APPENDIX

APPENDIX-I

Sl. No.	HLA Class I Supertype	HLA Class II Supertype Alleles
1	HLA-A*02:01	HLA-DRB1*01:01
2	HLA-A*02:03	HLA-DRB1*03:01
3	HLA-A*02:06	HLA-DRB1*04:01
4	HLA-A*03:01	HLA-DRB1*04:05
5	HLA-A*11:01	HLA-DRB1*07:01
6	HLA-A*24:02	HLA-DRB1*11:01
7	HLA-A*31:01	HLA-DRB1*13:02
8	HLA-A*68:01	HLA-DRB1*15:01
9	HLA-A*68:02	HLA-DRB5*01:01
10	HLA-B*07:02	HLA-DRB1*08:02
11	HLA-B*35:01	HLA-DRB1*09:01
12	HLA-B*44:03	HLA-DRB1*12:01
13	HLA-B*51:01	HLA-DRB4*01:01
14	HLA-B*53:01	HLA-DQA1*05:01/DQB1*02:01
15	HLA-B*58:01	HLA-DQA1*03:01/DQB1*03:02
16	HLA-A*01:01	HLA-DQA1*01:01/DQB1*05:01
17	HLA-A*33:01	HLA-DQA1*01:02/DQB1*06:02
18	HLA-B*15:01	HLA-DRB3*01:01
19	HLA-B*44:02	HLA-DRB3*02:02
20	HLA-B*57:01	HLA-DQA1*05:01/DQB1*03:01
21	HLA-A*23:01	HLA-DQA1*04:01/DQB1*04:02
22	HLA-A*26:01	HLA-DPA1*02:01/DPB1*01:01
23	HLA-A*30:01	HLA-DPA1*01:03/DPB1*02:01
24	HLA-A*30:02	HLA-DPA1*01/DPB1*04:01
25	HLA-A*32:01	HLA-DPA1*03:01/DPB1*04:02
26	HLA-B*08:01	HLA-DPA1*02:01/DPB1*05:01
27	HLA-B*40:01	HLA-DPA1*02:01/DPB1*14:01

