A new antigen scanning strategy for monitoring HIV-1 specific T-cell immune responses.

Delineation of the immune correlates of protection in natural infection or after vaccination is a mandatory step for vaccine development. Although the most recent techniques allow a sensitive and specific detection of the cellular immune response, a consensus on the best strategy to assess their magnitude and breadth is yet to be reached. Within the AIDS Vaccine Integrated Project (AVIP http://www.avip.eu.org) we developed an antigen scanning strategy combining the empirical-based approach of overlapping peptides with a vast array of database information. This new system, termed Variable Overlapping Peptide Scanning Design (VOPSD), was used for preparing two peptide sets encompassing the candidate HIV-1 vaccine antigens Tat and Nef. Validation of the VOPSD strategy was obtained by direct comparison with 15mer or 20mer peptide sets in a trial involving six laboratories of the AVIP consortium. Cross-reactive background responses were measured in 80 HIV seronegative donors (HIV-), while sensitivity and magnitude of Tat and Nef-specific T-cell responses were assessed on 90 HIV+ individuals. In HIV-, VOPSD peptides generated background responses comparable with those of the standard sets. In HIV-1+ individuals the VOPSD pools
showed a higher sensitivity in detecting individual responses (Tat VOPSD vs. Tat 15mers or 20mers: 
$p<=0.01$) as well as in generating stronger responses (Nef VOPSD vs. Nef 20mers: $p<0.001$) than 
standard sets, enhancing both CD4 and CD8 T-cell responses. Moreover, this peptide design allowed 
a marked reduction of the peptides number, representing a powerful tool for investigating novel HIV-1 
candidate vaccine antigens in cohorts of HIV-seronegative and seropositive individuals.

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