Abstract

Background:
The failure of Merck STEP and Phambili trials and the modest effect of RV144 trial emphasize the importance of understanding the correlates of protective immunity. Our study showed that the epitope recognition of HLA alleles associated with protection from HIV-1 infection is very narrow, thus vaccines focus on the key sites of HIV-1 might work better. Since the protease cleavage sites of HIV-1 are highly conserved among major subtypes, direct immune responses against these sites would yield two major advantages. First, the immune response could destroy the virus before it can establish permanently in the host. Second, the vaccine could force the virus to accumulate mutations eliminating the normal function of the HIV protease thus eliminating viable virions. For this vaccine strategy to work a given individual must have a HLA class I allele that can recognize one of the peptides overlapping one of the 12 protease cleavage sites of HIV-1. In this study we examined the population coverage of this vaccine approach using several approaches.

Methods:
The population coverage was predicted using computational algorithms, the Population Coverage Calculator (http://www.immuneepitope.org/) with the clade A and D peptides overlapping the protease cleavage sites (PCSs). The population coverage was also calculated based on the T cell epitopes that have already been identified at these sites. Furthermore, the peptides overlapping the 12 PCSs were screened with 8 HLA class I alleles using iTopia Epitope Discovery system and confirmed using IFNc ELISPOT assays with PBMCs.

Results:
Analysis using all three approaches showed that the percentage of populations in the world can recognize peptides overlapping at least one PCS is very high, including more than 90% population in Sub-Saharan Africa. iTopia epitope Discovery System screen showed that the eight common HLA alleles have epitopes in multiple PCSs (4 to 12).

Conclusion:
This vaccine approach has good population coverage.