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Research Article

Analysis of predicted proteasomal cleavages in the methyltransferase domain from JEV

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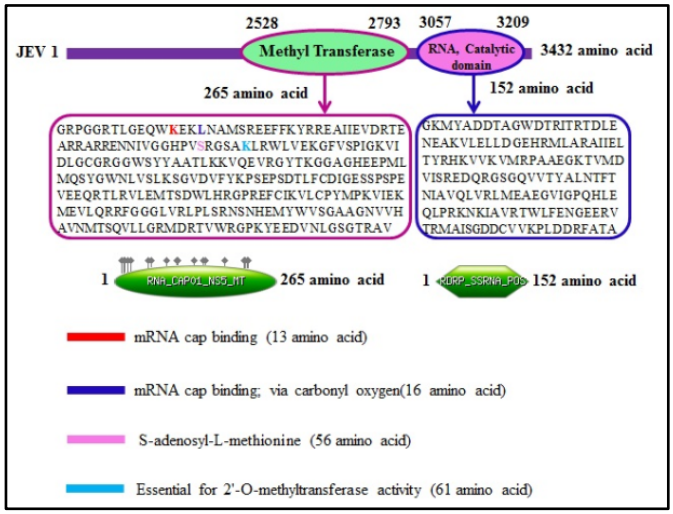
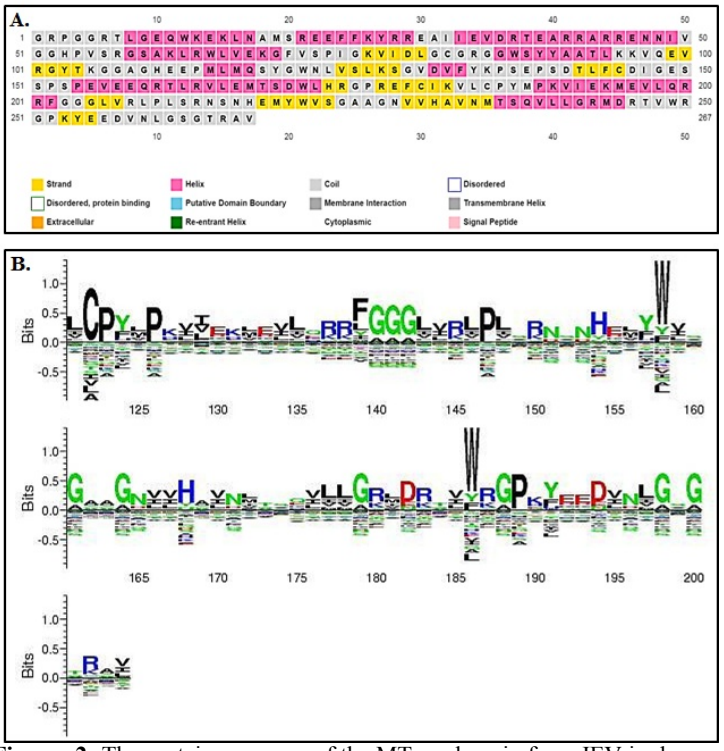
Abstract:
The methyltransferase (MTase, a 265 amino acid residues long region at the N-terminal end of the viral nonfunctional supermolecule NS5 domain) is key for viral replication in Japanese Encephalitis Virus (JEV). Sequence to structure to functional information with adequate knowledge on MTase from JEV is currently limited. Therefore, it is of interest to document a report on the comprehensive analysis of predicted proteasomal cleavage data in the methyltransferase domain from JEV. This data is relevant in the design and development of vaccine and other therapeutic candidates for further consideration.

Keywords: Japanese encephalitis (JEV), infection, methyltransferase, proteasome, cleavage

Background:
Japanese Encephalitis (JEV) is an infection, which belongs to the family of Flaviviridae. It is the cause for Viral Encephalitis worldwide with 50,000 cases every year and 15,000 deaths **[1].** The genome of the Flavivirus is a reclusive stranded RNA having a positive end **[2, 3].** The genome of the Flavivirus encodes a polyprotein with proteases divided into 7 nonstructural proteins such as NS1, NS2A, NS2B, NS3, NS4A, NS4B & NS5 and NS3 along with envelope proteins [4]. The non-structural 5 protein contains a N-terminal region named MTase (methyltransferase) & a C-terminal region named RdRp (RNA dependent RNA polymerase) **[5-7].** The link between proteasomal cleavage and cell mediated immune response well documented **[8].** Several methods to study proteasome cleavage are available **[9-12].** It is of interest to document a report on the comprehensive analysis of predicted proteasomal cleavage data in the methyltransferase domain from JEV towards the development of suitable therapeutics against the virus.



Figures 1: Domain organization in the JEV proteome is shown. It consists of two domains (MTase and RdRP) as shown.



Figures 2: The protein sequence of the MTase domain from JEV is shown with (A) secondary structures and (B) conserved domains.

