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## **AIDS virus escape from cytotoxic T lymphocyte containment in monkeys**

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### **Abstract**

Cytotoxic T lymphocyte (CTL)-based vaccine protection of rhesus monkeys against simian immunodeficiency virus (SIV) and simian-human immunodeficiency virus (SHIV) infection confers clinical benefit, but allows persistent viral replication. The intense selective pressure by CTLs on this replicating virus should rapidly select for viral escape variants. We demonstrated such escape in 7 of 9 vaccinated and control monkeys in a group of plasmid *gag* DNA vaccinated monkeys after a heterologous SIVsm challenge during a 3-year period of follow-up. The viral mutations all occurred in dominant CTL epitopes and were associated temporally with clinical deterioration of the infected monkeys. In contrast to the frequency of this occurrence in monkeys following SIVsm infection, only 1 of 8 monkeys optimally vaccinated with cytokine-augmented plasmid *gag* and *env* DNA developed such a clinically significant dominant epitope escape variant after SHIV-89.6P infection during a similar period of follow-up. Studies demonstrated that this dominant epitope was structurally constrained in SHIV-89.6P, and a coincident mutation in a region of the virus flanking the epitope was required to facilitate the generation of an optimally replicating variant virus with a dominant epitope mutation. These studies illustrate the potential complexity of the biologic events leading to the escape of an AIDS virus from a vaccine-elicited CTL response.

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