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Short communication

Alternate vaccine strain selection in the wake of emerging foot-and-mouth disease virus serotype A antigenic variants in India

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ABSTRACT

'National foot-and-mouth disease (FMD) control programme' is being implemented in India and therefore predicting vaccine match is a key surveillance task. Recently, a considerable proportion of field viruses (75.6%) showed antigenic drift from the existing serotype A vaccine strain A IND 40/2000 necessitating search for an alternate strain. Here, antigenic relationship ('r_1' value) of 87 field viruses with each of the 8 candidate strains was estimated by virus neutralization test. A IND 27/2011 strain emerged to be the one with the widest spectrum of antigenic coverage showing 'r_1' value of more than 0.3 with 81.6% of field strains. It achieved a reasonably high titre of $\log_{10}$ 7.5 $TCID_{50}$/ml in BHK-21 suspension cell which was accompanied by positive charge gaining substitutions (E_{82}–K and E_{131}–K in VP2) thought to have adaptive significance. However, potency trial remains to be conducted before A IND 27/2011 finds a place in the vaccine formulation.

1. Introduction

Foot-and-mouth disease (FMD), caused by FMD virus (FMDV) within the family *Picornaviridae*, is one of the most widespread viral diseases of cloven-hoofed animals. India has embarked on a preventive vaccination based 'national FMD control programme' since 2003 to combat the three prevalent serotypes O, A and Asia 1 [1]. ICAR-Directorate of FMD (ICAR-DFMD), Mukteswar, is entrusted with the responsibility of updating the vaccine strains. The antigenic diversity of serotype A has led not only to incorporation of multiple strains in the same vaccine [2,3] but also to frequent changes in the vaccine strains in Africa, Argentina, the Middle East and India in the past [2,4–6]. Considerable antigenic drift of the recent serotype A field viruses from the Indian vaccine strain [7] prompted this study to find out an alternate vaccine strain in response to the perceived epidemiological risk. One-way antigenic relationship coefficient ('r_1' value) of the field isolates was determined with each of the strains from a panel comprising 8 characterized field viruses in two-dimensional virus neutralization test (2D-VNT) using rabbit antiserum followed by bovine vaccinal serum (BVS). Their 'r_1' value profiles reflecting the breadth of antigenic coverage were compared to select the best candidate vaccine strain.

2. Methods

2.1. Field viruses and candidate vaccine strains

Virus isolates ($n = 87$) recovered from outbreaks investigated between 1999 and 2015, at the same passage level at which capsid coding (P1) region sequences were determined, were included in this study (Fig. 1). A total of 8 field isolates from various genetic groups/clades of genotype 18 (Fig. 1) showing reasonably high infectivity titre ($\log_{10}$ 7.3–8.1 $TCID_{50}$/ml) in BHK-21 cell monolayer were selected as the candidate vaccine strains.

2.2. Production of rabbit antiserum against the 8 candidate vaccine strains

BHK-21 cell-derived virus was inactivated by binary-ethyleneimine (BEI) and purified as described earlier [8]. A total of 20 μg of the purified antigen was emulsified with Freund's complete adjuvant and injected in the New Zealand White rabbits (3 per strain) by both sub-cutaneous and intramuscular route. After 3 weeks, a booster using the antigen blended with Freund's incomplete adjuvant was administered and blood was collected one week post-booster.