Methodology:
Conserved domain:
The MTase domain sequence was downloaded from NCBI Genome database is 265 amino acids. We analyzed the sequence using BLASTP for identifying homologs. The sequence was further analyzed using Prosite, SMART, PANTHER, Pfam and InterProScan for functional annotation of the MTase sequence **[13-15].** The MTase domain consisted of a mRNA cap binding region containing 13 amino acids along with a carbonyl oxygen region

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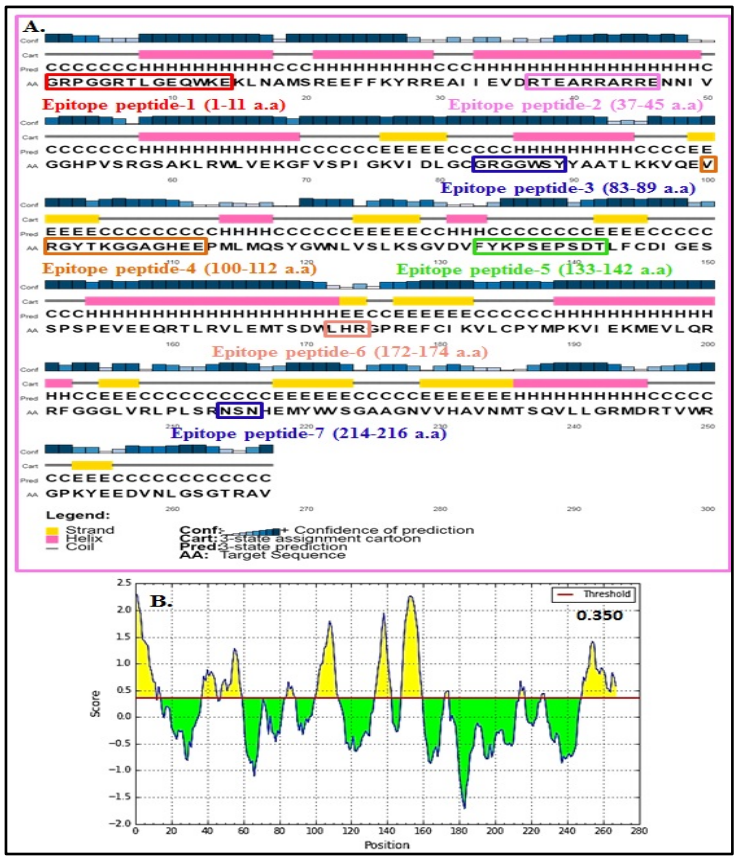
containing 16 amino acids and a S-adenosyl-L-methionine containing 56 amino acids. These are necessary for the activity of 2′-O-methyltransferase made of 61 amino acids. Moreover, the ends of MTase comprises of some coils, helices and strands.



Figures 3: MTase with secondary structures (A) and conformational epitopes (B) is shown.

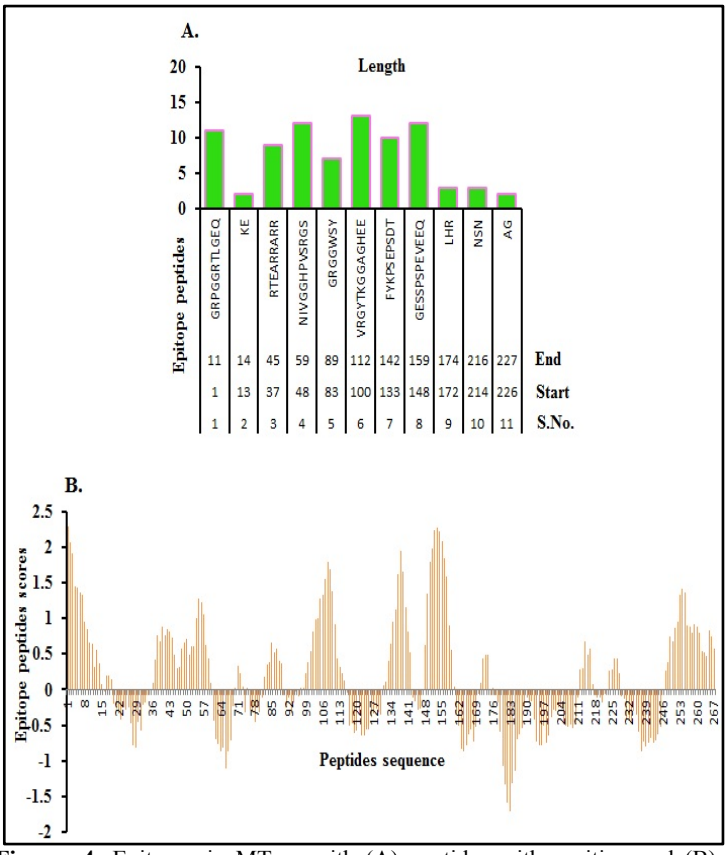
Sequence logo analysis:
We analyzed the MTase sequence using a Sequence Logo Generator as described elsewhere **[16, 17]** to identify patterns as logos in the protein.

