**Table 1: Summary of accession numbers of virus and vaccine/serum isolates included in this study. All viruses were obtained from studies by these 4 studies** (Mahapatra et al., 2017;Tesfaye et al., 2020; Upadhyaya et al., 2021; Yang et al., 2014)

| **Study (reference)** | **Year** | **# of r₁ pairs** | **Topotypes represented** | **Accession Numbers** |
| --- | --- | --- | --- | --- |
| Mahapatra M et al. Vaccine (2017) | 2011 | 4 | SAT 1, SAT 2, SAT 3 | KJ831676.1, DQ164880.1, DQ164881.1, KM243162.1, KM243163.1 |
| Tesfaye Y et al. Arch Virol (2020) | 2020 | 39 | EA-3, EA-4 | MZ851288.1, MZ851289.1, MZ851290.1, MZ851291.1, MZ851292.1, MZ851293.1, MZ851294.1, MZ851295.1, MZ851296.1, MZ851297.1, MZ851298.1, MZ851299.1, MZ851300.1, MZ851301.1, MZ851302.1, MZ851303.1 |
| Yang M et al. Virology J (2014) | 2014 | 30 | ME-SA, EA-3, SEA, WCSA | KJ606977.1, KJ606980.1, KJ606981.1, KJ606983.1, KJ606984.1, KJ606978.1, KC519630.1, KJ606979.1, KJ606982.1 |
| Upadhyaya S et al. Viruses (2021) | 2021 | 35 | PanAsia-2, IND-R2/75 | MN518164.1, MN518166.1, MN518152.1, MN518153.1, MN518154.1, MN518157.1, MN518149.1, MN518151.1, MN518142.1, MN518146.1, MN518147.1, MN518143.1, MN518155.1, MN518144.1, MN518145.1, MN518148.1 |

**List of serum/vaccines used in the model:** KF321732.1, KJ831676.1, AF204276.1, AY593823.1, FJ798108.1, KR401172.1

|  |  |  |  |
| --- | --- | --- | --- |
| **Field strain** | **Vaccine strain** | **Model r1 prediction** | **Published Lab results** |
| **Eltahir et al. study** | | | |
| OR425051.1\_UAE/1/2021 | JF968170.1\_3039 | >0.3 | >0.3 |
| OR425057.1\_UAE/15/2021 | JF968170.1\_3039 | <0.3 | >0.3 |
| OR425053.1\_UAE/9/2021 | JF968170.1\_3039 | >0.3 | >0.3 |
| OR425051.1\_UAE/1/2021 | LQ465469.1\_Campos | >0.3 | >0.3 |
| OR425057.1\_UAE/15/2021 | LQ465469.1\_Campos | >0.3 | >0.3 |
| OR425053.1\_UAE/9/2021 | LQ465469.1\_Campos | >0.3 | >0.3 |
| OR425051.1\_UAE/1/2021 | AY593823.1\_O1\_Manisa | >0.3 | >0.3 |
| OR425057.1\_UAE/15/2021 | AY593823.1\_O1\_Manisa | >0.3 | >0.3 |
| OR425053.1\_UAE/9/2021 | AY593823.1\_O1\_Manisa | >0.3 | >0.3 |
| OR425051.1\_UAE/1/2021 | KF321732.1\_PanAsia-2 | >0.3 | >0.3 |
| OR425057.1\_UAE/15/2021 | KF321732.1\_PanAsia-2 | >0.3 | >0.3 |
| OR425053.1\_UAE/9/2021 | KF321732.1\_PanAsia-2 | >0.3 | >0.3 |
| OR425051.1\_UAE/1/2021 | MT443823.1\_TUR/5/2009 | >0.3 | >0.3 |
| OR425057.1\_UAE/15/2021 | MT443823.1\_TUR/5/2009 | >0.3 | >0.3 |
| OR425053.1\_UAE/9/2021 | MT443823.1\_TUR/5/2009 | >0.3 | >0.3 |
| **Bachanek-Bankowska study** | | | |
| MH784405.1\_PAK/14/2017 | JF968170.1\_3039 | >0.3 | >0.3 |
| MH784405.1\_PAK/14/2017 | AY593823.1\_o\_1manisa | >0.3 | >0.3 |
| MH784405.1\_PAK/14/2017 | MT443823.1\_TUR/5/2009 | >0.3 | >0.3 |
| MH784403.1\_PAK/10/2016 | JF968170.1\_3039 | >0.3 | <0.3 |
| MH784403.1\_PAK/10/2016 | AY593823.1\_o\_1manisa | >0.3 | <0.3 |
| MH784403.1\_PAK/10/2016 | MT443823.1\_TUR/5/2009 | >0.3 | <0.3 |
| MH784404.1\_PAK/4/2017 | JF968170.1\_3039 | >0.3 | <0.3 |
| MH784404.1\_PAK/4/2017 | AY593823.1\_o\_1manisa | >0.3 | <0.3 |
| MH784404.1\_PAK/4/2017 | MT443823.1\_TUR/5/2009 | >0.3 | <0.3 |
| **Singanallur et al. study** | | | |
| KY696708.1\_O/ME-SA/Ind-2001d | JF968170.1\_3039 | >0.3 | >0.3 |
| KY696708.1\_O/ME-SA/Ind-2001d | AY593823.1\_o\_1manisa | >0.3 | <0.3 |
| **Tsefaye et al. study** | | | |
| MN987470.1\_ETH/21/2018 | FJ798108.1\_ETH/38/2005 | >0.3 | >0.3 |
| MN987469.1\_ETH/20/2018 | FJ798108.1\_ETH/38/2005 | >0.3 | >0.3 |
| MN987474.1\_ETH/25/2018 | FJ798108.1\_ETH/38/2005 | >0.3 | >0.3 |
| MN987471.1\_ETH/22/2018 | FJ798108.1\_ETH/38/2005 | >0.3 | >0.3 |
| MN987468.1\_ETH/19/2018 | FJ798108.1\_ETH/38/2005 | >0.3 | >0.3 |

