Immunogenicity Of Sequences Around Hiv-1 Protease Cleavage Sites: Potential Targets And Population Coverage Analysis For A Hiv Vaccine Targeting Protease Cleavage Sites.

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Date: 2013-06

Abstract:

Developing an effective preventative vaccine against HIV-1 has proved to be a great challenge. The classical and proven vaccine approach has failed so far or produced a modest effect, new approaches are needed. In this study we evaluated the immunogenicity of the sequences around the protease cleavage sites (PCS) and the population coverage of a vaccine targeting HIV-1 PCS. The sequence conservation was evaluated by comparing entropy score of sequences around PCS with Gag and Pol. The immunogenicity of sequences around the 12 PCS (+10/-10 amino acids) was analyzed by identifying epitopes of HLA class I alleles in PCS region using four approaches: (1) identification of previously reported HLA class I allele epitopes around PCS region; (2) screening and validating epitopes of 8 HLA class I alleles common to most world populations using iTopia Epitope Discovery system and IFN-γ ELISpot assays; (3) screening of 151 patients of Pumwani cohort for PBMC IFN-γ ELISPOT responses to the subtype A and D consensus around PCS region; and (4) prediction of HLA alleles with epitopes around the PCS using NetMHCpan. Population coverage was calculated using the web-based analysis tool of the Immune Epitope Database based on HLA class I genotype frequencies from dbMHC database. The results showed that many HLA class I alleles have multiple epitopes in the 12 PCS regions, indicating sequence immunogenicity around PCS. Multiple epitopes of many HLA class I alleles common to >95% world populations have been identified around the 12 PCS region. Targeting these sites is a feasible vaccine approach.