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HLA B17, B37, NYTPGPGVRYPLT, HLA B7; and GVRYPLTFGWCYK-LVP, HLA B18).

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HLA-B*57 is over-represented in slow progressors. HLA*5801 is a closely related molecule, and while the defined anchor residues of HLA*5801 can be used to predict epitopes in HIV-1 proteins, the CTL from HLA-B*57 positive individuals have limited cross-presentation capacity with HLA*5801 targets. In this paper five new HLA-B*57 epitopes were defined.

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[Hamajima (1997)] K. Hamajima, J. Fukushima, H. Bukawa, T. Kaneko, T. Tsuji, Y. Asakura, S. Sasaki, K. Q. Xin, & K. Okuda. Strong augment effect of IL-12 expression plasmid on the induction of HIV-specific cytotoxic T lymphocyte activity by a peptide vaccine candidate. *Clin Immunol Immunopathol* **83**:179–84, 1997. (Medline: 97288401) Notes: We previously reported that repeated inoculation of VC1, a macromolecular multicomponent peptide vaccine emulsified with Freund's adjuvant (VC1-F), induced high cytotoxic T lymphocyte (CTL) levels and a substantial level of multivalent antibodies which neutralized various human immunodeficiency virus type 1 (HIV-1) isolates. In the present study, we report that inoculation of VC1-F plus interleukin (IL)-12 expression plasmid can induce a higher

antigen-specific CTL response compared to that with VC1-F alone. VC1-F plus IL-12 expression plasmid or VC1-F alone were inoculated to BALB/c mice twice at interval of 2 weeks. Two weeks after the second inoculation, spleen effector cells from these mice were examined. Stronger CTL responses against target cells were observed from the inoculation of VC1-F plus IL-12 plasmid than from that with VC-1F alone, but there was no difference in antibody induction. The inoculation of VC1 plus IL-12 plasmid also produced higher CTL activity than the inoculation of VC1 alone. These augmented CTL activities were not observed using target cells pulsed with non-HIV-specific peptides and different class I haplotype cells. These data demonstrate that co-inoculation of cell-mediated immune potent antigen and IL-12 plasmids can enhance the antigen-specific CTL response. This may be a potential approach for the induction of cellular immunization against HIV-1 and other diseases.

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antagonized by naturally occurring HIV-1 Gag variants. *Nature* **369**:403–407, 1994. (Medline: 94255016) Notes: This paper documents that naturally occurring peptide variants can serve as antagonists, that is they can inhibit normal lysis of cells presenting the original epitope. The variants studied could serve as antagonists when they were processed from recombinant vaccinia, replicated HIV, or when they were synthetic peptides. Both agonist and antagonist sequences were found in the study subjects from whom the CTL clones were derived.

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[Rowland-Jones (1998a)] S. Rowland-Jones, T. Dong, P. Krausa, J. Sutton, H. Newell, K. Ariyoshi, F. Gotch, S. Sabally, T. Corrah, J. Kimani, K. MacDonald, F. Plummer, J. Ndinya-Achola, H. Whittle, & A. McMichael. The role of cytotoxic T cells in HIV infection. *Dev Biol Stand* **92**:209–14, 1998a. (Medline: 98214896) Notes: In this paper CTL response to previously defined conserved epitopes was found in exposed but uninfected prostitutes in Nairobi. Subtypes A and D are circulating in this regions, and the reactive epitopes tended to be conserved. Similarly previous studies in the Gambia showed that exposed but uninfected prostitutes tended to have B35 presented CTL epitopes conserved between HIV-1 and HIV-2. It was suggested that what was special about B35 is simply that it presents epitopes found both in HIV-1 and HIV-2.

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TAP gene polymorphism. *Eur J Immunol* **23**:1999–2004, 1993. (Medline: 93345604) Notes: Individual fails to present HLA-B8-restricted influenza epitope, but can present an HLA-B8-restricted HIV-1 gag epitope.

