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Blast Comparision of Denv Serotypes

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Abstract: *Dengue virus (DENV) has emerged as major health concern, as DENV infection has been shown to be associated with severe disease symptoms. As the largest protein component within the DENV replication complex, NS5 plays key roles in the life cycle and survival of the virus through its N-terminal methyltransferase (MTase) and C-terminal RNA-dependent RNA polymerase (RdRp) domains. Here, we present the blast result of DENV NS5 RdRp. We have identified the conserved features of DENV NS5 RdRp structures that could lead to development of current antiviral inhibitors being used against dengue virus, including flaviviruses.Our structural analysis should inform and accelerate the structure-based design of antiviral compounds against DENV.This leads to the identification of a potential drug-binding site of DENV NS5, which might facilitate the development of novel antivirals for DENV.*

Key Words -Flavivirus, Denv, NS5, Blast, Drug-

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I. Introduction

The viral family *Flaviviridae* includes three genera of enveloped viruses: Flavivirus, Pestivirus, and Hepacivirus[1].About 70 viruses have thus far been found to contain a flavivirus-specific antigen and are classified as belonging to the genus Flavivirus [2]. Many flaviviruses are significant human pathogens, including dengue virus serotypes (DENV) 1–4, yellow fever virus (YFV), tick-borne encephalitis complex virus (TBEV), Japanese encephalitis virus (JEV), Murray Valley encephalitis virus (MVEV), St. Louis encephalitis virus (SLEV), and West Nile virus (WNV). The spectrum of diseases caused by flaviviruses ranges from a mild febrile illness to hepatitis, hemorrhagic syndromes, and encephalitis and can be fatal [3].The World Health Organization estimates that almost half the global population is at risk of dengue virus infection and 900 million people live in areas endemic for yellow fever transmission [4]. Each year there are an estimated 200,000 cases of yellow fever and 400 million cases of dengue fever leading to ~30,000 and ~20,000 deaths respectively [5]; and alarmingly, flavivirus transmission rates have continued to rise over the last two decades. Currently, there are no effective treatments for diseases caused by flavivirus infections. Thus, there is an immediate need to validate anti-flaviviral drug targets and identify compounds with the ability to inhibit flaviviral replication.

Flavivirus GenomeFlavivirusvirions are spherical in shape with a diameter of 50 to 60 nm [6].The icosahedral nucleocapsid, about 30 nm in diameter, consists of capsid protein and genomic RNA, and is surrounded by a lipid bilayer in which the viral envelope and membrane proteins are embedded.The flavivirus genome RNA is single-stranded and of positive (i.e., mRNA-sense) polarity. A cap is present at the 5′ end, followed by the conserved dinucleotide sequence 5′-AG-3′ [7]. The 3′ end of the genome terminates with 5′-CU_{OH}-3′ [8] rather than with a poly(A) tract. The viral genome is approximately 11 kb in length, consisting of a 5′ untranslated region (UTR), a single long open reading frame (ORF), and a 3′ UTR (Fig. 1)[9]. The single ORF of WNV, for instance, encodes a polyprotein of about 3433 amino acids, and has a gene order of 5′-C-prM-E-NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5-3′ (Fig. 1A). The polyprotein is co-and post-translationally processed by viral and cellular proteases into three structural proteins (capsid [C], premembrane [prM] or membrane [M], and envelope [E]) and seven nonstructural (NS) proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) [10]. The NS proteins are assumed to be involved primarily in the replication of viral RNA as part of a replicase complex. The majority of the WNV NS proteins are multifunctional. NS1, NS3 and NS5 are large and highly conserved, while NS2A, NS2B, NS4A and NS4B are relatively small and hydrophobic. Glycoprotein NS1 and its interaction with NS4A are required for RNA replication [11]. It was recently reported that NS2A functions during assembly and/or release of infectious flavivirus particles [12]. NS2B forms a complex with NS3 and is a required cofactor for the protease activity of NS3 [13]. NS3 is a multi-functional protein with activities of serine protease (with NS2B as a cofactor), 5′-RNA triphosphatase (RTPase), nucleoside triphosphatase (NTPase), and helicase [14].The functions of the membrane-associated NS4A and NS4B are not known. NS5 has RNA-dependent RNA polymerase (RdRp) activity [15] and has homology with MTases, which are involved in methylation of the 5′ RNA cap structure [16].

