

PHENOTYPIC DIFFERENCES BETWEEN AMERICAN AND SOUTHEAST ASIAN STRAINS OF DENGUE SEROTYPE 2 VIRUSES

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Dengue virus continues to be a global health concern with considerable morbidity and mortality in the tropical and subtropical regions of the world. Previous studies have demonstrated that American strains of dengue serotype 2 (D2) viruses are genetically different from Southeast Asian strains and infection results in at most mild dengue disease without hemorrhagic manifestations or shock. Previous studies have reported that heparan sulfate is a specific receptor for dengue virus. Heparin has been demonstrated to competitively inhibit dengue virus infection though this effect varies by the dengue serotype suggesting differences in heparan sulfate avidity and possible alternate receptor pathways for viral entry. In our study, the interaction of D2 virus (Asian and American strains) with its cellular receptor and inhibition of virus binding by heparin was determined and compared using cell binding assay with H³-labeled D2(NGC) and D2 American (Peru) virus strains. Binding activities of 3H5, 4G2 and 2H2 monoclonal antibodies against both strains were determined by enzyme immunoassay (EIA). Our results demonstrated that heparin inhibition of virus binding and endpoint binding reactivity of 3H5, (serotype-specific neutralizing activity) and 4G2 (flavivirus group determinant) to D2 (Peru) and D2 (NGC) are significantly different between the Asian and American D2 virus strains indicating phenotypic differences between these two viruses. Competitive infection assays between heparin and monoclonal antibodies showed that in D2 (Peru), heparin inhibited binding of 3H5 while in D2 (NGC), binding to both sites was promoted. Our results suggest that the heparan sulfate-binding site and 3H5 neutralizing epitopes are different for the two strains and are adjacent to or overlap with each other. Understanding the phenotypic differences in these two viruses will increase our understanding of the differences in virus entry and infectivity of these viruses and their role in producing subclinical to severe dengue disease.

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POSSIBLE RELATIONSHIP BETWEEN IMMUNE RESPONSE TO MOSQUITO (*Aedes aegypti*) SALIVARY PROTEINS AND DENGUE DISEASE SEVERITY

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Dengue viruses are arthropod-borne viruses transmitted by *Aedes aegypti* mosquitoes. These viruses can cause dengue fever (DF), which is a relatively benign disease, or the more severe dengue hemorrhagic fever (DHF) in humans. It is known that arthropod saliva contains proteins that can interfere with the host immune response as well as the coagulation cascade to facilitate the acquisition of blood during the intake of the blood meal. Salivary proteins have usually been characterized after extraction from dissected salivary glands. We developed a procedure