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[Sipsas (1997)] N. V. Sipsas, S. A. Kalams, A. Trocha, S. He, W. A. Blattner, B. D. Walker, & R. P. Johnson. Identification of type-specific cytotoxic T lymphocyte responses to homologous viral proteins in laboratory workers accidentally infected with HIV-1. *J Clin Invest* **99**:752–62, 1997. (Medline: 97197584) Notes: To examine a situation where the autologous strain and the reference reagents would be the same, the CTL response of three lab workers accidentally infected with HIV IIIB was studied. Both group specific and type specific epitopes were targets for CTL clones. One subject had a broadening of CTL response over time, using a broad range of restricting HLA class I alleles. Characterization of the cytotoxic T lymphocyte (CTL) response against HIV-1 has been limited by the use of target cells expressing viral proteins from laboratory isolates of HIV-1. This approach has favored identification of group-specific CTL responses and precluded assessment of the extent of type-specific CTL responses directed against HIV-1. Using cells expressing viral proteins from the HIV-1 IIIB strain, we performed a detailed characterization of HIV-1-specific CTL response in three laboratory workers accidentally infected with HIV-1 IIIB. Eight of the epitopes identified were group specific, lying in relatively conserved regions of Gag, reverse transcriptase, and envelope. Three type-specific epitopes were identified, two of them in highly variable regions of envelope. In longitudinal studies in one subject, seven different epitopes and five different restricting HLA class I alleles were identified, with a progressive increase in the number of CTL epitopes recognized by this subject over time. Our data demonstrate that type-specific CTL responses make up a significant proportion of the host cellular immune response against HIV-1 and that a broadening of epitope specificity may occur.

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[Tobery & Siliciano(1997)] T. W. Tobery & R. F. Siliciano. Targeting of HIV-1 antigens for rapid intracellular degradation enhances cytotoxic T lymphocyte (CTL) recognition and the induction of de novo CTL responses *in vivo* after immunization. *J Exp Med* **185**:909–20, 1997. (Medline: 97217373) Notes: CD8+ cytotoxic T lymphocytes (CTLs) have the ability to recognize and eliminate virally infected cells before new virions are produced within that cell. Therefore, a rapid and vigorous CD8+ CTL response, induced by vaccination, can, in principle, prevent disseminated infection in vaccinated individuals who are exposed to the relevant virus. There has thus been interest in novel vaccine strategies that will enhance the induction of CD8+ CTLs. In this study, we have tested the hypothesis that targeting an antigen to undergo more efficient processing by the class I processing pathway will elicit a more vigorous CD8+ CTL response against that antigen. Targeting a type I transmembrane protein, the HIV-1 envelope (env) protein, for expression in the cytoplasm, rather than allowing its normal co-translational translocation into the endoplasmic reticulum, sensitized target cells expressing this mutant more rapidly for lysis by an env-specific CTL clone. Additionally, a greatly enhanced de novo env-specifc CTL response was induced *in vivo* after immunization of mice with recombinant vaccinia vectors expressing the cytoplasmic env mutant. Similarly, targeting a cytoplasmic protein, HIV-1 nef, to undergo rapid cytoplasmic degradation induced a greatly enhanced de novo nef-specific CD8+ CTL response *in vivo* after immunization of mice with either recombinant vaccinia vectors or DNA expression plasmids expressing the degradation targeted nef mutant. The targeting of viral antigens for rapid cytoplasmic degradation represents a novel and highly effective vaccine strategy for the induction of enhanced de novo CTL responses *in vivo*.

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cells were used as stimulator cells of bulk PBMC cultures to determine precursor frequencies and identify epitopes.

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challenge with SHIV chimeric challenge stock. Not all immunized monkeys had a CTL response, probably due to the outbred nature of the animals and polymorphic MHC alleles. Two macaques had CTL to gag, and one macaque had CTL to the CD4 binding region, and one animal responded to gp120 pooled peptides; none had a response to the V3 peptide.

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Cross-clade envelope glycoprotein 160-specific CD8+ cytotoxic T lymphocyte responses in early HIV type 1 clade B infection. *AIDS Res Hum Retroviruses* **14**:925–37, 1998b. (Medline: 98349428).

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