FOOT AND MOUTH DISEASE VIRUS EXPRESSING CHIMERIC CAPSID PROTEIN: A TOOL FOR DELINEATION OF NEW ANTIGENIC SITES AND VACCINE STRAIN SELECTION

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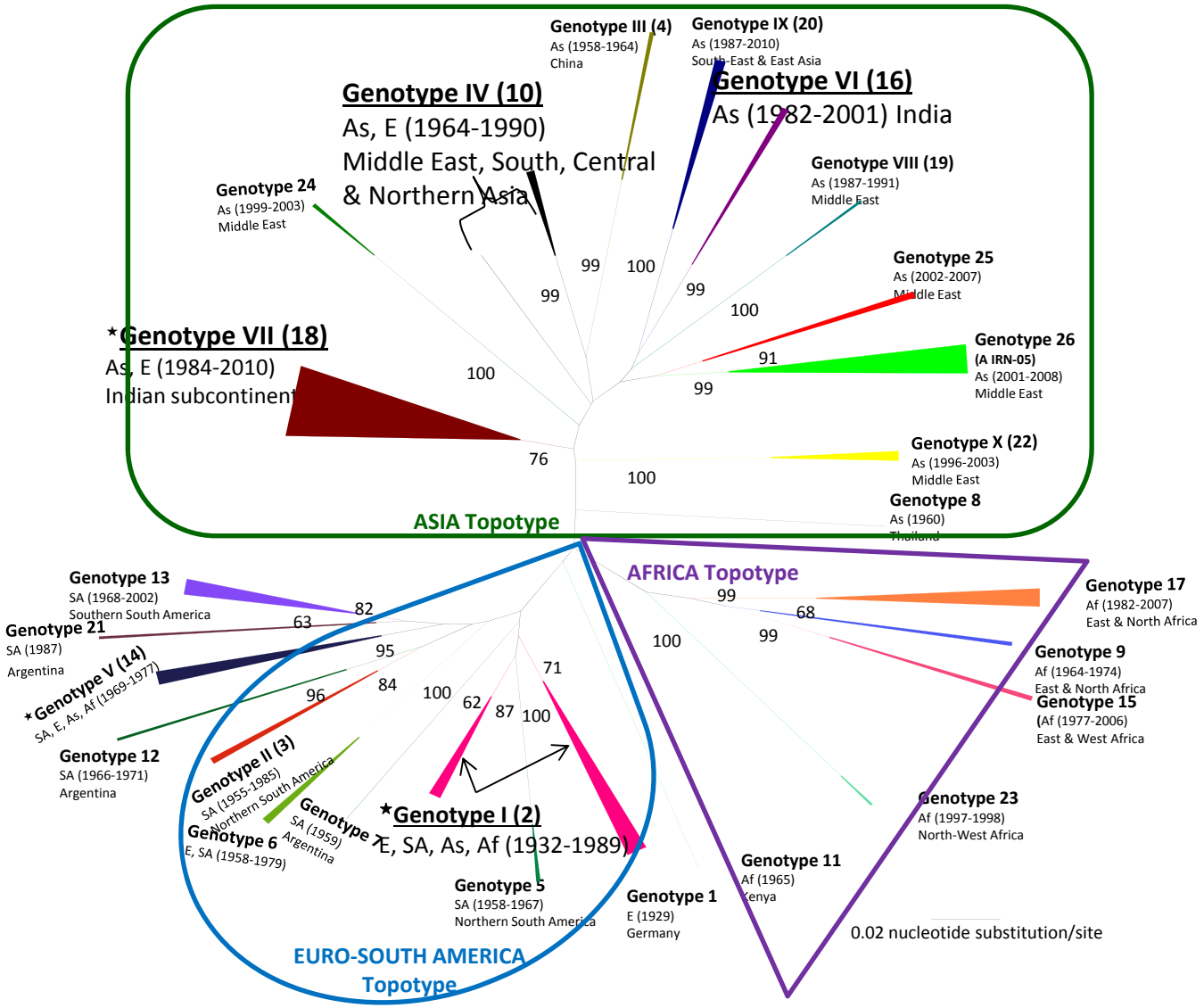
Overview

- Global distribution of FMDV serotype A and recent spread of Genotype VII (18)
- Lack of suitable vaccine strain against current genotype VII (18)
- Chimeric FMDV and evidences that the VP2 capsid protein has been responsible for the antigenic un-relatedness of the recent genotype-18
- Identification new putative antigenic epitope (VP2-74) and its role for antigenic un-relatedness.

