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could bind, which suggested that quantitative difference in binding constants may ultimately determine in vivo MHC restriction.

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class I molecules. *Eur J Immunol* **24**:777–780, 1994. (Medline: 94170859) Notes: Peptides from influenza and HIV-1 tested for their ability to promote the assembly of HLA-A2 and HLA-B51 molecules in T2 cell lysates. HIV Pol 476-484 allowed significant assembly of HLA-A2, and is a target for CTL. Nef peptide 186-194 produced significant assembly of HLA-B51. A hydrophobic anchor residue (V, L, I) at position 9 could occupy pocket F, and a hydrophobic residue (V, L) at position 3 or 4 may anchor to hydrophobic pocket D of HLA-B51. Proline at position 2 increases HLA-B51 anchoring.

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[Culmann (1991)] B. Culmann, E. Gomard, M.-P. Kieny, B. Guy, F. Dreyfus, A.-D. Saimot, D. Sereni, D. Sicard, & J.-P. Levy. Six epitopes with human cytotoxic CD8+ cells in the central region of the HIV-1 Nef protein. *J Immunol* **146**:1560–1565, 1991. (Medline: 91132023) Notes: Nef specific CTL were generated from six seropositive donors. Six epitopes were defined, all localized to two regions in the central part of Nef. Some epitopes could be recognized in the contexts of several HLA class I molecules. Peptides were based on BRU epitopes: QVPLRPMTYK, HLA A3, A11, B35; AAVDLSHFLKEK, HLA A11; HTQGYFPQWQ, HLA B17;TQGYFPQWQNYT, HLA B17, B37, NYTPGPGVRYPLT, HLA B7; and GVRYPLTFGWCYKLVP, HLA B18).

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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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alpha (TNF-α), and TNF-β upon contact with target cells presenting viral antigen was assessed. Epitopes: p17: KIRLRPGGKKKYKLKHIVWASRELE, A3; gp41: VERYLKDQQL, B14 and A28, ERYLKDQQL, B14; RT: AIFQSSMTKILEPFRKQNPDIVIYQ, A11; and Nef SQRRQDILDLWIYHTQGYFPDWQNY, B13.

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[Porgador (1997)] A. Porgador, H. F. Staats, B. Faiola, E. Gilboa, & T. J. Palker. Intranasal immunization with CTL epitope peptides from HIV-1 or ovalbumin and the mucosal adjuvant cholera toxin induces peptide- specific CTLs and protection against tumor development in vivo. *J Immunol* **158**:834–41, 1997. (Medline: 97146054) Notes: To evaluate the ability of mucosal immunization protocols using peptide immunogens to induce CTL responses, BALB/c and C57BL/6 mice were immunized intranasally (i.n.) with peptides corresponding to a known CTL epitope in HIV-1 glycoprotein 120 or OVA, respectively, and the mucosal adjuvant cholera toxin (CT). Intranasal immunization of BALB/c mice with a 10- or 15-amino acid peptide corresponding to a CTL determinant in HIV-1 glycoprotein 120 and CT induced peptide-specific CTLs in spleen cells that persisted through 35 days after the last immunization. Intranasal immunization of C57BL/6 mice with the octameric OVA peptide and CT produced similar results with detectable peptide-specific CTL in both the cervical lymph node and spleen. To test whether CTL induced by i.n. immunization with OVA peptide and CT were functional in vivo, groups of C57BL/6 mice were injected with E.G7- OVA tumor cells that express the OVA protein and monitored for tumor growth. Animals immunized i.n. with OVA and CT were protected against tumor development as efficiently as animals immunized by the potent CTL induction protocol of i.v. injection with OVA-pulsed dendritic cells. Intranasal immunization with peptides corresponding to known CTL epitopes and CT provides a noninvasive route of immunization for the induction of CTL responses in vivo.

[Price (1997)] D. A. Price, P. J. Goulder, P. Klenerman, A. K. Sewell, P. J. Easterbrook, M. Troop, C. R. Bangham, & R. E. Phillips. Positive selection of HIV-1 cytotoxic T lymphocyte escape variants during primary infection. *Proc Natl Acad Sci USA* **94**:1890–5, 1997. (Medline: 97203157) Notes: Cytotoxic T lymphocytes (CTLs) are thought to play a crucial role in the termination of the acute primary HIV-1 syndrome, but clear evidence for this presumption has been lacking. Here we demonstrate positive selection of HIV-1 proviral sequences encoding variants within a CTL epitope in Nef, a gene product critical for viral pathogenicity, during and after seroconversion. These positively selected HIV-1 variants carried epitope sequence changes that either diminished or escaped CTL recognition. Other proviruses had mutations that abolished the Nef epitope altogether. These results provide clear evidence that CTLs exert selection pressure on the viral population in acute HIV-1 infection.

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release from stimulated CTL clones derived from either the peripheral blood or CSF of 3 patients was studied. HLA restriction was determined for two of seven clones. GM-CSF and TNF-α and IFN-γ were produced by all clones; most clones produced low amounts of IL-2, IL-3, and IL-4.

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[Rowland-Jones(1995)] S. Rowland-Jones. 1995. Notes: Personal communication.

[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 HIV-1 and HIV-2.

