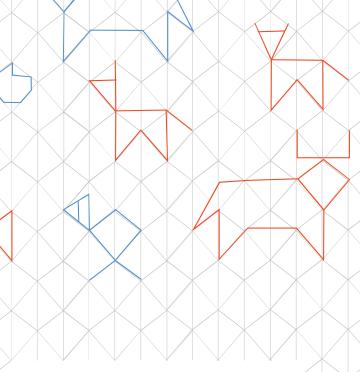




# 1<sup>st</sup> GF-TADs Regional Conference in the European region

FMD full genome sequencing and comparing strains: Overview of the Footand-Mouth Disease outbreaks in Europe in 2025

**ANSES - EURL for FMD** 



Funded by

the European Union







### **Foot-and-Mouth Disease (FMD)**

# An ancient disease but still with us, and a threat for zones free from FMD socio-economic impact, losses, embargos...

- Highly contagious transboundary animal disease
- Infecting cloven-hoofed animals (cattle and wildlife, more than 70 species are sensitive)
- Incubation period : between 2 and 14 days
- Main symptoms: fever, vesicles, hypersalivation...
- Economic losses can be dramatic in FMD-free countries.









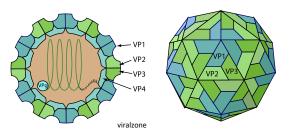


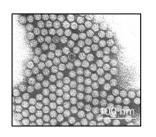




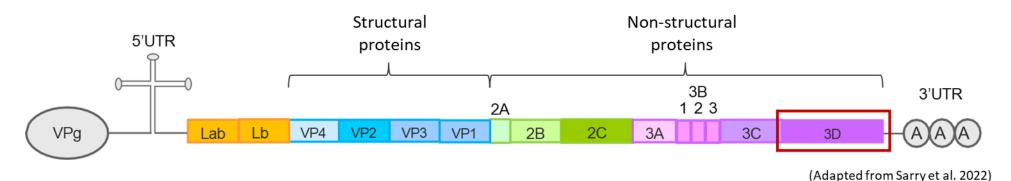
Reflections on the Foot-and-Mouth Disease Epidemic of 2001: a United Kingdom Perspective

### **Foot-and-Mouth Disease virus (FMDV)**





- Family: *Picornaviridae*, genus: *Aphtovirus*
- Non-enveloped virus (small virus of 25nm), icosaedric capside
- Genome: positive single strand RNA
- Genome size of 8,5 kb coding :
  - 4 structural proteins
  - 11 non structural proteins

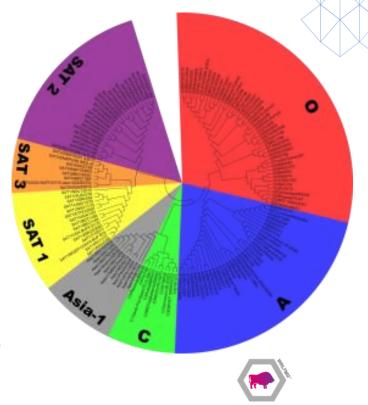


### **Foot-and-Mouth Disease virus (FMDV)**

- High genetic and antigenic variability:
  - 7 serotypes (O, A, C, Asia1, SAT1, SAT2, SAT3)
  - Many subtypes (Topotypes, lineages and sublineages)
- Sequencing of VP1 is commonly used to identify strains
- Vaccination exists, but forbidden in EU since 1991
- No cross-protection between serotypes

