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Inhibition of enterovirus 71 entry by peptides targeting I β-sheet of VP1 protein

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The binding of enterovirus capsid protein VP1 on the host receptors is the first step for virus entry during the infection. Peptides blocking the binding of VP1 and its receptors can be used not only for antiviral treatment but also for probing functional important motifs or residues involved in this biological process. Based on the crystal structure of VP1-VP4 complex of enterovirus 71 (EV71), we applied molecular modeling approaches to revisit the potential antiviral peptides in an antienterovirus 71 screening study. We showed that a β -sheet structure (I β) is unique and locates at a very favorable position for drug target. More importantly, the sequence of I β -sheet is highly conserved among subtypes of EV71, suggesting an idea target sites for antiviral drug design. Peptides targeting I β -sheet potently inhibited EV71 infections. Further attachment and single-round pseudovirus infection assays revealed that the attachment of virions on host cells was effectively blocked by peptides. Alanine scan analysis demonstrated that residues Arg250, Arg254, Met255 and Lys256 are critical for virion binding on host cells. This study demonstrated the importance of I β -sheet structure for EV71 entry and an effective peptide for block virion-host cell interactions.

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