

CTL References

- [Achour et al.(1996)] A. Achour, F. Bex, P. Hermans, A. Burny, & D. Zagury. Induction of anti-gp160 cytotoxic T cells cross-reacting with various V3 loop P18 peptides in human immunodeficiency virus type 1 envelope-immunized individuals. *J Virol* **70**:6741–6750, 1996.
- NOTE: (Medline: 96386561).
- [Achour et al.(1994)] A. Achour, S. Lemhammedi, O. Picard, J. P. M'Bika, J. F. Zagury, Z. Moukrim, A. Willer, F. Beix, A. Burny, & D. Zagury. Cytotoxic T lymphocytes specific for HIV-1 gp160 antigen and synthetic P18IIB peptide in an HLA-A11-immunized individual. *AIDS Res Hum Retroviruses* **10**:19–25, 1994.
- NOTE: (Medline: 94235369) CTL restricted by several different class I molecule HLA types can present this V3 antigen: RIQRGPGRAFVTIGK.
- [Achour et al.(1993)] A. Achour, O. Picard, J. P. M'Bika, A. Willer, R. Snart, B. Bizini, C. Carell, A. Burny, & D. Zagury. Envelope protein and P18 IIB peptide recognized by cytotoxic T-lymphocytes from humans immunized with AIDS virus envelope. *Vaccine* **11**:699–701, 1993.
- NOTE: (Medline: 93342850) Both HLA A2 and A3 class I molecules types can present this V3 antigen: RIQRGPGRAFVTIGK.
- [Achour et al.(1990)] A. Achour, O. Picard, D. Zagury, P. Sarin, R. Gallo, P. Naylor, & A. Goldstein. HGP-30, a synthetic analogue of human immunodeficiency virus p17, is a target for cytotoxic lymphocytes in HIV-infected individuals. *Proc Natl Acad Sci* **87**:7045–7049, 1990.
- NOTE: (Medline: 90384945) This epitope serves as a B cell epitope as well as an HLA-A2 T-cell epitope. The peptide is also called HGP-30.
- [Ahlers et al.(1997a)] J. D. Ahlers, N. Dunlop, D. W. Alling, P. L. Nara, & J. A. Berzofsky. Cytokine-in-adjuvant steering of the immune response phenotype to HIV-1 vaccine constructs: granulocyte-macrophage colony-stimulating factor and TNF-alpha synergize with IL-12 to enhance induction of cytotoxic T lymphocytes. *J Immunol* **158**:3947–58, 1997a.
- NOTE: (Medline: 97256624).
- [Ahlers et al.(1997b)] J. D. Ahlers, N. Dunlop, C. D. Pendleton, M. Neuman, P. L. Nara, & J. A. Berzofsky. Candidate HIV type 1 multideterminant cluster peptide-P18MN vaccine constructs elicit type 1 Helper T cells, cytotoxic T cells and neutralizing antibody, all using the same adjuvant immunization. *AIDS Res Hum Retroviruses* **12**:259–272, 1997b.
- NOTE: (Medline: 97256624).
- [Ahlers et al.(1997c)] J. D. Ahlers, T. Takeshita, C. D. Pendleton, & J. A. Berzofsky. Enhanced immunogenicity of HIV-1 vaccine construct by modification of the native peptide sequence. *Proc Natl Acad Sci USA* **94**:10856–10861, 1997c.
- NOTE: (Medline: 97454543).
- [Alexander-Miller et al.(1996)] M. A. Alexander-Miller, K. C. Parker, T. Tsukui, C. D. Pendleton, J. E. Coligan, & J. A. Berzofsky. Molecular analysis of presentation by HLA-A2.1 of a promiscuously binding V3 loop peptide from the HIV-1 Envelope protein to human cytotoxic T lymphocytes. *Int Immunopharmacol* **8**:641–649, 1996.
- NOTE: (Medline: 96324787).
- [Altman et al.(1996)] J. D. Altman, P. A. H. Moss, P. J. R. Goulder, D. H. Barouch, M. G. McHeyzer-Williams, J. I. Bell, A. J. McMichael, & M. M. Davis. Phenotypic analysis of antigen-specific T lymphocytes. *Science* **274**:94–6, 1996.
- NOTE: (Medline: 96412252) Published erratum appears in *Science* 1998 Jun 19;280(5371):1821.
- [Barber et al.(1997)] L. D. Barber, L. Percival, K. L. Annett, J. E. Gumperz, L. Chen, & P. Parham. Polymorphism in the $\alpha 1$ Helix of the HLA-B Heavy Chain Can Have an Overriding Influence on Peptide-Binding Specificity. *J Immunol* **158**:1660–1669, 1997.
- NOTE: (Medline: 97180884).
- [Barnett et al.(1997)] S. W. Barnett, S. Rajasekar, H. Legg, B. Doe, D. H. Fuller, J. R. Haynes, C. M. Walker, & K. S. Steimer. Vaccination with HIV-1 gp120 DNA induces immune responses that are boosted by a recombinant gp120 protein subunit. *Vaccine* **15**:869–873, 1997.
- NOTE: (Medline: 97378939).

