Identification and characterization of HLA-A*0301 epitopes in HIV-1 gag proteins using a novel approach

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Abstract:

Identification of CTL epitopes correlated to immune protection is important for the development of vaccines that enhance T-cell mediated immune responses. The correlation of positively selected amino acids (PS) of HIV-1 with host HLA alleles can identify regions containing potential T-cell epitopes. However, the specific epitopes have to be identified and characterized using overlapping peptides through T-cell functional assays. In this study we used a new approach to identify and characterize potential epitopes in the gag region containing PS mutations that significantly correlated with HLA-A*0301. The iTopia Epitope Discovery System was used to rapidly screen a panel of peptides overlapping the regions containing PS mutations and the peptides identified were assessed for relative affinity and complex stability. The potential epitopes were then validated by interferon gamma (IFN-γ) ELISpot assays with patient PBMCs. Using this approach we identified/confirmed the predicted HLA-A*0301 epitopes in two regions of gag containing PS mutations V7I and K403R, one previously reported and the other novel. Five of the seven peptides that bound to A*0301 contained the K403R mutation and corresponded to the documented LARNCRAPRK-A3 supertype epitope. Two epitope variants, RASVLSGGK and RASILSGGK containing the V7I mutation, were identified using the iTopia Epitope Discovery System, however only the consensus variant (RAK9C) was confirmed using the ELISpot assay and it represents a novel A*0301 epitope.