Abstract

Background: Current HIV vaccine candidates have been based on the conventional views of viral infection and attempt to induce broad T cell responses to HIV-1. Until now, the candidate vaccines based on such approach either failed to provide protection or produced modest effect that is not satisfactory for an effective vaccine. Since these vaccine candidates were not based on the correlates of protection against HIV-1 infection, improving such understanding could be critical for successful vaccine development.
Methods: A subset of women enrolled in the Pumwani Sexworker Cohort remain uninfected by HIV-1 despite repeated exposures through sex work. This resistance to HIV-1 infection is associated with several alleles of Human Leukocyte Antigens (HLAs) and specific CD8+ and CD4+ T cell responses. In this study we systematically analyzed HIV-1 clade A and D Gag epitope profiles of two HLA class I alleles associated with different outcomes of HIV-1 infection, A*0101 is significantly associated with slower seroconversion while B*0702 is associated with rapid seroconversion. We screened a Gag peptide library with iTopia Epitope Discovery System to compare the peptide binding capacity of these two alleles. The identified peptides were characterized by affinity and off-rate assays and confirmed by interferon gamma ELISPOT assays using patient peripheral blood mononuclear cells.
Results: A*0101, an allele associated with protection from HIV-1 infection, only binds to 3 epitopes in Gag. Whereas, B*0702, an allele associated with rapid disease progression, has 30 Gag epitopes. There is no significant difference in peptide binding affinity, off-rate, ELISPOT SFU values and epitope specific Tem/Tcm frequencies.
Conclusion: In contrast to the broad peptide binding spectrum of B*0702, A*0101's epitopes are narrowly directed. Observations of this study question the current approach for HIV-1 vaccine development and propose a different vaccine development strategy.