Recently, NS5 was also found to carry RNA guanylyltransferase (GTase) activity [17]. Upon flavivirus infection, the plus-strand genomic RNA is transcribed into a complementary minus-strand RNA, and that, in

turn, serves as the template for the synthesis of more plus-strand genomic RNA [18]. The synthesis of flavivirus plus-sense and minus-sense RNAs is asymmetric; plus-sense RNA is produced in 10- to 100-fold excess over minus-sense RNA [19].

Ns5 Protein

With a molecular mass of 104 kDa, NS5 is the largest of the DENV proteins. The NS5 protein from dengue virus is bifunctional and contains 900 amino acids. The *S*-adenosyl methionine transferase activity resides within its N-terminal domain, and residues 270 to 900 form the RNA-dependent RNA polymerase (RdRp) catalytic domain. Viral replication begins with the synthesis of minus-strand RNA from the dengue virus positive-strand RNA genome, which is subsequently used as a template for synthesizing additional plus-strand RNA genomes. This essential function for the production of new viral particles is catalyzed by the NS5 RdRp. We performed blast of all denv NS5 serotypes (1-4) and summarize NS5 is the largest (102 kDa) and the most conserved protein (with ~70% sequence identity among the four serotypes). These results should facilitate structure- based efforts for the design of antiviral compounds against DENV.

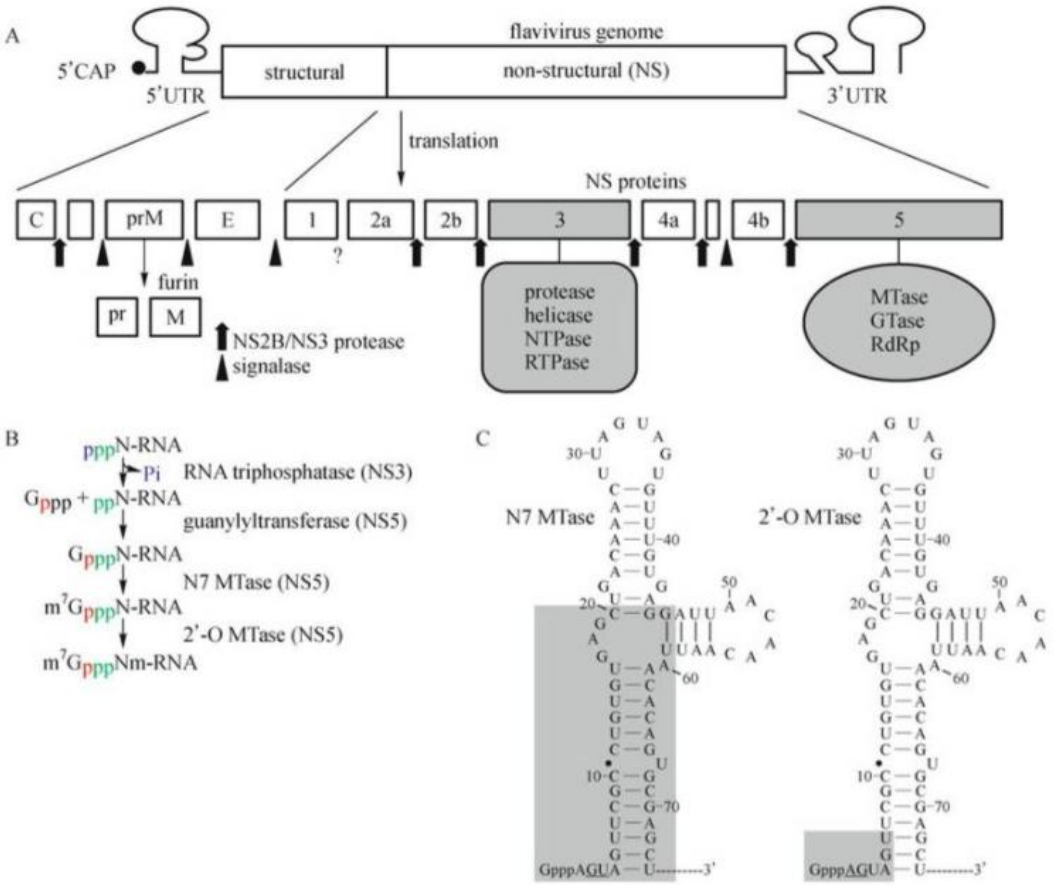

Fig 1. Schematic representations of flavivirus genome structure (A), RNA cap formation (B), and substrate specificities of the WNV MTase (C)

