Anti-viral activity of marine sulfated polysaccharide targeting dengue virus envelope protein

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Flavivirus infection is initiated by the interaction between envelope (E) protein and protein, lipid, or carbohydrate host receptor(s) that exist in a complex extracellular matrix structure. It is speculated that interaction of viral particle with these molecules determines tissue tropism, host range, and virulence. To date, DC-SIGN (dendritic cell-specific ICAM3-grabbing non-integrin), heparan sulfate-containing proteoglycans and nLc4Cer (neolactotetraosylceramide) have been reported as putative receptor molecules for dengue viruses.

Among flaviviruses, Dengue virus (DEN) and Japanese encephalitis virus (JEV) transmitted by mosquitoes cause dengue fever and dengue hemorrhagic fever, and encephalitis, respectively. Mechanisms on flavivirus infection such as adsorption are not well defined. There are no effective anti-viral agents available so far. To understand the host range, tissue tropism of this pathogen, which is transmitted to humans by infected mosquitoes, it is critical to elucidate the molecular mechanisms on the interaction of the viral surface glycoprotein, E protein, with host receptors. In this study, we investigated sulfated carbohydrate molecules specifically recognized by DEN.

We examined whether sulfated polysaccharides can inhibit infection of mammalian cells by dengue viruses. Fucoidan and heparin significantly inhibited infection by these viruses as well as direct virus binding to cells. We also found that dengue viruses interact directly with fucoidan and heparin. These results strongly suggest that common structures shared by these sulfated molecules, fucoidan and heparin could be essential epitopes for dengue virus–host cell interaction. These findings will contribute to determination of the mechanisms of early stages of dengue virus infection and will aid in the development of effective antiviral drugs such as entry inhibitors.

References

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