

# Dengue Virus Nonstructural-1 Protein And Its Structural Correlation To Human Integrin/Adhesin Proteins

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## Abstract

Dengue infection is a major public health problem, yearly affecting thousands of children in the tropical countries. Although most infections present as fever, headache, chill and rash there is a severe form of dengue infection called dengue hemorrhagic fever. The mechanisms underlying severe bleeding in dengue DHF are not completely understood. Recently, it is noted that the dengue virus nonstructural-1 protein (NS1) generated antibodies to common epitopes on platelet integrin/adhesin proteins. Although the phylogenetic analysis revealed the closed phylogenetic relationship between dengue NS1 and integrin/adhesin proteins it does not mean the structural homology. Here, the author performs a structural analysis to answer the question how dengue virus NS1 protein the related to platelet integrin/adhesin relating proteins. Answering this question, the author performed a structural analysis of dengue virus NS1 and integrin/adhesin proteins. According to this study, no significant similarity in the structure of the studied protein can be detected. Therefore, the previous detected correlation between dengue virus NS1 and integrin/adhesin proteins is not supported.

## INTRODUCTION

Dengue infection is a major public health problem, yearly affecting thousands of children in the Southeast Asia Region <sup>1</sup>. Although most infections present as fever, headache, chill and rash <sup>2, 3, 4</sup> there is a severe form of dengue infection called dengue hemorrhagic fever. In this case, the host immunological response host is the important factor in the course of disease <sup>5</sup>. These responses are immune complex formation, complement activation, increase histamine release and a massive release of many cytokines into the circulation, leading to shock, vasculopathy, thrombopathy and disseminated intravascular coagulation (DIC) <sup>5</sup>.

However, the mechanisms underlying severe bleeding in dengue DHF are not completely understood. Recently, Falconar proposed that the dengue virus nonstructural-1 protein (NS1) generated antibodies to common epitopes on human blood clotting and integrin/adhesin proteins on the platelet <sup>6</sup>. In addition, several anti-NS1 monoclonal antibodies produced haemorrhage in mice, cross-reacted with integrin/adhesin proteins present on the platelets <sup>6</sup>. Therefore, the role of NS1 as an important protein causing the unwanted immunological reaction bringing DHF is hypothesized. However, the proof on the correlation between dengue virus NS1 and platelet integrin/adhesin proteins is

needed. Here, the author performs a structural analysis to answer the question how dengue virus NS1 protein the related to platelet integrin/adhesin relating proteins. Answering this question, the author performed a structural analysis of dengue virus NS1 and integrin/adhesin proteins.

## MATERIALS AND METHODS

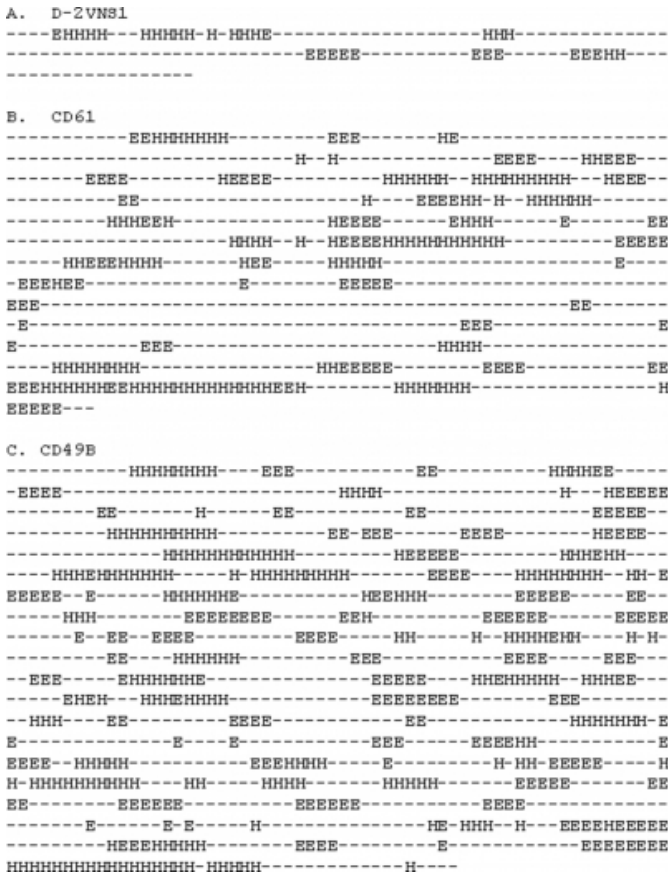
The database Pubmed (<http://www.pubmed.com>) and ExPASy <sup>7</sup> was used for data mining of the protein sequences of dengue virus NS1 proteins (D-2VNS1) and platelet integrin/adhesin relating proteins (CD49B, CD41 and CD61). Secondary structure prediction was performed for each protein. Concerning modeling, the author performs protein secondary structure predictions of all studied proteins from its primary sequence using NNPREDICT server<sup>8</sup>. The calculated secondary structures were presented and compared.