Secondary structures:
We used PSIPRED (http://bioinf.cs.ucl.ac.uk/psipred/) to assign secondary structures in the MTase domain sequence.

Epitope prediction
We used the Penchant scale (http://tools.immuneepitope.org) for assign epitope properties in the MTase domain under analysis **[18].**

B-cell epitope prediction
Conformational B-cell epitopes were predicted using the tool available at http://tools.immuneepitope.org and as described elsewhere **[18-24].**

Proteasomal cleavage prediction
Proteosomal cleavage prediction was completed using NetCTL **[25]**, NetChop and NetCTLpan **[26]**.



Figures 4: Epitopes in MTase with (A) peptides with position and (B) predicted antigen score

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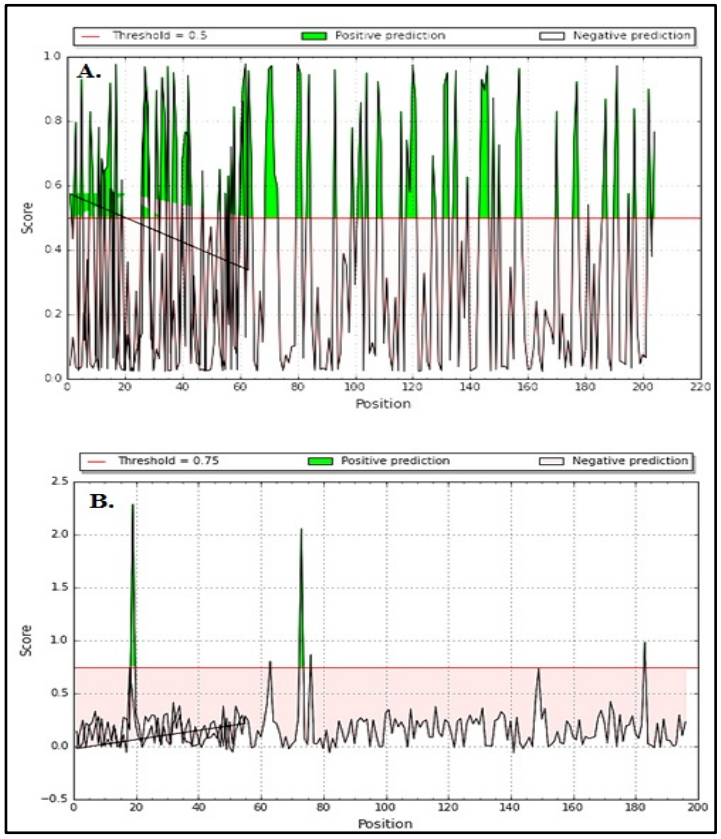

Figures 5: Predicted cleavage sites in MTase with (A) score and expanded region with score (B)

Results and Discussion:

The methyltransferase (MTase, a 265 amino acid residues long region at the N-terminal end of the viral nonfunctional supermolecule NS5 domain) is key for viral replication in Japanese Encephalitis Virus (JEV). Sequence to structure to functional information with adequate knowledge on MTase from JEV is currently limited. Therefore, it is of interest to document a report on the comprehensive analysis of predicted proteasomal cleavage data in the methyltransferase domain from JEV. Domain organization in the JEV proteome is shown in **Figure 1**. It consists of two domains (MTase and RdRP). The protein sequence of the MTase domain from JEV is shown with secondary structures and conserved domains in **Figure 2** as described elsewhere **[27]**. MTase with secondary structures and conformational epitopes is shown in **Figure 3** as described elsewhere **[28-30]**. Epitopes (antigenic regions) in MTase with short peptides with residue position and predicted antigen score is given in **Figure 4** as described elsewhere **[28-30]**. Data on predicted cleavage sites in MTase with score and expanded region with score is given in **Figure 5** as described elsewhere **[31-34]**. Thus, a comprehensive analysis of the MTase domain in JEV is highly important for further understanding of the sequence to structure to functional analysis of the protein. This data is relevant in the design and development of vaccine and other relevant therapeutic candidates for further consideration.

Conclusion:

We report a preliminary analysis of predicted proteasomal cleavage data in the methyltransferase domain from JEV. This data is relevant in the design and development of vaccine and other therapeutic candidates for further consideration.

Conflict of Interests:

The authors declare no conflict of interest

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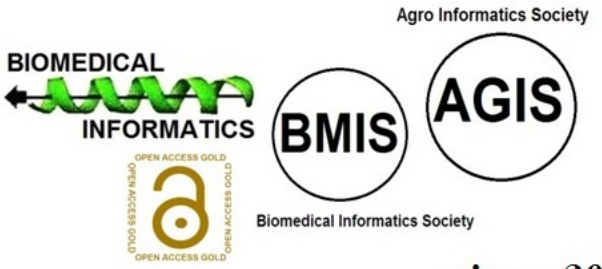

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