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Novel Dengue virus epitopes identified In Silico: Implications as vaccine candidates

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We used T cell epitope prediction tools to identify epitopes from a representative sample of Dengue virus (DENV) polyprotein sequences, and evaluated in vivo and in vitro the immunogenicity and antigenicity of the corresponding synthetic vaccine candidates. Balb/c mice were immunized subcutaneously with 5 distinct synthetic peptides (50μg each) in Freund's complete adjuvant (v/v). Two weeks later, mice received a second dose of the same peptide in Freud's incomplete adjuvant. Mock immunized mice only received doses of the same adjuvants. Three weeks after the last immunization, mice were sacrificed to collect blood and spleen cells for the analysis of the immune response. In subsequent experiments, mice were immunized with subsets of 9-11 peptides mixtures as described above, for confirmation of their immunogenicity. Twenty two epitopes were predicted to have a high affinity for MHC class I ($H\text{-}2K^d$, $H\text{-}2D^d$, $H\text{-}2L^d$ alleles) or class II (IA^d alleles). These epitopes were conserved between the four virus serotypes, but with no similarity to human and mouse sequences. Thirteen synthetic peptides induced specific antibodies production with or without T cells activation in mice. Three synthetic peptides induced mostly IgG antibodies, and one of these from the E gene induced a neutralizing response. Ten peptides induced a combination of humoral and cellular responses by CD4+ and CD8+ T cells. Twelve peptides were novel B and T cell epitopes. These results indicate that our bioinformatics strategy is a powerfull tool for the identification of novel antigens and its application to human HLA may lead to a potent epitope-based vaccine against Dengue virus and many other pathogens.