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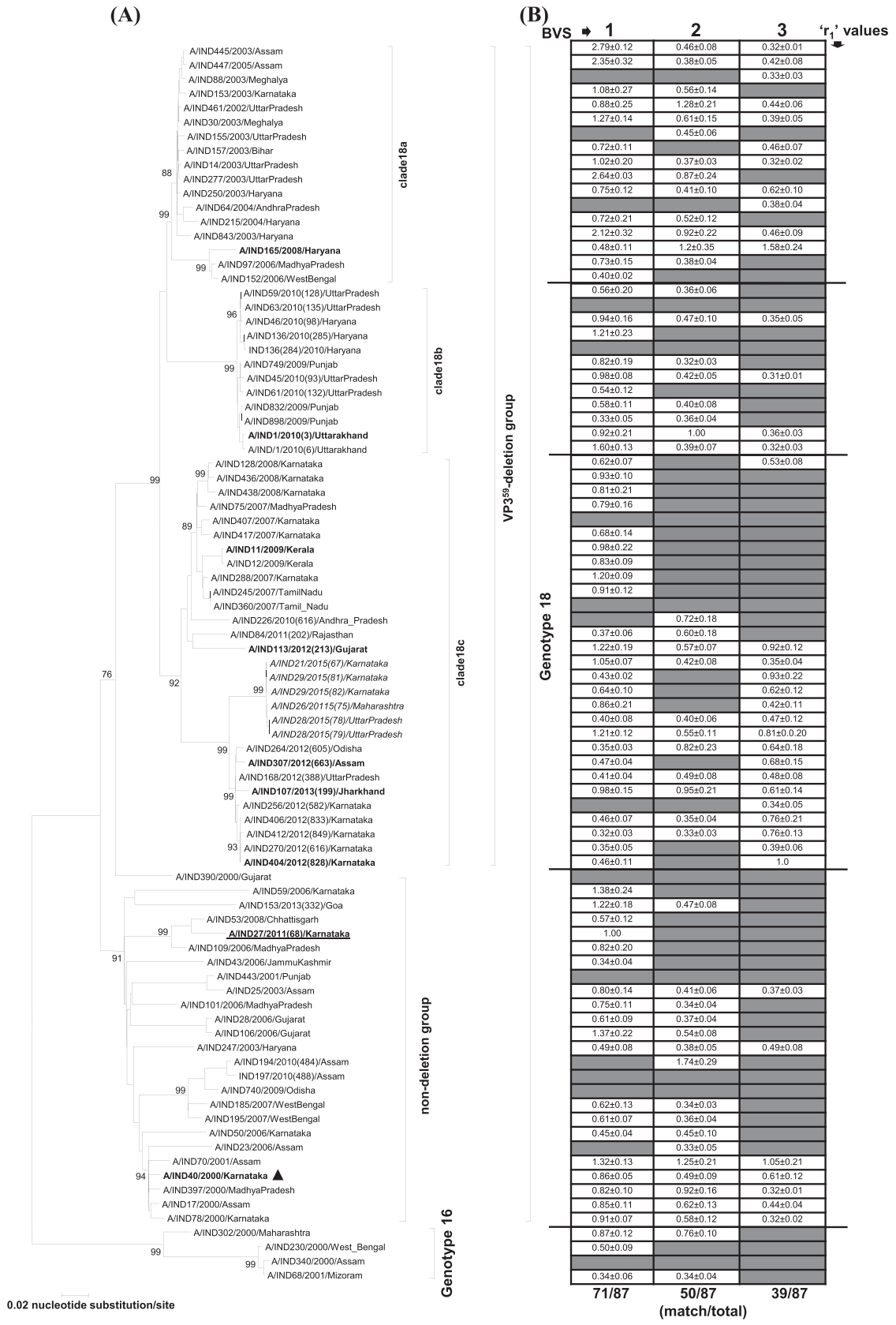

Fig. 1. (A) *Maximum likelihood phylogenetic tree based on P1 sequence* data depicting the genetic clustering of FMD virus serotype A. Isolates sequenced in this study are shown in italics and the candidate vaccine strains are shown with bold font. The existing vaccine strain A IND 40/2000 is marked with a filled triangle and the most suitable candidate vaccine strain A IND 27/2011 is underlined. The numbers within parentheses denote the sample number when multiple samples were collected from the same outbreak. The genotypes and clades are shown adjacent to the tree. (B) Table showing the antigenic relationship (mean ± SD 'r_1' values determined from 2 runs of 2D-VNT using BVS) of field isolates with the candidate vaccine strains (1, A IND 27/2011; 2, A IND 1/2010; 3, A IND 404/2012). The respective 'r_1' values are aligned with the isolates in the tree and cells are filled with grey shade in case the 'r_1' values are less than 0.3.

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