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Novel mechanism for invasion of EV71 virus demonstrated

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A new study determines glycosylation and pH-dependent conformational changes of virus receptor SCARB2 as crucial for EV71 attachment, entry and uncoating.

Enterovirus 71 (EV71) is the major causative agent of hand, foot and mouth disease (HFMD) in the Asia-Pacific region, having caused 8.8 million infections and 3,000 deaths in China in the past five years. Unlike other enteroviruses (e.g. Coxsackievirus), EV71 can cause severe aseptic meningitis, encephalitis, myocarditis and acute flaccid paralysis, thus leading to significant fatality rates. Unfortunately, the molecular mechanism of EV71 invasion remains poorly understood and there are still no clinically approved therapeutics. Researchers from the Institute of Biophysics, Chinese Academy of Sciences, reported in a study published in Springer's open access journal *Protein & Cell* a novel mechanism for EV71 entry mediated by its receptor SCARB2. These findings make a significant conceptual advance in the understanding of non-enveloped virus entry, to which EV71 belongs.

In this study, the authors determined the crystal structures of the SCARB2 ectodomain at physiological pH (7.5) and acidic pH (4.8). Comparison of these structures revealed an unexpected pH-dependent conformational change in the EV71 binding sites. At acidic condition, SCARB2 opens up a lipid-transfer tunnel to trigger viral uncoating, releasing the viral genome into the host cell. In addition, the authors demonstrated that the glycosylation of SCARB2 plays a crucial role in attachment and infection of EV71. These results demonstrate how

SCARB2 mediates both attachment and uncoating of EV71, and provide valuable information for SCARB2-related drug design against EV71 infection.

More information: Dang, M. Wang, X. et al. (2014). Molecular mechanism of SCARB2-mediated attachment and uncoating of EV71. *Protein & Cell*. DOI: 10.1007/s13238-014-0087-3

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