Global Distribution of Serotype A



Genotype 18 (VII)

- Since 2001, genotype VII (18) has been exclusively responsible for all the field outbreaks

- Within the genotype-18 a divergent and unique lineage emerged in late part of 2002, which showed an amino acid (aa) deletion at 59th position of VP3 (VP3^{59}-deletion group). From 2007–2008, there is an upsurge in incidence of outbreaks due to this lineage.

- In 2015, it appeared for the 1st time in the **Middle East**, during the same year, by Iran, Turkey and Armenia. Most recently (May 2017), this virus was identified in Northern Israel, on the Lebanese and Syrian borders, Nepal and Bhutan.

Antigenic relatedness

- Currently, majority of the field isolates belonging to the VP3[59]-deletion group were found antigenically unrelated to the in-use vaccine strain through the 2D-VNT assay.
- Considering the antigenic diversity, a panel of 3 candidate vaccine strains were selected, and one strain provided good antigenic coverage (79 out of 84 tested isolates were matched).
- Sequence analysis in the countrywide longitudinal data-set could not determine any specific fixation of amino acid substitution at the known antigenically critical positions.

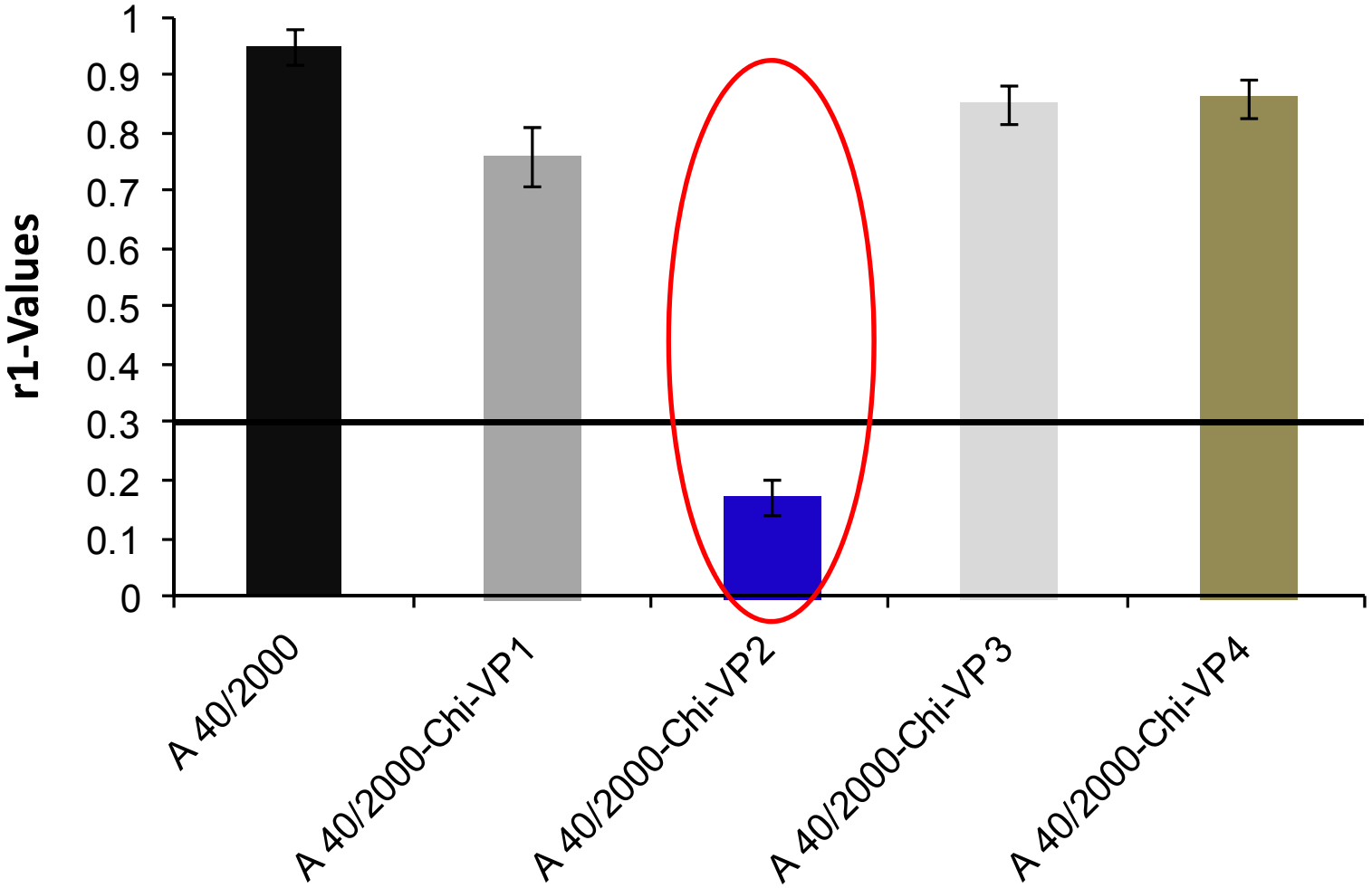
Domain Swapping Mutagenesis and chimeric cDNA clones