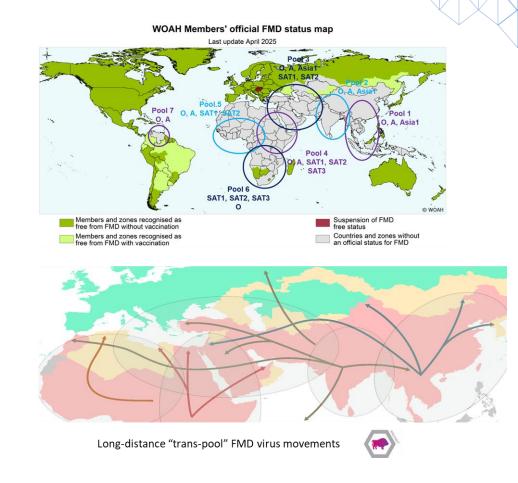


FMD control remains a challenge, due to vaccination and viral persistence



### **Epidemiology of FMD**

- Six serotypes (O, A, Asia-1, SAT-1,-2, and -3) are circulating globally
- Serotype O is the most prevalent worldwide
- Serotype C not reported since 2004 (Extinction ?)
- Unpredictable spread of lineages between pools and over long-distance
- Identification and characterisation of circulating strains help to understand the transmission pathways and to identify future lineages that may pose a threat



# **Recent FMD events**

### FMD outbreak in Europe: Germany, January 2025

- Outbreak reported by Germany in Brandenburg on a farm of water buffaloes (14 animals, 3 dead)
- Lineage O/ME-SA/SA-2018 identified
  - initially identified in South Asia, and then spread to West Asia
- Most closely related sequence on VP1: O/TUR/Igdir/2024 (99.84%)
- Vaccine matching test performed at EURL : effective vaccines available

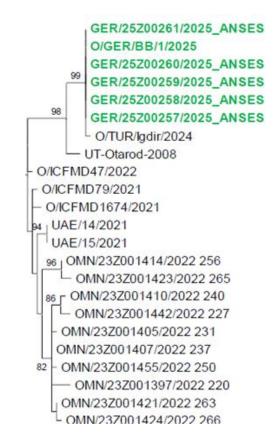




### rtRT-PCR for the detection of O/ME-SA/SA-2018 FMDV

This real-time RT-PCR is a molecular tool for detection of Foot-and-mouth disease virus lineage O/ME-SA/SA-2018, as it is an emerging lineage in South Asia since 2018.

https://eurl-fmd.anses.fr/





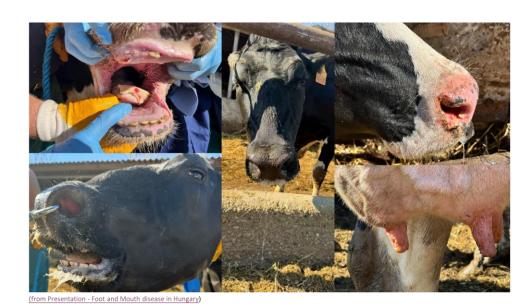






### FMD outbreak in Europe: Hungary, March-April 2025

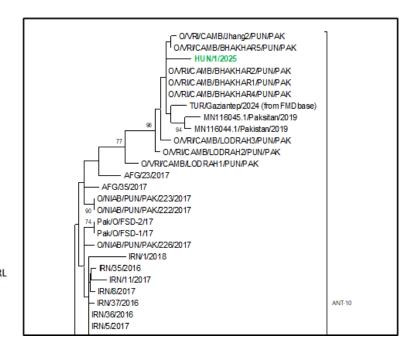
- Outbreak reported by Hungary on a dairy farm close to the border with Slovakia (2,5 km)
- Sublineage O/ME-SA/PanAsia-2<sup>ANT-10</sup> identified (also named O/ME-SA/PanAsia-2<sup>PUN-16</sup>)
- Most closely related sequences are from Pakistan (2017, 2018: 99,22%) and Türkiye (2024: 98,58%)
- No epidemiological link with the German case (same serotype, different lineage)
- Vaccine matching test performed at EURL : effective vaccines available
- 5 outbreaks between March and April