Table A1- HLA-I and II supertype alleles

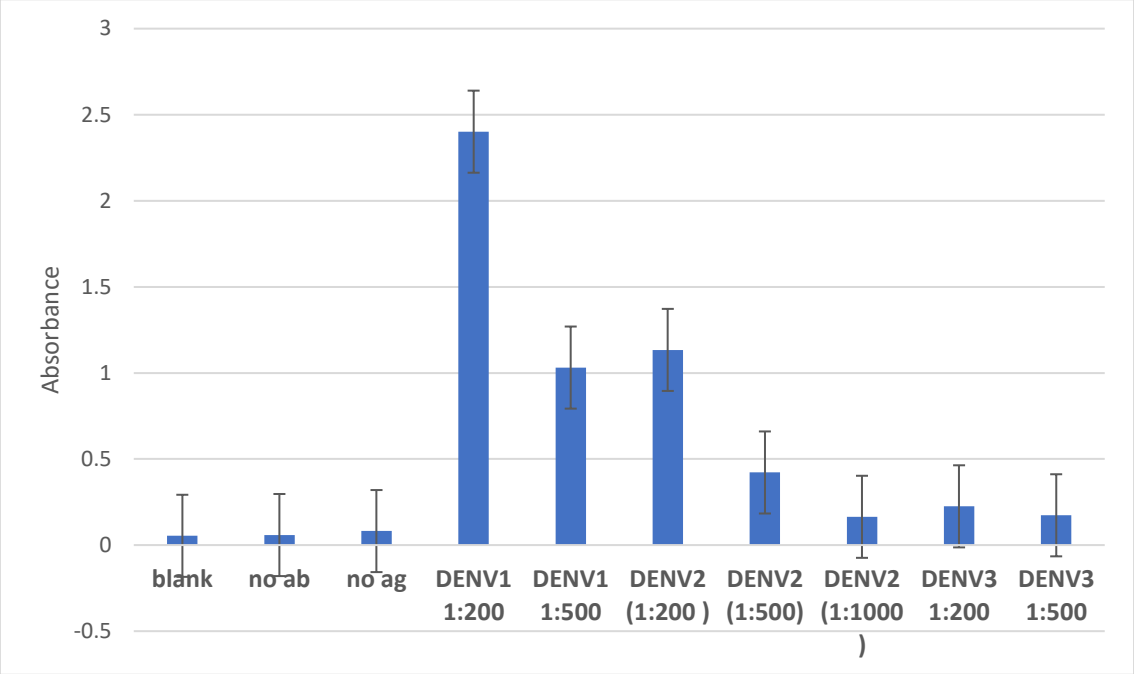

Figure A1: Standardization of indirect ELISA with DENV1-3 monoclonal antibodies

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ORIGINAL RESEARCH ARTICLE

Identification of Immunodominant Epitopes of Dengue Virus 2 Envelope and NS1 Proteins: Evaluating the Diagnostic Potential of a Synthetic Peptide

Sushmita Singha[1] · Neena Nath[2] · Vaishali Sarma[2] · Kangkana Barman[1] · Gurumayum Chourajit Sharma[1] · Lahari Saikia[2] · Shashi Baruah[1]

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Abstract

Background and Objective Dengue is a major infectious disease with potential for outbreaks and epidemics. A specific and sensitive diagnosis is a prerequisite for clinical management of the disease. We designed our study to identify epitopes on the Dengue virus (DENV) envelope (E) and non-structural protein 1 (NS1) with potential for diagnosis.

Methods Serology and immunoinformatic approaches were employed. We collected DENV-positive, DENV-negative and Japanese encephalitis virus-positive samples from collaborating hospitals in 2019 and 2022–2023. Seropositive peptides in 15–18 mer peptide arrays of E and NS1 proteins of DENV2 were determined by an indirect enzyme-linked immunosorbent assay. B-cell linear and conformational epitopes were predicted using BepiPred2.0 and ElliPro, respectively. A consensus recombinant peptide was designed, synthesised and evaluated for its diagnostic potential using patient sera.

Results Eight peptides of E protein and six peptides of NS1 protein were identified to be the most frequently recognised by Dengue-positive patients. These peptide sequences were compared with B-cell epitope regions and found to be overlapped with predicted B-cell linear and conformational epitopes. EP11 and NSP15 showed a 100% amino acid sequence overlap with B-cell epitopes. EP1 and NSP15 had 14 whereas EP28, EP31, EP60 16, NSP12 and NSP32 had more than 15 interacting interface residues with a neutralising antibody, suggesting a strength of interaction. Interestingly, potential epitopes identified were localised on the surface of proteins as visualised by PyMOL. Validation with a recombined synthetic peptide yielded 92.3% sensitivity and 91.42% specificity.

Conclusions Immunodominant regions identified by serology and computationally predicted epitopes overlapped, thereby showing the robustness of the methodology and the peptide designed for diagnosis.

Key Points

Immunodominant peptides of Dengue virus envelope and non-structural protein 1 proteins were identified.

Computationally predicted epitope regions overlapped with immunodominant peptide sequences.

Evaluation of the diagnostic potential of a synthetic peptide yielded 92.3% sensitivity and 91.42% specificity.

1 Introduction

Dengue virus (DENV) infection is a globally important vector (*Aedes aegypti* and *Aedes albopictus* mosquitoes) borne disease, with approximately half of the world's population at risk of Dengue (100–400 million infections/year), where 70% of the global burden is from Asia [1]. Dengue virus is a single-stranded positive-sense RNA virus belonging to the family *Flaviviridae* with four distinct serotypes DENV1, DENV2, DENV3 and DENV4. With a non-segmented genome of 11 kb in size, it is packed inside an icosahedral nucleocapsid and is further covered by the host membrane and viral envelope protein. It has a single open reading frame that encodes for a single polyprotein and is further cleaved into three structural proteins: the capsid, membrane and

Extended author information available on the last page of the article

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