The evolutionary history of Bovine Papillomavirus-1 in equine sarcoids

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Papillomaviruses are a family of slowly evolving, host-adapted DNA viruses, making them unlikely candidates for host shifts. However, while Bovine Papillomavirus-1 (BPV-1) primarily causes warts in its natural host the cow, it also leads to locally aggressive and invasive skin tumours in equids known as sarcoids. Sarcoids are a common disease of equids worldwide, difficult and costly to treat, and of significant welfare importance. Here we describe the first phylogenetic analysis of BPV-1 in equine sarcoids. This study gives several novel insights into the evolutionary history of BPV-1 and its cross-species association with equine sarcoids, and highlights the high prevalence of a potentially equine-adapted sequence variant.

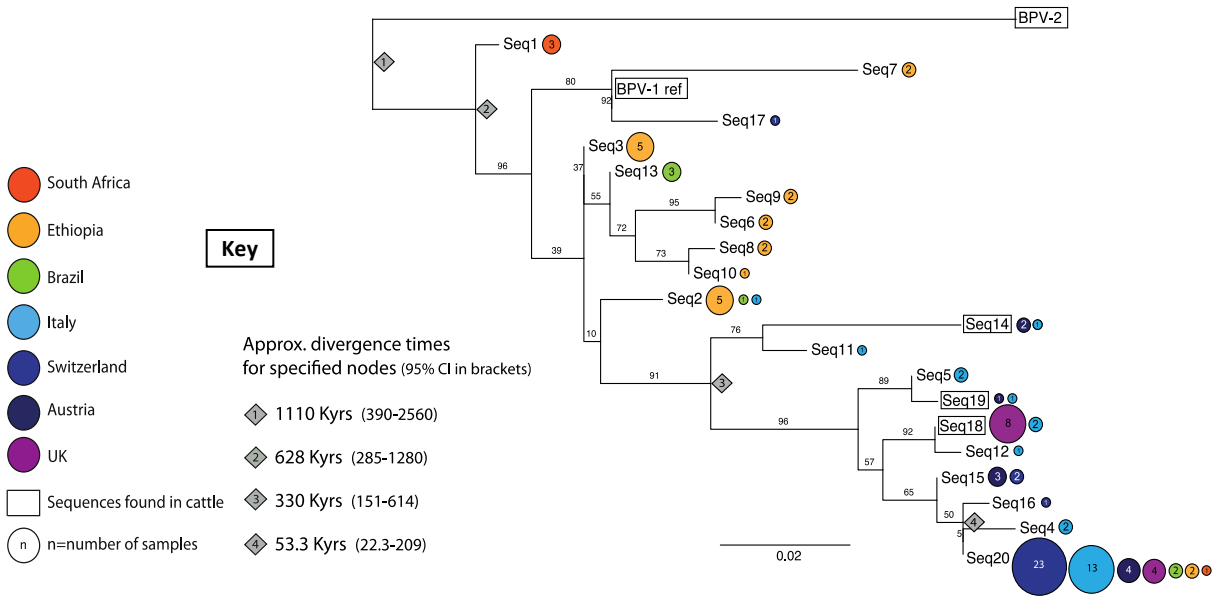

Figure 1: Maximum Likelihood phylogeny for the BPV-1 LCR sequences.

Sequences found in cattle are surrounded by rectangles. Circles next to the sequence name give the distribution of equine samples as described in the key. Estimated divergence times are given for nodes indicated by numbered diamonds. Numbers above the branches give branch support (bootstrap %). The scale bar indicates genetic distance (nucleotide substitutions per site).

The Bayesian phylogeny was identical except for the position of the BPV-1 ref/Seq7/Seq17 clade.

Materials and Methods

The BPV-1 transcriptional promoter region (the Long Control Region (LCR), 695bp) was sequenced from 119 tissue samples, collected from equine sarcoids (n=104) and cattle papillomas (n=15). Samples originated in three different continents (Africa, Europe and South America) and consisted of 21 unique LCR sequence variants. One of these corresponded with the BPV-1 reference sequence, and the rest were assigned numbers from 1–20. The BPV-2 reference sequence was included as an outgroup.

Phylogenies were constructed for the 21 aligned BPV-1 sequences and the BPV-2 outgroup using Maximum Likelihood and Bayesian methods. Divergence dates were calculated using the Beast program and the nucleotide substitution rate estimated by Rector *et al*.[6]

Discussion

The BPV-1 phylogeny (Figure 1) gives rise to the following observations:

Age of the most recent common ancestor The viral sequences show considerable diversity which appears to have accumulated over millennia. Estimated divergence dates (diamonds in Figure 1) substantially predate domestication of both cattle and equids

Geographic segregation Sequences show significant ($p<0.001$) geographic segregation, with an ancestral African group and a more evolved European group. Intriguingly, this separation is mirrored by the distribution of the two different subspecies of cattle and thus could potentially reflect host specialisation

Cross-species transmission The distribution of (UK) cattle samples (rectangles in Figure 1) throughout the European group suggests cross-species transmission of BPV-1 between cattle and equids has occurred multiple times. Given known biological behaviour of BPV-1[2,3,4], we suggest BPV-1 may be preferentially maintained in the cattle population with a relatively high frequency of cross-species transmission to equids.

Sequence 20 The high prevalence of Sequence 20 in equids from all countries sampled, and its absence from cattle, implies this variant may have a selective advantage in the equine population.

In conclusion The emergence of this slowly evolving DNA virus in horses is unlikely to be a recent phenomenon and cannot be attributed to a single cross-species transmission event. However, a recently evolved variant (Sequence 20) appears to be preferentially adapted to its new host and, unlike other variants, has reached a global distribution.

References

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This work was funded by a BBSRC Doctoral Training Grant