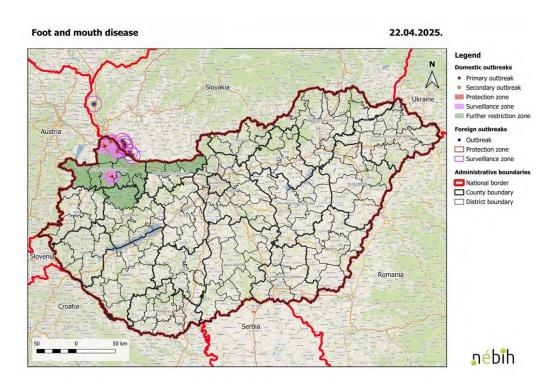


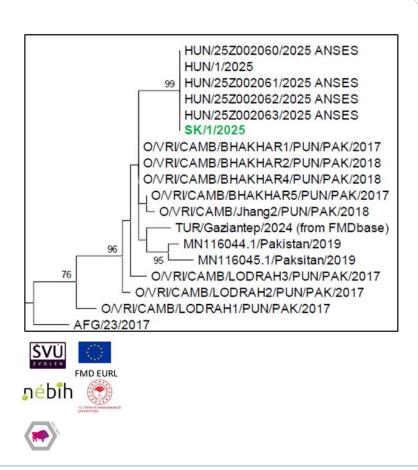




### FMD outbreak in Europe: Slovakia, March-April 2025

- Three outbreaks reported by Slovakia on March 21<sup>st</sup>, close to the border with Hungary
- Sublineage O/ME-SA/PanAsia-2<sup>ANT-10</sup> identified (also named O/ME-SA/PanAsia-2<sup>PUN-16</sup>)
- Same VP1 sequence as in Hungary
- Vaccine matching test performed at EURL : effective vaccines available
- 6 outbreaks between March and April





### Full Genome Sequencing (FGS) vs VP1 sequencing : advantages

Rev. Sci. Tech. Off. Int. Epiz., 2016, 35 (1), 175-189

### Genomics and outbreaks: foot and mouth disease

a) VPI

G.L. Freimanis, A. Di Nardo, K. Bankowska, D.J. King, J. Wadsworth, N.J. Knowles & D.P. King\*

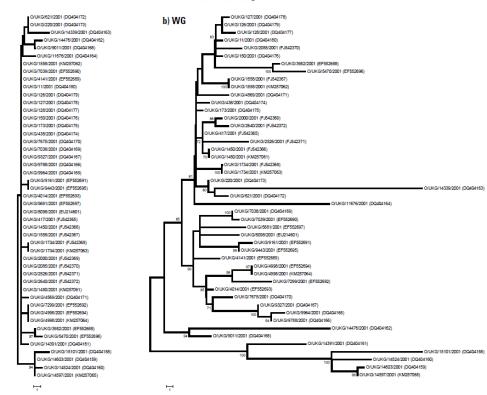


Fig. 4

A comparison between phylogenetic analysis of data generated from the same foot and mouth disease virus isolates collected during the 2001 foot and mouth disease epidemic in the United Kingdom using VP1 only or WG (whole genome)

Maximum likelihood trees were produced using MEGAv.6.06 (70)

With access to the full genome, you increase the resolution and you can find more differences between isolates that can be identical based on VP1 analysis

### The use of Full Genome Sequencing

JOURNAL OF VIROLOGY, Nov. 2006, p. 11274–11282 0022-538X/06/\$08.00+0 doi:10.1128/JVI.01236-06 Copyright © 2006, American Society for Microbiology. All Rights Reserved. No. 22 OPEN ACCESS Freely available online

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PLOS ONE

Molecular Epidemiology of the Foot-and-Mouth Disease Virus Outbreak in the United Kingdom in  $2001^{\circ}$ 

Eleanor M. Cottam, 1,2\* Daniel T. Haydon, 2 David J. Paton, 1 John Gloster, 4† John W. Wilesmith, 3 Nigel P. Ferris, 1 Geoff H. Hutchings, 1 and Donald P. King 1 Transmission Pathways of Foot-and-Mouth Disease Virus in the United Kingdom in 2007