A: Flavivirus genome structure. Flavivirus genomic RNA consists of a 5′ untranslated region (UTR), a single open reading frame (ORF), and a 3′-UTR. The single ORF encodes three structural and seven nonstructural (NS) proteins. Sites of polyprotein cleavage mediated by the viral NS2B-NS3 and by host signalase and furin are shown, and the enzymatic activities of NS3 and NS5 are also indicated. B: Cap formation of flavivirus RNA. Four enzymatic modifications are required for flavivirus RNA cap formation. Phosphates from different molecules are colored individually to indicate their sources. The putative steps presented here are modified from cellular mRNA cap formation. C: Summary of RNA substrate requirements for the N7 and 2′-O activities of the WNV MTase [20]. The stem-loop structure formed by the 5′ terminal 74 nt of the WNV genome was predicted by the Mfold program [21]. The shaded regions are important for N7 (left panel) and 2′-O (right panel) methylations. Essential wild-type nucleotides are underlined.

II. Methodology

To analyze sequence similarity among all four DENV NS5, We performed BLAST (the Basic Local Alignment Search Tool) between DENV2 and DENV3 NS5. BLAST finds regions of local similarity between sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance of matches. BLAST can be used to infer functional and evolutionary relationships between sequences as well as help identify members of gene families.

For Blast we obtained gi code of both denv3 and denv2 NS5 from protein database of ncbi. With these sequences we found following result.

