Identification of a short, highly conserved, motif required for picornavirus capsid precursor processing at distal sites

Many picornaviruses cause important diseases in humans and other animals including poliovirus, rhinoviruses (causing the common cold) and foot-and-mouth disease virus (FMDV). These small, non-enveloped viruses comprise a positive-stranded RNA genome (ca. 7-9 kb) enclosed within a protein shell composed of 60 copies of three or four different capsid proteins. For the aphthoviruses (e.g. FMDV) and cardioviruses, the capsid precursor, P1-2A, is cleaved by the 3C protease (3Cpro) to generate VP0, VP3 and VP1 plus 2A. For enteroviruses, e.g. poliovirus, the capsid precursor is P1 alone, which is cleaved by the 3C protease to generate just VP0, VP3 and VP1. The sequences required for correct processing of the FMDV capsid protein precursor in mammalian cells were analyzed. Truncation of the P1-2A precursor from its C-terminus showed that loss of the 2A peptide (18 residues long) and 27 residues from the C-terminus of VP1 (211 residues long) resulted in a precursor that cannot be processed by 3Cpro although it still contained two unmodified internal cleavage sites (VP0/VP3 and VP3/VP1 junctions). Furthermore, introduction of small deletions within P1-2A identified residues 185-190 within VP1 as being required for 3Cpro-mediated processing and for optimal accumulation of the precursor. Within this C-terminal region of VP1, five of these residues (YCPRP), are very highly conserved in all FMDVs and are also conserved amongst other picornaviruses. Mutant FMDV P1-2A precursors with single amino acid substitutions within this motif were highly resistant to cleavage at internal junctions. Such substitutions also abrogated virus infectivity. These results can explain earlier observations that loss of the C-terminus (including the conserved motif) from the poliovirus capsid precursor conferred resistance to processing. Thus, this motif seems essential for maintaining the correct structure of picornavirus capsid precursors prior to processing and subsequent capsid assembly; it may represent a site that interacts with cellular chaperones.

General information
State: Published
Organisations: National Veterinary Institute, Virology
Contributors: Kristensen, T., Belsham, G.
Number of pages: 22
Publication date: 1 Jan 2019
Peer-reviewed: Yes

Publication information
Journal: PLOS Pathogens
Volume: 15
Issue number: 1
ISSN (Print): 1553-7366
Ratings:
BFI (2019): BFI-level 2
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 6.05 SJR 4.006 SNIP 1.548
Web of Science (2017): Impact factor 6.158
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.46 SJR 4.736 SNIP 1.639
Web of Science (2016): Impact factor 6.608
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 7.14 SJR 5.144 SNIP 1.785
Web of Science (2015): Impact factor 7.003
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 7.67 SJR 5.324 SNIP 1.933
Web of Science (2014): Impact factor 7.562
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 8.22 SJR 5.511 SNIP 2.004
Web of Science (2013): Impact factor 8.057
ISI indexed (2013): ISI indexed yes