Eleanor M. Cottam<sup>1,2</sup>, Jemma Wadsworth<sup>1</sup>, Andrew E. Shaw<sup>1</sup>, Rebecca J. Rowlands<sup>1</sup>, Lynnette Goatley<sup>1</sup>, Sushila Maan<sup>1</sup>, Narender S. Maan<sup>1</sup>, Peter P. C. Mertens<sup>1</sup>, Katja Ebert<sup>1</sup>, Yanmin Li<sup>1</sup>, Eoin D. Ryan<sup>1</sup>, Nicholas Juleff<sup>1</sup>, Nigel P. Ferris<sup>1</sup>, John W. Wilesmith<sup>3</sup>, Daniel T. Haydon<sup>2</sup>, Donald P. King<sup>1</sup>, David J. Paton<sup>1</sup>, Nick J. Knowles<sup>1</sup> Reconstruction of the Transmission History of RNA Virus Outbreaks Using Full Genome Sequences: Foot-and-Mouth Disease Virus in Bulgaria in 2011

Begoña Valdazo-González<sup>1</sup>\*, Lilyana Polihronova<sup>2</sup>, Tsviatko Alexandrov<sup>2</sup>, Preben Normann<sup>4</sup>, Nick J. Knowles<sup>1</sup>, Jef M. Hammond<sup>1</sup>, Georgi K. Georgiev<sup>2</sup>, Fuat Özyörük<sup>3</sup>, Keith J. Sumption<sup>6</sup>, Graham J. Belsham<sup>4</sup>, Donald P. King<sup>1</sup>

- TCS statistical parsimony analysis clearly showed the genetic evolutionary history of the virus.
- Transmission routes can be determined by traditional contact tracing (black arrows) and by genetic data (gray arrows) (slight differences can be observed)

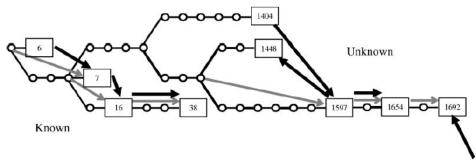
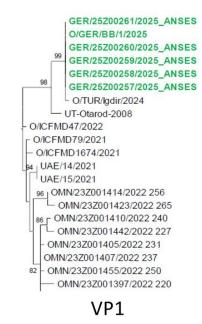
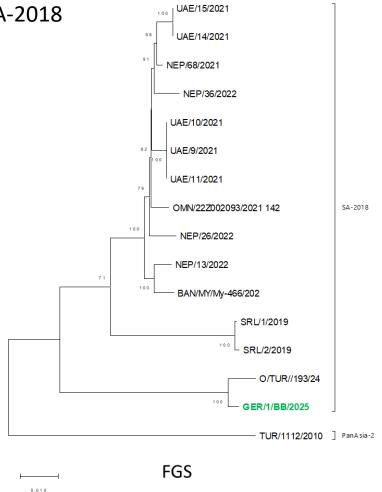


FIG. 5. TCS analysis of two clusters of infected premises. Statistical parsimony analysis of known and unknown virus transmission events. Each connecting branch line represents a nucleotide substitution, with each dot representing a putative ancestor virus. Black arrows indicate the transmission route determined by traditional contact tracing, gray arrows indicate the route supported by the genetic data. The data show the close genetic relationship of IP1692 to IP1597 and IP1654, although epidemiological tracing suggested IP1692 was infected from a more distantly related source.

### **FGS in Germany**

- As for VP1, proximity with a strain that circulated in Türkiye in 2024
- Very small number of full genomes are available for O/ME-SA/SA-2018
- More FGS are required to have a global picture



