

Defining the Evolutionary Space and Mode of Foot-and-Mouth Disease Virus Lineages Emergence

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Introduction

Studying the genomics of foot-and-mouth disease virus (FMDV) improves our understanding of the principles and processes that drives the evolutionary fitness and geographical structure of FMDV lineages in endemic systems, as well as the virus adaptation and virulence evolution in response to resistance variability among host populations.

Methods

Sequence Data. A dataset comprising n=2495 sequences of the FMDV VP1 coding region (639bp) were compiled from the FAO WRLFMD repository. These were of contemporary O/ME-SA/PanAsia2 (n=1321), A/ASIA/Iran-05 (n=843), and Asia-1/ASIA/Sindh-08 (n=331) FMDV lineages co-circulating in the Middle East, Central and Southern Asia regions from 2001 to 2018. **Phylogenetic Inference and Geographic History Reconstruction.** Patterns of FMDV lineage diffusion were reconstructed using Bayesian phylogeographic methods in BEAST 10.0.2 with post-processing analysis in R 3.2.1.

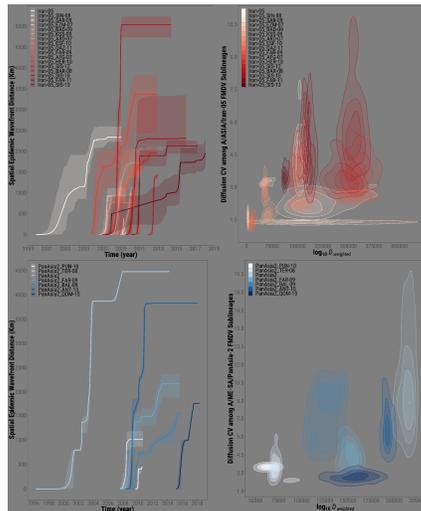


Figure 4. Spatial epidemic wavefront (left) and kernel density of the diffusion coefficient (right) estimated for each of the FMDV sublineages belonging to the A/ASIA/Iran-05 (up) and O/ME-SA/PanAsia-2 (down) lineage.

Results

Evolutionary trajectories of FMDV lineages revealed a cyclical dynamic of virus transmissions by alternating serotypes, with single lineages predominating at time intervals (**Fig. 1**). Different FMDV serotypes were reported to move at the very same geographical scale, with transitions being reconstructed in a westerly direction from the Southern Asia region to Western Asia and North Africa (**Fig. 5**). Emergence of new lineages were sustained by virus transmissions periodically originated from countries of the Southern Asia region, with Pakistan, Afghanistan and Iran acting both as primary conveyor of infections and for generating virus diversity (**Fig. 2**). Spatial diffusion and epidemic wavefront through time were linked to the evolutionary fitness of FMDV sublineage (**Tab. 1**), with some generating sustained infections on a large host population size at a wider geographic range (**Fig. 3-4**).

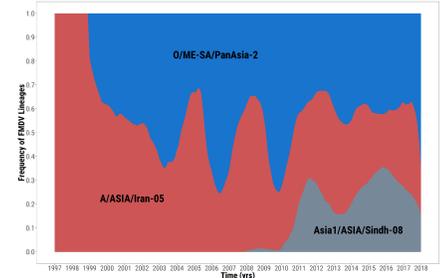


Figure 1. Estimated frequency of FMDV lineages through time as established by the ancestral reconstruction.

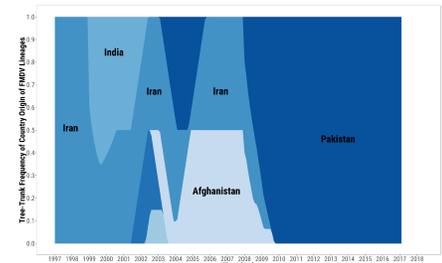


Figure 2. Estimated frequency of country-specific origin of FMDV lineages along the tree-trunk as established by the ancestral reconstruction.

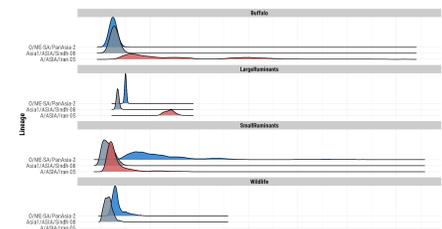


Figure 3. Estimated posterior density of the host-specific FMDV lineage persistence measured as the waiting time in years for a virus to be transmitted between hosts.

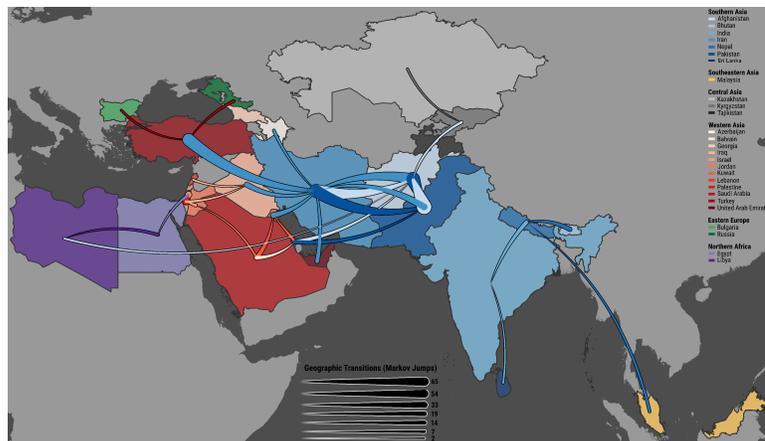


Figure 5. Migration history of FMDV lineages reconstructed from 1997 to 2018 over the Middle East region. Curved lines indicate median counts of transitions inferred between countries. Start and end point locations are centroids.

Acknowledgements

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Conclusion

The evolutionary dynamics of multiple FMDV serotypes at the endemic level is a complex process involving competition between geographically co-existing lineages, co-evolving within the same host population structure. Successful fixation of FMDV lineages strongly depends on the genotype and landscape in which they interact. In this context, the Southern Asia region represents the 'mixing vessel' ecosystem for maintaining and moving viruses along with livestock trade pathways both westwards to West Eurasia and into North Africa, and eastwards into Southeast and East Asia.

FMDV Lineage	tMRCA	tMRS	D_w (km ² /year) [95% HPD]	Epidemic Wavefront (km/year) [95% HPD]
Asia-1/ASIA/Sindh-08	2008.6	2018.1	626.7 [587.9 - 664.3]	357.5 [0 - 2647.4]
A/ASIA/Iran-05	1992.2	2018.1	726.8 [695.2 - 761.6]	102.4 [0 - 759.7]
O/ME-SA/PanAsia-2	1996.3	2018.3	726.5 [706.1 - 751.3]	243.5 [0 - 1899.3]

Table 1. Evolutionary time and spatial statistics estimated for the of FMDV lineages circulating in Middle East from 1997 to 2018. tMRCA=time of the most recent common ancestor; tMRS=time of the most recent sample.