Original Article
Characterization of a nonhemagglutinating mutant of mink enteritis virus in China

Bin Tan*, Shu-Qin Zhang*, Jian-Ke Wang, Hang Zhao, Li-Zhi Chen, Wei Wu, Shi-Peng Cheng


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Abstract: Parvoviruses are small eukaryotic DNA viruses that infect a variety of animal species, including humans. Canine parvovirus type-2, feline panleukopenia virus and mink enteritis virus are all host-range variants of the carnivore parvovirus subgroup. These viruses could hemagglutinate (HA) swine or rhesus monkey erythrocytes in buffered saline solutions at pHs between 6.0 and 6.8. Here we report a nonhemagglutinating mutant of MEV and the amino acid differences compared with other MEV, FPV and CPV strains. Further studies and investigations on MEV are needed to clarify whether this mutant is fixed in the MEV population as a consequence of the mechanisms of antigenic escape or further adaptation to broader host range. It turns crucial to have a better understanding of the epidemiology and evolution of parvovirus.

Keywords: MEV, hemagglutination, amino acids

Introduction

Parvoviruses (family Paroviridae) are small eukaryotic DNA viruses that infect a variety of animal species, including humans. Canine parvovirus (CPV), feline panleukopenia virus (FPV), and mink enteritis virus (MEV) are all host-range variants of the carnivore parvovirus subgroup [1, 2]. Strikingly, although these single-stranded viruses have a DNA genome and use cellular replication machinery, their rate of nucleotide substitution and the underlying rate of mutation is same as that of RNA viruses [3]. CPV emerged in the mid-1970s as a new pathogen of dogs and has since become endemic in the global dog population. Despite widespread vaccination, CPV has remained a persistent disease of dogs. The new genetic and antigenic variants have arisen and extended host range. The CPV represents a rare and important model of disease emergence through cross-species transmission [4]. It is known that several amino acids in the capsid protein of CPV coordinately determined the canine host range, specific antigenic and HA properties [5]. MEV is genetically and antigenically closely related to CPV. These viruses could hemagglutinate (HA) swine or rhesus monkey erythrocytes in buffered saline solutions at pHs between 6.0 and 6.8 [6]. The first nonhemagglutinating MEV was identified and designated MEV-S in 1984 Sweden [7]. However, the nature of hemagglutination (HA) by parvovirus is not well understood. Differences of amino acids in the capsid protein sequences between HA and Non-HA MEV strains have not been reported previously. Here we report a nonhemagglutinating mutant of MEV and the amino acid differences compared with other MEV strains.

In 2009, an infectious enteritis outbreak occurred, which affected more than 5,000 minks at a breeding mink farm in Shandong province of China. Nearly all minks showed clinical and pathological signs of enteritis and the mortality was estimated at 50%. We successfully isolated the pathogenic agent from the fecal samples of infected minks by repeated passages in Crandell Rees feline kidney (CRFK) cells. It was designated as MEV-SDNH. Virus isolation (VI) was conducted as previously described [8]. Two days after incubation, the inoculated cells were tested by direct immunofluorescence (IF) assay using anti-CPV monoclo-
Nonhemagglutinating mink enteritis virus

Table 1. Changes of amino acid in capsid protein VP2 for MEV, FPV and CPV strains

<table>
<thead>
<tr>
<th>Amino acid position</th>
<th>GenBank accession no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strains</td>
<td></td>
</tr>
<tr>
<td>MEV-Abashiri</td>
<td>Thr Ala Asp Asn</td>
</tr>
<tr>
<td>MEV-d</td>
<td></td>
</tr>
<tr>
<td>MEV-e</td>
<td></td>
</tr>
<tr>
<td>MEV-Antigenic type 1</td>
<td>Val</td>
</tr>
<tr>
<td>MEV-Antigenic type 2</td>
<td>Val Asp</td>
</tr>
<tr>
<td>MEV-DL</td>
<td>Val Gly</td>
</tr>
<tr>
<td>MEV-LN10</td>
<td>Val Asp</td>
</tr>
<tr>
<td>MEV-SDNH</td>
<td>Ser Ile Asn Lys</td>
</tr>
<tr>
<td>FPV</td>
<td>Thr Ala Asp Asn</td>
</tr>
<tr>
<td>CPV-2</td>
<td>Ala</td>
</tr>
<tr>
<td>CPV-2a</td>
<td>Gly</td>
</tr>
<tr>
<td>CPV-2b</td>
<td>-</td>
</tr>
<tr>
<td>CPV-2c</td>
<td>-</td>
</tr>
</tbody>
</table>

In order to simplify the presentation of results, the amino acid sequences identical with the above positions are represented by dashes.

A non-hemagglutinating mutant of MEV was derived and identified by VI, IF, HA, and animal infection tests. There were 4 amino acid changes in the capsid protein VP2 compared to HA MEV strains. It was noteworthy that the mutation at the residues position 426 led to Asn→Lys replacement.

In order to simplify the presentation of results, the amino acid sequences identical with the above positions are represented by dashes.
to acquire definite advantages over the original CPV. Changes at residue 426 have modified the antigenic profile of CPV since it is located in the major antigenic region over the three-fold spike of the CPV capsid, and molecular epidemiological studies have demonstrated that complicated selection dynamics act on this residue [13, 14]. However CPV-2 was unable to replicate in cats, the new variants of canine parvovirus, CPV-2a and CPV-2b/2c have also penetrated the feline host-range and they were able to infect and replicate in cats [15]. Residue 426 has undergone two mutations since the emergence of CPV, and is the only coding changes capable of distinguishing the CPV-2a strains from CPV-2b/2c strains [16]. The adaptation of CPV was likely dependent on a high rate of mutation and the positive selection of mutations in the major capsid gene [3]. Mutations involving residue 426 have not been reported previously for MEV. Analogously to CPV, it may be hypothesized that this change may affect the antigenic profile of MEV and confer an evolutionary advantage to the virus. Further studies and investigations on MEV are needed to clarify whether this mutant is fixed in the MEV population as a consequence of the mechanisms of antigenic escape or further adaptation to broader host range. It turns crucial to have a better understanding of the epidemiology and evolution of parvovirus.

Acknowledgements

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Disclosure of conflict of interest

None.

Address correspondence to: Shi-Peng Cheng, Institute of Special Animal and Plant Sciences, 4899 Juye Street, Changchun 130112, Jilin, China. Tel: 86-431-81919845; Fax: 86-431-81919845; E-mail: tcsscp@126.com

References


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