A IND 40/2000

A PD 26/2015

Chimeric infectious clones were generated through Mega-primer mediated domain swapping method (Biswal et al., 2015)

2D-VNT with A IND 40/2000 BVS



Chimeric-VP2 cDNA clones

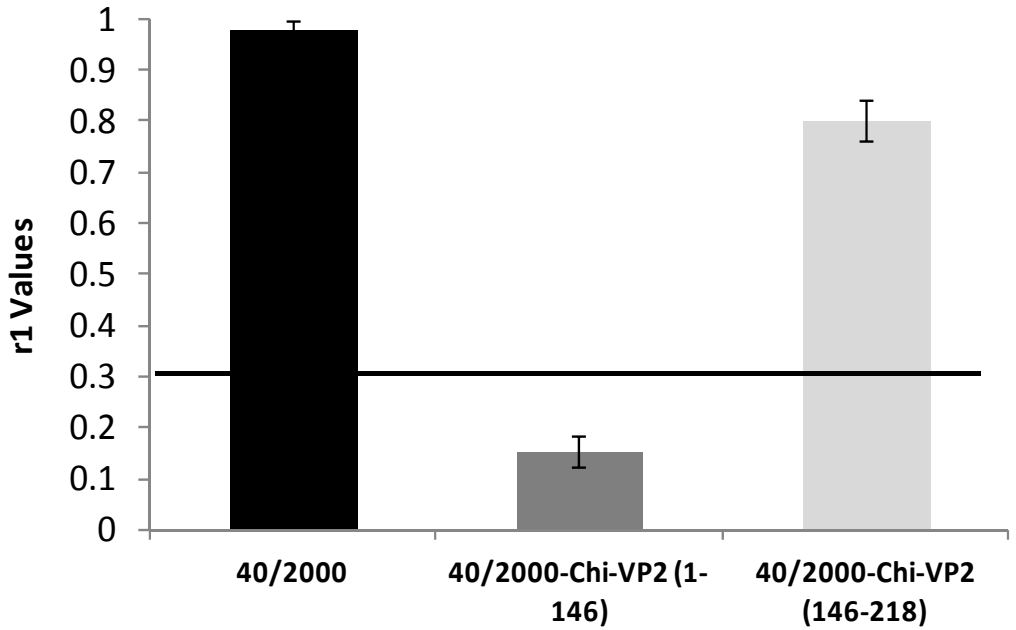
A IND 40/2000

A PD 26/2015

Chimeric VP2

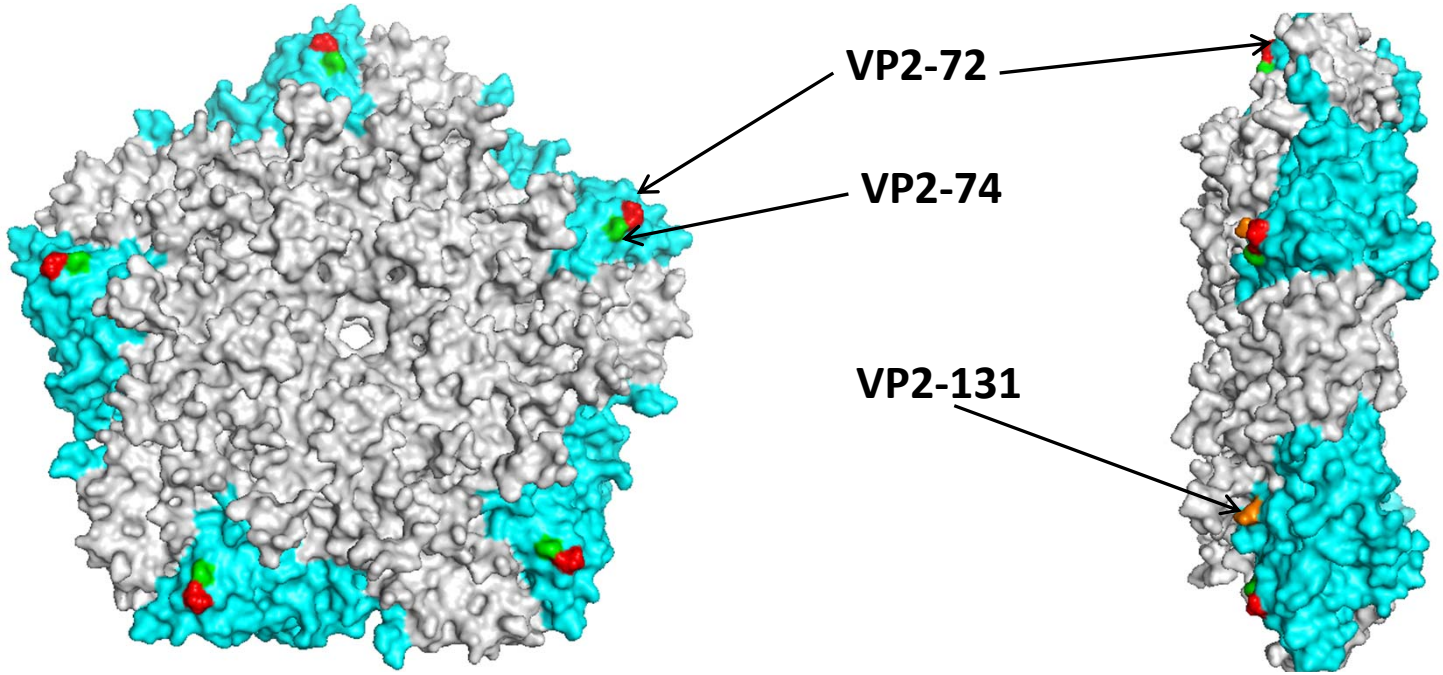