## RESULTS

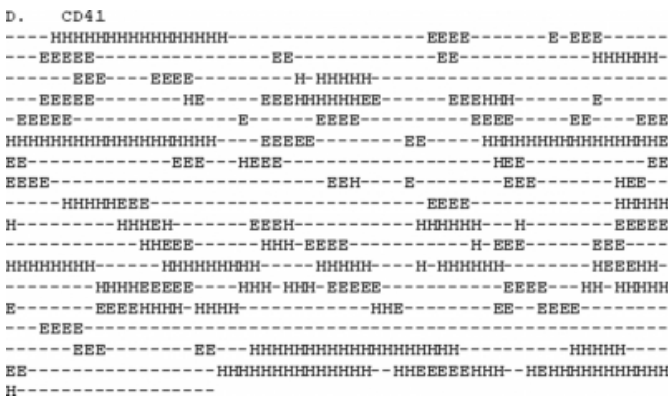
From searching of the databases, the sequences of D-2VNS1, CD49B, CD41 and CD61 were derived. These sequences were further predicted for secondary structure and the calculated structures were presented in Figure 1.

**Figure 1**

Figure 1: Calculated secondary structures of dengue NS1 and integrin/adhesin proteins (Secondary structure prediction: )



**Figure 2**



**DISCUSSION**

It is mentioned that antibody responses generated by mice to the dengue NS1 protein were influenced by MHC class II (I-A) haplotype but each antiserum cross-reacted with human fibrinogen, thrombocytes and endothelial cells <sup>6</sup>. Therefore, the homology of NS1 and other mentioned proteins can be a potential role of both antigenic and biochemical mimicry in

dengue haemorrhagic fever pathogenesis, consistent with clinical data <sup>6</sup>. Wiwanitkit proposed that platelet integrin/adhesin relating proteins, especially CD61, might play an important role in causing hemorrhagic complication in dengue infection <sup>9</sup>. Indeed, Chang et al reported that dengue NS1 immobilized on coverslips resulted in more cell adhesion than did the control proteins and indicated that integrin relating peptides structural mimicry existed within the NS1 antigen <sup>10</sup>. Although the phylogenetic analysis revealed the closed phylogenetic relationship between dengue NS1 and integrin/adhesin proteins it does not mean the structural homology. Since structure reflect more direct to the molecular to molecular interaction, the homology in structure is more accurate to the real phenomenon than similarity in sequence <sup>9</sup> or phylogenetic.

Modeling for the structure is needed to verify the homology in the structure. Here, the author use the structural analysis technique to clarify the correlation between dengue virus NS1 protein the related to platelet integrin/adhesin relating proteins. According to this study, no significant similarity in the structure of the studied protein can be detected. Therefore, the previous detected correlation between dengue virus NS1 and integrin/adhesin proteins is not supported.

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**References**

1. Thisyakorn U, Thisyakorn C. Diseases caused by arboviruses-dengue hemorrhagic fever and Japanese B encephalitis. Med J Aus 1994; 160: 22 - 6
2. Guzman MG, Kouri G. Dengue: an update. Lancet Infect Dis. 2002;2:33-42
3. da Fonseca BA, Fonseca SN. Dengue virus infections. Curr Opin Pediatr 2002;14:67-711
4. Solomon T, Mallewa M. Dengue and other emerging flaviviruses. J Infect. 2001;42:104-15
5. Mittrakul C. Bleeding problem in dengue haemorrhagic fever: platelets and coagulation changes. Southeast Asian J Trop Med Public Health. 1987;18:407-12
6. Falconar AK. dengue virus nonstructural-1 protein (NS1) generates antibodies to common epitopes on human blood clotting, integrin/adhesin proteins and binds to human endothelial cells: potential implications in haemorrhagic fever pathogenesis. Arch Virol 1997;142:897-916
7. Gasteiger E, Gattiker A, Hoogland C, Ivanyi I, Appel RD, Bairoch A. ExPASy: The proteomics server for in-depth protein knowledge and analysis. Nucleic Acids Res 2003;31:3784-8
8. Kneller DG, Cohen FE, Langridge R. Improvements in Protein Secondary Structure Prediction by an Enhanced Neural Network. J Mol Biol 1990; 214: 171-182
9. Wiwanitkit V. Platelet CD61 might play an important role

in causing hemorrhagic complication in dengue infection.  
Clin Appl Thrombo Hemostat (in press)

10. Wang S, He R, Patarapotikul J, Innis BL, Anderson R. Antibody-enhanced binding of dengue-2 virus to human platelets. Virology 1995;213:254-7

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