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[Rowland-Jones (1993a)] S. L. Rowland-Jones, D. F. Nixon, M. C. Aldhous, F. Gotch, K. Ariyoshi, N. Hallam, J. S. Kroll, K. Froebel, & A. McMichael. HIV-specific cytotoxic T-cell activity in an HIV-exposed but uninfected infant. *Lancet* **341**:860–861, 1993a. (Medline: 93218363) Notes: The factors necessary for protective immunity against HIV-1 are unknown. Important information about these factors should come from study of people at high risk of HIV infection who have not apparently become infected. Among these are the estimated 60-85who may be exposed in utero or perinatally to HIV-1 but do not become infected. We observed the transient appearance of HIV-specific cytotoxic T-lymphocyte (CTL) activity in a baby born to HIV-1-infected parents, in whom all standard markers of infection remained negative. These findings suggest that HIV-specific CTLs may be a marker for recently exposed, but uninfected, individuals.

[Rowland-Jones (1993b)] S. L. Rowland-Jones, S. H. Powis, J. Sutton, I. Mockridge, F. M. Gotch, N. Murray, A. B. Hill, W. M. Rosenberg, J. Trowsdale, & A. J. McMichael. An antigen processing polymorphism revealed by HLA-B8-restricted cytotoxic T lymphocytes which does not correlate with TAP gene polymorphism. *Eur J Immunol* **23**:1999–2004, 1993b. (Medline: 93345604) Notes: Individual fails to present HLA-B8-restricted influenza epitope, but can present an HLA-B8-restricted HIV-1 gag epitope.

[Rowland-Jones (1995)] S. L. Rowland-Jones, J. Sutton, K. Ariyoshi, T. Dong and , F. Gotch, S. McAdam, D. Whitby, S. Sabally, A. Gallimore, T. Corrah, M. Takiguchi, T. Schultz, A. McMichael, & H. Whittle. HIV-specific cytotoxic T-cells in HIV-exposed but uninfected Gambian women. *Nature Medicine* **1**:59–64, 1995. (Medline: 96071373) Notes: Four HIV-1 and -2 cross-reactive epitopes that are presented to CTL from HIV-infected Gambians by HLA-35 were identified. These peptides could elicit HIV specific CTLs from 3 of 6 repeatedly exposed but seronegative sex workers who carry the HLA-B35 allele. Most CTL derived from HIV-2 positive donors also recognized the HIV-2 peptide and the analogous HIV-1 peptide.

[Safrit (1994a)] J. T. Safrit, C. A. Andrews, T. Zhu, D. D. Ho, & R. A. Koup. Characterization of human immunodeficiency virus type 1-specific cytotoxic T lymphocyte clones isolated during acute seroconversion: recognition of autologous virus sequences within a conserved immunodominant epitope. *J Exp Med* **179**:463–472, 1994a. (Medline: 94125027) Notes: HIV-1 specific CTL clones were isolated from two individuals at acute seroconversion. In one patient, two HLA A31-restricted clones recognized the same fragment of gp41, peptide RLRDLLLIVTR, but one was sensitive to a Thr to Val substitution, while the other was not. A CTL HLA A32-restricted clone from the other patient recognized the gp41 peptide VLSIVNRVRQGYSPLSFQTH. Autologous viral sequences from seroconversion were recognized by the CTL clones, but not the HIV-1 strain MN.

[Safrit (1994b)] J. T. Safrit, A. Y. Lee, C. A. Andrews, & R. A. Koup. A region of the Third Variable Loop of HIV-1 gp120 is recognized by HLA-B7-Restricted CTLs from two acute seroconversion patients. *J Immunol* **153**:3822–3830, 1994b. (Medline: 95015873) Notes: HIV-1 envelope-specific CTL clones were isolated from the peripheral blood of two patients within weeks of seroconversion. These clones were CD8+ and restricted by the HLA-B7 molecule. The minimum epitope was defined, RPNNNTRKSI, with anchor residues at the proline and isoleucine; the anchor residues are relatively well conserved. A serine to arginine change at position 9 of the epitope abrogated clone recognition in one of the patients. This amino acid change is one factor that has been associated with a change from a nonsyncytium-inducing to a syncytium-inducing phenotype of HIV-1.

[Salmon-Ceron (1999)] D. Salmon-Ceron, J. L. Excler, L. Finkielsztejn, B. Autran, J. C. Gluckman, D. Sicard, T. J. Matthews, B. Meignier, C. Valentin, R. El Habib, C. Blondeau, M. Raux, C. Moog, J. Tartaglia, P. Chong, M. Klein, B. Milcamps, F. Heshmati, & S. Plotkin. Safety and immunogenicity of a live recombinant canarypox virus Expressing HIV Type 1 gp120 MN tm/gag/protease LAI (ALVAC-HIV, vCP205) Followed by a p24E-V3 MN Synthetic Peptide (CLTB-36) Administered in Healthy Volunteers at Low Risk for HIV Infection. *AIDS Res Hum Retroviruses* **15**:633–45, 1999. (Medline: 99260285).

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[Shankar (1998)] P. Shankar, H. Sprang, & J. Lieberman. Effective lysis of HIV-1-infected primary CD4+ T cells by a cytotoxic T- lymphocyte clone

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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.

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construct, stimulated with peptides: SITKGPGRVIYATGQ, RF; RIQRGPGRAFVTIGK, IIIB; and RIHIGPGRAFYTTKN, MN.

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totoxic T cells and neutralizing antibodies induced in rhesus monkeys by virus-like particle HIV vaccines in the absence of protection from SHIV infection. *Virology* **245**:65–74, 1998b. (Medline: 98277073) Notes: A VLP is a non-infectious virus like particle self-assembled from HIV Pr55 gag. Macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains. Gag and Env specific CTL were stimulated in each case, and Ab response to Gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4. Despite the CTL and Ab response, immunized macaques were infected by intervenous 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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