Chimeric VP2

2D-VNT with A IND 40/2000 BVS



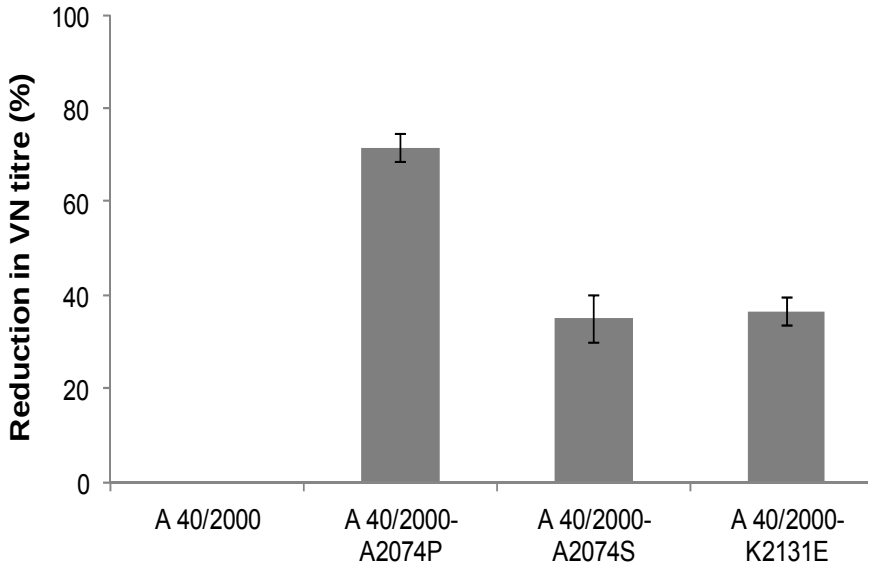
Putative antigenic residue(s) on the VP2-protein of the antigenic variants

Position and Amino Acid	Secondary Structure	Entropy Values	Consurf Values	Consensus between genetic and antigenic variants
55-V/K/E/L/N/T	αZ helix	0.403	-0.340	Not found
