# Hiv-specific T Cells: Strategies For Fighting A Moving Target.

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## Abstract:

HIV vaccine development faces many hurdles, including the failure of empirical approaches, an incomplete understanding of protective immunity, and the extreme genetic diversity of HIV-1. HIV is a moving target in at least two key ways: 1) within an infected individual, years of evolution lead to the formation of quasispecies, and selection of variants with increased fitness, and 2) during the course of the pandemic, subtypes change in frequency as they are transmitted from host to host. In spite of this, CD8+ T cells are often able to overcome HIV diversity, leading to relatively high levels of cross-reactive and cross-clade responses. Recent research suggests that the cross-reactivity of HIV-specific CD8+ T cell responses should be evaluated comprehensively, using multiple immunological assays (including those that correlate best with protective immunity), and taking into account subtle differences in epitopic variation, presenting HLA allele, and cognate TCR that all influence recognition and escape. In addition, although escape and cross-reactivity are often predictable, important differences can present, particularly in the setting of multiple and different clades. Finally, strategies to optimize the induction of protective, cross-reactive T cells, and towards the likely infecting strain in the mucosa where exposure occurs and opportunities to prevent infection are greatest, are urgently needed. Though some cues can be found from observational studies, more in depth analyses of past and ongoing HIV vaccine trials will be needed to know if and how HIV genetic diversity can be overcome by vaccine-induced T cells.