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European bat lyssavirus type 2 (EBLV-2) in Finland

European bat lyssavirus type 2 (EBLV-2) was first isolated in Finland from a Daubenton's bat (*Myotis daubentonii*) in 2009. Rabies in bats was already suspected in 1985, when a Swiss biologist died in Finland of lyssavirus infection, later identified as EBLV-2 infection. However, the origin of the infection could not be confirmed at that time. In 1986, 183 bats were analyzed for lyssaviruses in active surveillance, and passive rabies surveillance was ongoing, but lyssavirus was not detected in bats before 2009. In 2010 - 2011, during another active surveillance study, samples from 774 bats were analyzed for EBLV viral RNA. In addition, sera from 423 bats were analyzed for the presence of lyssavirus antibodies. Antibodies were detected in 2010 and 2011 from two locations and from one location, respectively. All seropositive bats were Daubenton's bats. All locations where seropositive bats were detected were in close proximity to where the EBLV-2-positive Daubenton's bat was found in 2009. No EBLV viral RNA was detected in any of these bats. In 2016, EBLV-2 was detected from a diseased Daubenton's bat for the second time from a location about 100 kilometers from where the Daubenton's bat was found in 2009. These data provide proof that EBLV-2 is endemic in the Finnish Daubenton's bat population.

In phylogenetic analysis, the Finnish EBLV-2 strains formed a monophyletic group separate from other bat- type lyssaviruses with significant support. EBLV-2 shared the most recent common ancestry with Bokeloh bat lyssavirus (BBLV) and Khujand virus (KHUV). EBLV-2 showed limited diversity compared to RABV and appears to be well adapted to its host bat species. The slow tempo of viral evolution was evident in the estimations of divergence times for EBLV-2: the current diversity was estimated to have built up during the last 2000 years. In a phylogenetic tree of partial N gene sequences, the Finnish EBLV-2 strains clustered with strains from Central Europe, supporting the hypothesis that EBLV-2 circulating in Finland might have a Central European origin. The Finnish EBLV-2 strains and a Swiss strain (1993) were estimated to have diverged from other EBLV-2 strains during the last 1000 years, and the Finnish strains (1985 and 2009) appear to have evolved from a common ancestor during the last 200 years.

Rabies vaccine is used to protect against rabies virus before potential exposure. Since all the currently available vaccines are based on RABV, the vaccines are also used to protect against other lyssaviruses, and additionally against EBLV-2 infection based on cross-protection. We assessed the level of protection afforded by two commercial rabies vaccines, one for humans and one for animals, against intracerebral challenge in mice with European bat lyssavirus type 2 (EBLV-2) isolated from a Finnish bat in 2009. We compared this with protection using the same mouse model against challenge with classical rabies virus (RABV) isolated from a Finnish raccoon dog in 1989. When challenged with RABV, all the vaccinated mice survived. When challenged with EBLV-2, 75 % to 85 % of the vaccinated mice survived. All vaccinated mice developed sufficient to high virus-neutralizing antibody (VNA) titers against RABV, ranging from 0.5 to 128 IU/ml. RABV-based vaccines also appear to offer good cross-protection against EBLV-2 circulating in the Finnish bat population.

To investigate the factors influencing the response to rabies vaccination, we assessed the success of vaccination measured from the antibody response in dogs ( $n = 10\,071$ ) and cats ( $n = 722$ ) sampled during 2009 - 2013. We examined the factors influencing the response to vaccination when animals failed to reach a rabies antibody titer of  $\geq 0.5$  IU/ml. Of the dog and cat samples, 10.7 % (95% confidence interval CI 10.1 - 11.3) and 3.5 % (95 % CI 2.3 - 5.0), respectively, had a vaccination antibody titer 60 cm or larger (OR from 2.3 to 3.2) resulted in a higher risk of failing to reach an antibody level of at least 0.5 IU/ml. In dogs up to a year old, these risks were higher than in older dogs. In cats, the type of vaccine did not appear to play a role.