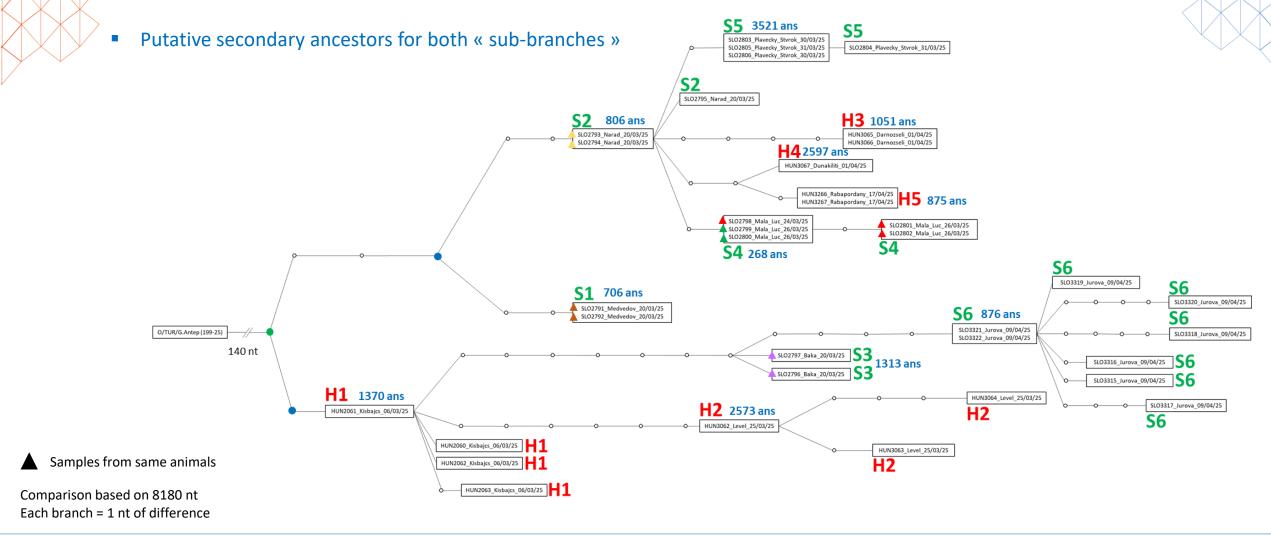


### **FGS in Hungary-Slovakia**

Country	Outbreak number	Date of confirmation of the outbreak	Number of animals in the farm	Nb of samples received	FGS performed
Hungary	H1 (Kisbajcs)	06/03/2025	1370	4	Yes (4/4)
Slovakia	S1 (Medvedov)	21/03/2025	706	3	Yes (2/3)
Slovakia	S2 (Narad)	21/03/2025	806	3	Yes (3/3)
Slovakia	S3 (Baka)	21/03/2025	1313	2	Yes (2/2)
Slovakia	S4 (Mala Luc)	25/03/2025	268	5	Yes (5/5)
Slovakia	S5 (Plavecky Stvrtok)	30/03/2025	3521	4	Yes (4/4)
Hungary	H2 (Levél)	26/03/2025	2573	3	Yes (3/3)
Hungary	H3 (Darnózseli)	02/04/2025	1051	2	Yes (2/2)
Hungary	H4 (Dunakiliti)	02/04/2025	2597	1	Yes (1/1)
Hungary	H5 (Rábapordány)	17/04/2025	875	2	Yes (2/2)
Slovakia	S6 (Jurova)	04/04/2025	876	8	Yes (8/8)

### TCS tree (statistical parsimony analysis)

Presence of a single putative common ancestor for all the sequences recovered from infected animals provides
evidence for a single introduction of the virus.



### Take-home messages on the HUN-SK cases

- Full genome analyses of 36 samples (12 from Hungary and 24 from Slovakia) was performed at EURL
- FGS give a picture of the outbreaks related to available data (Not all samples have been retrieved from all animals)
- Single introduction of the virus
- "Real" ancestor of the outbreak not sampled (probably originated from Hungary few days before the sampling of the first animal; date of first infection was estimated 27-28 February 2025 (EUVET report))
- The Turkish strain identified in the VP1 phylogenetic tree has been sequenced and confirm that a similar virus has circulated in West Asia, but as for the VP1 analysis (98,58% of nt identity), it is not a "perfect match" (98,26 % of identity with HUN2061)
- More information is required on strains circulating in West Asia



**Cooperation is mandatory to combat FMD (sharing information, sharing data)** 















## THANK YOU





