ANALYSIS OF THE HOST REACTION BY DENGUE VIRAL NONSTRUCTURAL PROTEIN 1

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Background: Vascular leakage and shock are the major causes of death in patients with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). It has been suggested that several factors are involved in plasma leakage, such as an excessive production of cytokines, an activation of complement, and apoptosis-related phenomenon. However, it is still unclear. Several groups reported that patients with an elevated level of the free soluble form of dengue virus (DV) nonstructural protein 1 (sNS1) are at risk of developing DHF. However, the role of NS1 is still unknown.

Objectives: To understand the role of sNS1 in blood, we searched for the host molecule with which NS1 interacts in human plasma. Besides, we analyzed the effect of the membrane bound NS1 to host cells, complement systems, etc.

Methods: To find the host factor interacting NS1 in plasma, affinity purification using a GST-fused NS1 was performed. For the analysis of the effect of NS1 to host cells, membrane bound form NS1 was expressed in cell and analyzed by immunofluorescence, etc

Results: he affinity chromatography with GST-NS1 detected 34-36 kDa protein. A complement inhibitory factor clusterin (Clu), which naturally inhibits the formation of terminal complement complex (TCC), was identified by mass spectrometry. This result suggests the possibility that the complement terminal pathway may be involved in the dengue pathogenesis. In addition, the membrane bound NS1 caused an unbalance of complement system, etc.

Conclusions: The activation of complement system has been observed in DV-infected patients. The activation of complement system possibly causes vascular leakage. Clu is thought to inhibit the activation of the complement terminal pathway and may be involved in pathogenesis of severe cases. For instance, the removal of Clu by anti-dengue antibody through NS1 may cause failure of the repression of activated complement by DV infection. However, the mechanism of the complement activation in dengue infection remains unknown. In other words, it is unclear how the complement system is activated. Further study is needed to understand the pathogenesis of DV infection.

Keywords: pathogenesis**,** dengue virus**,** nonstructural protein