Sequence adaptations affecting cleavage of the VP1/2A junction by the 3C protease in foot-and-mouth disease virus-infected cells.

The foot-and-mouth disease virus (FMDV) capsid protein precursor P1-2A is cleaved by the virus-encoded 3C protease to VP0, VP3, VP1 and 2A. It was shown previously that modification of a single amino acid residue (K210E) within the VP1 protein and close to the VP1/2A cleavage site, inhibited cleavage of this junction and produced 'self-tagged' virus particles. A second site substitution (E83K) within VP1 was also observed within the rescued virus [Gullberg et al. (2013). J Virol 87, 11591-11603]. It was shown here that introduction of this E83K change alone into a serotype O virus resulted in the rapid accumulation of a second site substitution within the 2A sequence (L2P), which also blocked VP1/2A cleavage. This suggests a linkage between the E83K change in VP1 and cleavage of the VP1/2A junction. Cells infected with viruses containing the VP1 K210E or the 2A L2P substitutions contained the uncleaved VP1-2A protein. The 2A L2P substitution resulted in the VP1/2A junction being highly resistant to cleavage by the 3C protease, hence it may be a preferred route for 'tagging' virus particles.