REA_18 - Computational mapping of B Cell epitopes applied to the development of diagnostic tests for Arboviruses

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Introduction: Cross-epidemics of different arboviruses are frequently in tropical countries such as Brazil. Diagnostic methods for patients suspected by Dengue, Zika and Chikungunya virus are limited in many ways; include the structural characteristics conserved among the viral types. The development of accessible tools becomes essential, because molecular methods are inaccessible for public health. B lymphocytes are widely used in biotechnological applications and constitute a fundamental portion of the immune system. Experimental methods for epitope mapping are expensive, laborious and time consuming. Advances in B-cell epitope mapping by computational prediction have molecular insights into the antigen-antibody complex.

Objective: The objective was the Linear B-cell epitope prediction of homologous targets NS3 and NSP2, found respectively in the *Flaviviridae* and *Togaviridae* families. The identification of differential epitopes in each virus is the first step in developing diagnostic methods based on epitopes.

Methodology: To increase confidence in the predicted epitopes, two servers were chosen. BepiPred-2.0 is based a Random Forest algorithm trained in epitopes and non-epitope amino acids determined from crystalline structures. Residues above the 0.5 limit were considered epitopes. The statistical cutoff point is defined based on a training set of the server, which used physicochemical parameters of epitope sequences, elucidated experimentally. The ABCpred server was selected because it is the first server developed based on a recurrent neural network. The statistical cut-off was the standard of 0.5 in length with 16 residues. To filter the results, the location in the secondary structure and also Hydrophobicity (Eisenberg) are observed.

Results: BepiPred2.0 predicted 20 to 24 epitopes per viral type. Epitopes with differential composition in the sequences were located in external and accessible regions, outside β sheets, characteristics described in the literature as ideal for accessibility to the receptor. Epitopes predicted by ABCpred also predicted by BepiPred2.0 were selected, and ordered according to the ABCpred score. The 10 best results obtained from 0.98 (most likely to be epitope) to 0.86. Epitopes predicted in a similar region among viral types were marked with the same color in Pymol, to select epitopes with less conserved composition and have been reclassified based on solvent accessibility, lower hydrophilicity and preferred location on beta-sheet and alpha-helix.

Conclusion: The peptides have different characteristics in the NS3 target for each viral type. For NSP2 of Chikungunya the results were satisfactory and compared to other viruses of the family. It is intended to use the results in molecular docking simulations to predict interactions in the antigen-antibody complex. The Lead epitopes will be validated experimentally using ELISA.

Keywords: Arbovirus; Epitope prediction; Celular B