Supplementary table 1: Predicted cross-reaction classification between vaccine and field strains reported in vaccine matching experiments by studies in United Arab Emirates (6), Pakistan (7), Australia (8), and Ethiopia (9) respectively.

A graph of training

AI-generated content may be incorrect.

Supplementary Figure 1: Principal component analysis (PCA) of the original training set (left) and SMOTE-augmented training set (right). Points represent serum-virus pairs, with red circles denoting non-cross-neutralizing pairs (r1 < 0.3) and green triangles denoting cross-neutralizing pairs (r1 ≥ 0.3). SMOTE generated additional synthetic samples from the minority class (cross-neutralizing), expanding the feature space while preserving structure and avoiding distortion. Ellipses indicate 95% confidence regions.

**References**

1. Mahapatra M, Upadhyaya S, Aviso S, Babu A, Hutchings G, Parida S. Selection of vaccine strains for serotype O foot-and-mouth disease viruses (2007-2012) circulating in Southeast Asia, East Asia and Far East. Vaccine [Internet]. 2017 Dec 18 [cited 2024 Sep 17];35(51):7147–53. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29157957

2. Maree FF, Blignaut B, Esterhuysen JJ, de Beer TAP, Theron J, O’Neill HG, et al. Predicting antigenic sites on the foot-and-mouth disease virus capsid of the South African Territories types using virus neutralization data. J Gen Virol [Internet]. 2011 Oct 1 [cited 2023 Nov 14];92(10):2297–309. Available from: https://www.microbiologyresearch.org/content/journal/jgv/10.1099/vir.0.032839-0

3. Tesfaye Y, Khan F, Yami M, Wadsworth J, Knowles NJ, King DP, et al. A vaccine-matching assessment of different genetic variants of serotype O foot-and-mouth disease virus isolated in Ethiopia between 2011 and 2014. Arch Virol [Internet]. 2020 Aug 1 [cited 2023 Nov 14];165(8):1749–57. Available from: https://pubmed.ncbi.nlm.nih.gov/32435857/

4. Upadhyaya S, Mahapatra M, Mioulet V, Parida S. Molecular Basis of Antigenic Drift in Serotype O Foot-and-Mouth Disease Viruses (2013-2018) from Southeast Asia. Viruses [Internet]. 2021 Sep 1 [cited 2023 Nov 14];13(9). Available from: https://pubmed.ncbi.nlm.nih.gov/34578467/

5. Yang M, Xu W, Goolia M, Zhang Z. Characterization of monoclonal antibodies against foot-and-mouth disease virus serotype O and application in identification of antigenic variation in relation to vaccine strain selection. Virol J [Internet]. 2014 Aug 1 [cited 2023 Nov 14];11(1):136. Available from: /pmc/articles/PMC4125342/

6. Eltahir YM, Ishag HZA, Parekh K, Wood BA, Ludi A, King DP, et al. Foot and Mouth Disease Vaccine Matching and Post-Vaccination Assessment in Abu Dhabi, United Arab Emirates. Vet Sci 2024, Vol 11, Page 272 [Internet]. 2024 Jun 14 [cited 2024 Sep 24];11(6):272. Available from: https://www.mdpi.com/2306-7381/11/6/272/htm

7. Bachanek-Bankowska K, Wadsworth J, Henry E, Ludi AB, Bin-Tarif A, Statham B, et al. Genome Sequences of Antigenically Distinct Serotype O Foot-and-Mouth Disease Viruses from Pakistan. Bruno V, editor. Microbiol Resour Announc [Internet]. 2019 Jan 17 [cited 2023 Nov 14];8(3). Available from: https://journals.asm.org/doi/10.1128/mra.01397-18

8. Singanallur NB, Dekker A, Eblé PL, van Hemert-Kluitenberg F, Weerdmeester K, Horsington JJ, et al. Emergency FMD Serotype O Vaccines Protect Cattle against Heterologous Challenge with a Variant Foot-and-Mouth Disease Virus from the O/ME-SA/Ind2001 Lineage. Vaccines [Internet]. 2021 Sep 29 [cited 2024 Sep 24];9(10):1110. Available from: https://www.mdpi.com/2076-393X/9/10/1110/htm

9. Tesfaye Y, Khan F, Gelaye E. Vaccine matching and antigenic variability of foot-and-mouth disease virus serotypes O and A from 2018 Ethiopian isolates. Int Microbiol [Internet]. 2022 Jan 5 [cited 2024 Sep 24];25(1):47–59. Available from: https://link.springer.com/10.1007/s10123-021-00178-w