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Immunogenicity of novel dengue virus epitopes identified by immunoinformatics analysis

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Epitope-based vaccines provide a novel strategy for prophylactic and therapeutic application of pathogen-specific immunity. A critical requirement of this strategy is the identification and selection of T-cell epitopes that act as vaccine targets. This study describes current methodologies for the selection process, with dengue virus as a model system. Mosquito-borne dengue (DEN) viruse is the leading cause of arthropod-transmitted viral disease in humans. A licensed tetravalent vaccine that provides effective, long-term immunity against all four serotypes of DEN virus is needed, but is currently unavailable. Past and recent strategies for the development of new DEN vaccine include inactivated and live attenuated viruses, engineered viruses and chimeric viruses derived from infectious cDNA clones of DEN. The detection of T-cell epitopes is a critical step in vaccine design and a key problem in immunoinformatics.The study involves mapping of the helper T lymphocyte epitopes in the proteins of the of DEN virus, which may be expected to mediate the immune response to this virus. The success of an EV is determined by the choice of epitopes used in them. However, the experimental discovery of candidate epitopes is expensive in terms of time and money. In silico approaches have been used for the design of EVs. In particular, computational methods for MHC binding prediction have already become standard tools in immunology. In silico approaches to MHC binding prediction yield high accuracies. In the second part population coverage analysis will be done for the predicted epitopes to determine the proportion of various populations that may be expected to show T-cell response to each peptide. The conservancies of these predicted T-cell epitopes across various DEN genotypes will also assessed. This approach provides an experimental basis for the design of pathogen specific, T-cell epitope-based vaccines that are targeted to majority of the genetic variants of the pathogen, and are effective for a broad range of differences in human leukocyte antigens among the global human population. In the third part, the revelant epitopes studied in the second part of the approach would be synthesized as chimeras. The chimeric peptide(s) will be expressed and purified after cloning it into a suitable vector (pUC series / pET series). The chimeric peptides thus purified would be studied for immugenic responses. This new approach could bridge the gap between the traditional methods and immunoinformatics based approach which are more cost efficient and would cover all the four genotypes of dengue virus for epitope based vaccine design.

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