia, it is possible that LIV is also present in other countries in Europe.

Literature

Clark et al.
Population genomics of louping ill virus provide new insights into the evolution of tick-borne flaviviruses.
PLoS Negl. Trop. Dis. 2020, 14 (9): e0008133

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