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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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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 ELI Spot 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.

Biography

Ma Luo is an Adjunct Professor of Department of Medical Microbiology, University of Manitoba and Research Scientist, HIV Host Genetics, National HIV and Retrovirology Laboratory, National Microbiology Laboratory, Public Health Agency of Canada. She received her MSc from Chinese University of Science and Technology, Beijing, China and PhD from University of Manitoba, Canada. The major focus of her research in the recent years has been on uncovering the mechanism of resistance and susceptibility to HIV-1, to understand the interplay between host genetics, including human leukocyte antigens, KIR and other host genetic factors, with HIV virus, and to use this knowledge to develop vaccines and therapeutics.

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