

Evidence of escape mutations in HLA-A02 epitopes in HIV-1-positive patients after dendritic cell-based therapeutic vaccination with CD8 epitopes.

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HIV-1 evades the cell-mediated immune response by escape mutations in CD8 epitopes during infection, and possibly when exposed to a CD8 cell-stimulating vaccine. Whereas immunodominant epitopes are frequently subject to escape mutation, infrequently targeted subdominant epitopes remain relatively conserved.

We have completed testing of an HIV vaccine based on 7 highly conserved, subdominant CD8 epitopes. The cohort for this human study consists of 13 HIV-positive, HLA-A02-positive Danish males. Immunological investigations have shown that the vaccine epitopes stimulate epitope-specific CD8 responses in all vaccinees. CD8 responses were induced against several epitopes in most patients. To understand the molecular basis for these immune responses, and to investigate possible escape mutations, sequential sequences were obtained from cloned viral RNA. We have investigated the sequence of targeted and non-targeted CTL epitopes.

We confirmed the presence of the vaccine epitope targets in circulating virus of the vaccinees, to which immune responses could be induced. Our results indicate limited evolution in targeted epitopes despite the induction of additional immunity towards these. However, in some cases *de novo* immune responses are associated with viral evolution in targeted epitopes.