74 -A/P/S	βC–βC loop	0.798	3.033	Yes (A→P)
79-E/V/G/A/Q	βC strand	0.505	2.533	No
96 -D/G/N/K/E	αA helix	0.510	0.332	Not found
131-E/K/D/G/H/N	βE–βF loop	1.064	1.734	Not found

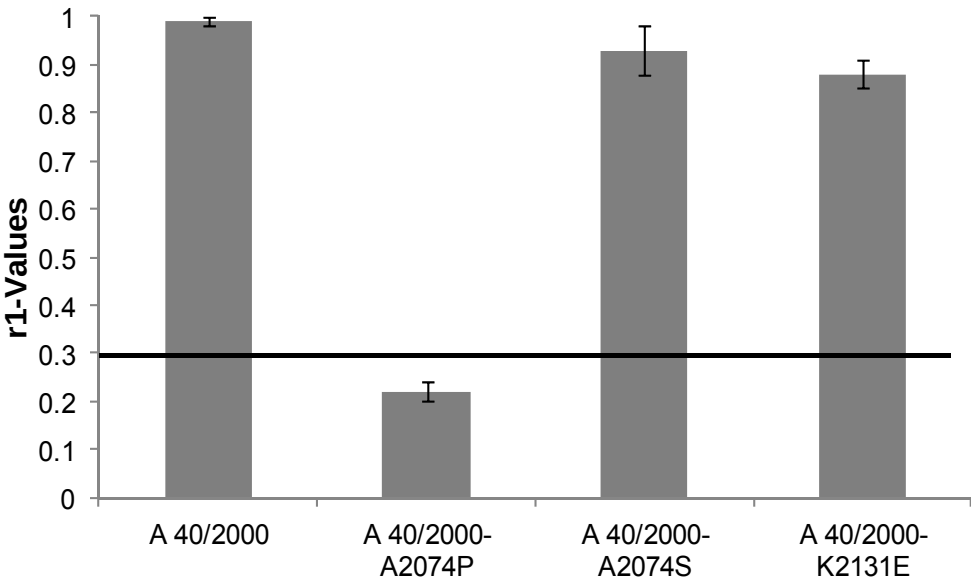


Reduction in Virus neutralization titre and associated ‘r1’-value after site-directed mutagenesis