III. Result And Discussion

Comparison between DENV2 and DENV 3 NS5 protein

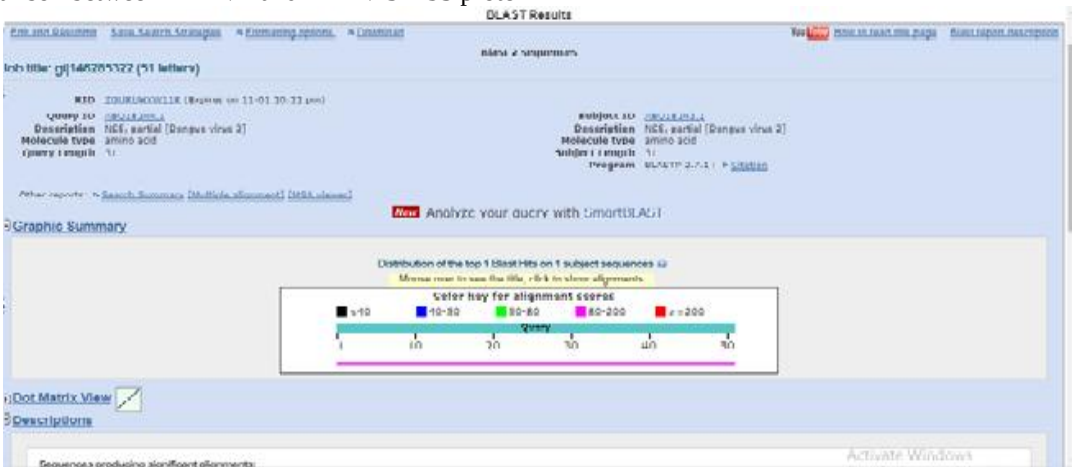

Fig 2. Blast result

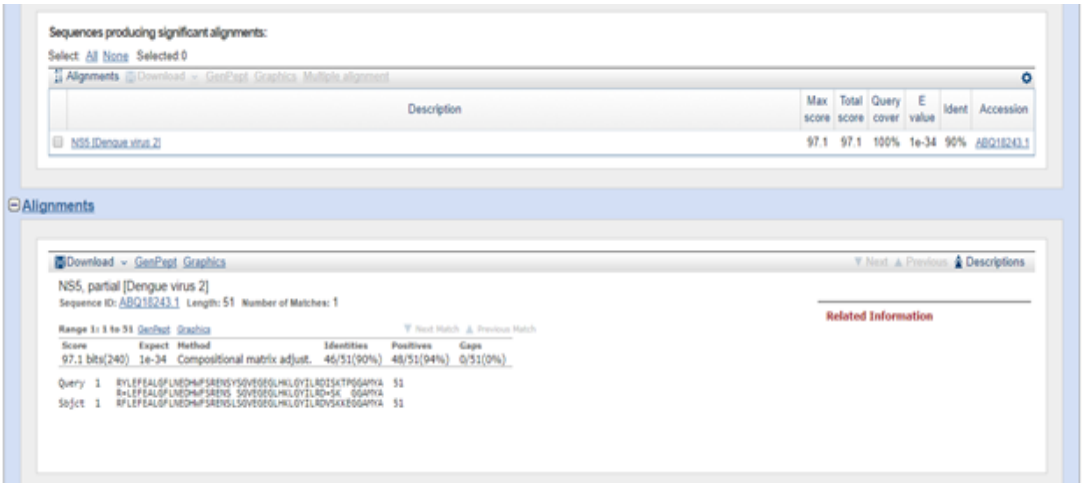

Fig 3. Statistics of similarity between denv serotypes

IV. conclusion

From the observation using the Bioinformatics software protein data base and Blast suggest that NS5 shows greatsimilarity in DENV serotypes. The NS5 protein in DENV plays an important role in pathogenesis. It plays key roles in the life cycle and survival of the virus through its N- terminal methyltransferase (MTase) and C- terminal RNA- dependent RNA polymerase (RdRp) domains. This studies shown that if research work on NS5 protein is encouraged, this will be a vital step to find the lifesaving drug in case of dengue.

Refrences

[1]. Brinton, 1981; Westaway et al., 1985; Brinton, 2002).
[2]. (Westaway et al., 1985).
[3]. Asnis et al., 2000; Asnis et al., 2001; Kramer and Bernard, 2001; Shi et al., 2001; Shi et al., 2002a, 2002b).
[4]. OrganizationWH (2014) Vector-borne diseases. Geneva, Switzerland: World Health Organization.
[5]. Guzman A, Isturiz RE (2010) Update on the global spread of dengue. Int J Antimicrob Agents 36: S40–
[6]. S42. doi: 10.1016/j.ijantimicag.2010.11.012 PMID: 21129927
[7]. Li et al., 2008; Perera and Kuhn, 2008; Yu et al., 2008.

[8]. Cleaves and Dubin, 1979.
[9]. Wengler and Wengler, 1981.
[10]. Rice et al., 1985; Shi et al., 2001.
[11]. Chambers et al., 1990.
[12]. Lindenbach and Rice, 1997; Muylaert et al., 1997; Lindenbach and Rice, 1999.
[13]. Kummerer and Rice, 2002.
[14]. Chambers et al., 1991; Arias et al., 1993; Chambers et al., 1993; Falgout et al., 1993.
[15]. Wengler and Wengler, 1991; Warrener et al., 1993; Li et al., 1999.
[16]. Tan et al., 1996; Ackermann and Padmanabhan, 2001; Guyatt et al., 2001
[17]. Koonin, 1993; Egloff et al., 2002; Ray et al., 2006.
[18]. Issur et al., 2009.
[19]. Chambers et al., 1990.
[20]. Muylaert et al., 1996; Diamond et al., 2000.
[21]. Dong H, Ray D, Ren S, Zhang B, Puig-Basagoiti F, Takagi Y, Ho CK, Li H, Shi PY. Distinct RNA elements confer specificity to flavivirus RNA cap methylation events. J Virol. 2007;81(9):4412–4421
[22]. Zuker M. Mfold web server for nucleic acid folding and hybridization prediction. Nucleic Acids Res. 2003;31(13):3406–3415.
[23]. Thai Leong Yap et al. Crystal Structure of the Dengue Virus RNA-Dependent RNA Polymerase Catalytic Domain at 1.85-Angstrom Resolution. Journal of virology. 2007, p. 4753–4765.

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