

P018 The integrin $\alpha\beta 8$ functions as a receptor for foot-and-mouth disease virus.

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Field isolates of foot-and-mouth disease virus (FMDV) have been shown to use three α v-integrins, $\alpha\beta 1$, $\alpha\beta 3$ and $\alpha\beta 6$ as cellular receptors. Binding to the integrin is mediated by a highly conserved RGD motif located on a surface exposed loop of VP1. The RGD tripeptide is a recognition motif for several other members of the integrin family which also have the potential to act as receptors for FMDV. In this report we show that FMDV binds to human $\alpha\beta 8$ on the surface of $\beta 8$ -transfected SW480 cells and that this binding leads to a productive infection. The interaction with the integrin can be inhibited by RGD-containing peptides, and by function blocking Mabs which recognise either the $\alpha\beta 8$ heterodimer or the α v-chain. The same results were obtained with a chimeric $\alpha\beta 8$ containing the cytoplasmic domain of the $\beta 6$ -chain ($\alpha\beta 8/6$). In contrast, replacing the $\beta 6$ cytoplasmic domain with the cytoplasmic domain of the $\beta 8$ chain ($\alpha\beta 6/8$) appeared to alter the conformation or activation state of the extracellular domain of $\alpha\beta 6$ at the cell surface since FMDV binding was reduced compared to wild-type $\beta 6$. In addition, FMDV binding to the $\beta 6/8$ chimera did not lead to infection demonstrating that the $\beta 8$ cytoplasmic domain, in contrast to the $\beta 6$ cytoplasmic domain does not promote receptor internalization. This suggests a novel mechanism of FMDV internalization mediated by the $\alpha\beta 8$ integrin.