A

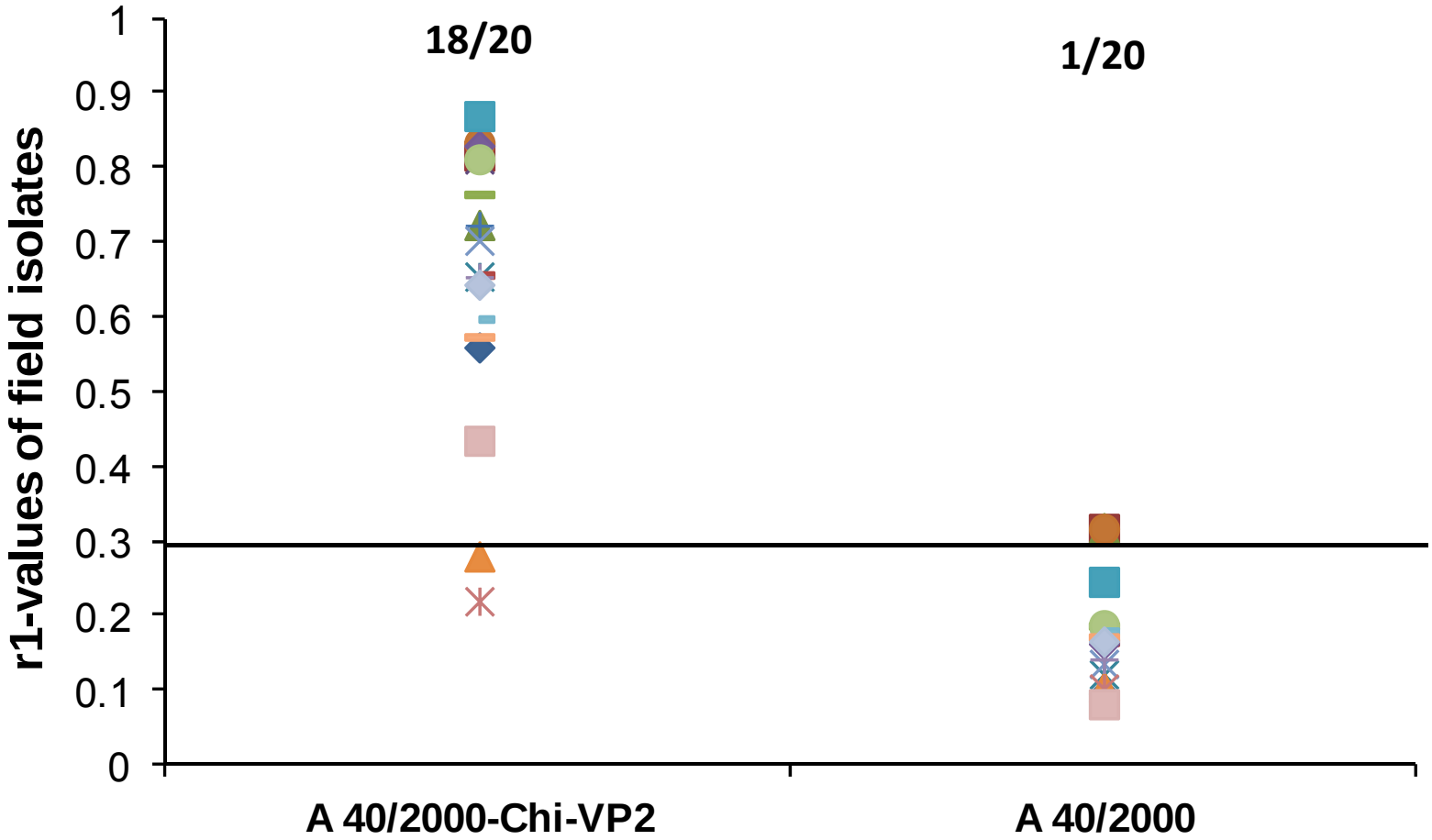


B



2D-VNT was carried out using BVS against A IND 40/2000

r1-values of serotype-A field isolates with Rabbit anti-146S serum



Conclusions

- Reverse genetics technology based chimeric FMDV is a handy tool for the determination of the role of individual capsid protein(s) in the viral-antigenicity .

- New antigenic epitope (VP2-74) was identified on the capsid surface of FMDV serotype A-genotype VII(18).

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