CTL References

- [Bauer et al.(1997)] M. Bauer, M. Lucchiari-Hartz, R. Maier, G. Haas, B. Autran, K. Eichmann, R. Frank, B. Maier, & A. Meyerhans. Structural constraints of HIV-1 Nef may curtail escape from HLA-B7-restricted CTL recognition. *Immunol Lett* **55**:119–22, 1997.
- NOTE: (Medline: 97289021).
- [Bertoletti(1998)] A. Bertoletti. 1998.
- NOTE: Personal communication.
- [Betts et al.(1997)] M. R. Betts, J. Krownka, C. Santamaria, K. Balsamo, F. Gao, G. Mulundu, C. Luo, N. N'Gandu, H. Sheppard, B. H. Hahn, S. Allen, & J. A. Frelinger. Cross-clade human immunodeficiency virus (HIV)-specific cytotoxic T-lymphocyte responses in HIV-infected Zambians. *J Virol* **71**:8908–11, 1997.
- NOTE: (Medline: 98001422).
- [Birk et al.(1998)] M. Birk, A. Vahlne, A. Sonnerborg, & M. Sallberg. Non-synonymous mutations within the human immunodeficiency virus type 1 p17 gene are clustered to sequences binding to the host human leukocyte antigen class I molecules. *AIDS Res Hum Retroviruses* **14**:241–8, 1998.
- NOTE: (Medline: 98150878).
- [Blazevic et al.(1995)] V. Blazevic, A. Ranki, & K. J. E. Krohn. Helper and cytotoxic T cell responses of HIV type 1-infected individuals to synthetic peptides of HIV type 1 Rev. *AIDS Res Hum Retroviruses* **11**:1335–1342, 1995.
- NOTE: (Medline: 96159130) The same set of four peptides from the Rev protein could stimulate proliferation of CD4+ cells and trigger CTL killing of autologous target cells transformed with EBV.
- [Boisgerault et al.(1996)] F. Boisgerault, I. Khalil, V. Tieng, F. Connan, T. Tabary, J. C. J. H. M. Cohen, D. Charron, & A. Toubert. Definition of the HLA-A29 peptide ligand motif allows prediction of potential T-cell epitopes from the retinal soluble antigen, a candidate autoantigen in birdshot retinopathy. *Proc Natl Acad Sci USA* **93**:3466–3470, 1996.
- NOTE: (Medline: 96194993).
- [Borrow et al.(1994)] P. Borrow, H. Lewicki, B. H. Hahn, G. M. Shaw, & M. B. Oldstone. Virus-specific CD8+ cytotoxic T-lymphocyte activity associated with control of viremia in primary human immunodeficiency virus type 1 infection. *J Virol* **68**:6103–6110, 1994.
- NOTE: (Medline: 94335134).
- [Borrow et al.(1997)] P. Borrow, H. Lewicki, X. Wei, M. S. Horwitz, N. Peffer, H. Meyers, J. A. Nelson, J. E. Gairin, B. H. Hahn, M. B. Oldstone, & G. M. Shaw. Anti-viral pressure exerted by HIV-1-specific cytotoxic T lymphocytes (CTLs) during primary infection demonstrated by rapid selection of CTL escape virus. *Nat Med* **3**:205–11, 1997.
- NOTE: (Medline: 97170967) Genetic pathways of virus escape from CTL pressure resembled virus escape from antiretroviral therapy.
- [Bouillot et al.(1989)] M. Bouillot, J. Choplin, F. Cornille, F. Martinon, T. Papo, E. Gomard, M. C. Fournie-Zaluski, & J. Levy. Physical association between MHC class I molecules and immunogenic peptides. *Nature* **339**:473–475, 1989.
- NOTE: (Medline: 8926208) Describes an assay for binding radiolabelled MHC class I molecules to specific peptides that are bound to a solid phase support. Both presenting and non-presenting MHC molecules could bind, which suggested that quantitative difference in binding constants may ultimately determine *in vivo* MHC restriction.
- [Brander et al.(1996)] C. Brander, G. Corradin, T. Hasler, & W. Pichler. Peptide immunization in humans: a combined CD8+/CD4+ T cell-targeted vaccine restimulates the memory CD4 T cell response but fails to induce cytotoxic T lymphocytes (CTL). *Clin Exp Immunol* **105**:18–25, 1996.
- NOTE: (Medline: 96280772).
- [Brander et al.(1998)] C. Brander, K. E. Hartman, A. K. Trocha, N. G. Jones, R. P. Johnson, B. Korber, P. Wentworth, S. P. Buchbinder, S. Wolinsky, B. D. Walker, & S. A. Kalams. Lack of strong immune selection pressure by the immunodominant, HLA-. *J Clin Invest* **101**:2559–66, 1998.
- NOTE: (Medline: 98282291).
- [Brander et al.(1995b)] C. Brander, W. J. Pichler, & G. Corradin. Identification of HIV-protein derived CTL epitopes for their potential use as synthetic vaccine. *Clin Exp Immunol* **101**:107–113, 1995b.
- NOTE: (Medline: 95347061).

CTL References

- [Brander et al.(1995a)] C. Brander, W. J. Pichler, & G. Corradin. Identification of HIV protein derived cytotoxic T-lymphocyte (CTL) epitopes for their possible use as synthetic vaccines. *Clin Exp Immunol* **101**:107–113, 1995a.
- NOTE: (Medline: 95325623) To identify CTL epitopes with potential as peptide-vaccine candidates, peptide sequences were screened for fulfilling the HLA-A2.1 binding motif and involvement in the natural immune response to HIV. Five peptides bound to HLA-A2.1, and HIV-infected persons showed a cytotoxic response against peptide-labeled target cells.
- [Brander & Walker(1995)] C. Brander & B. Walker. The HLA-class I restricted CTL response in HIV-1 infection: Identification of optimal epitopes. In B. Korber, C. Brander, B. Walker, R. Koup, B. Haynes, J. Moore, & G. Myers, editors, *HIV-1 Molecular Immunology Database*, volume 1, pages IV-1 to IV-9, Los Alamos, NM. Theoretical Biology and Biophysics, Los Alamos National Laboratory, 1995.
- NOTE: This database.
- [Brander & Walker(1997a)] C. Brander & B. Walker. The HLA-class I restricted CTL response in HIV-1 infection: Identification of optimal epitopes. In B. Korber, C. Brander, B. Walker, R. Koup, B. Haynes, P. D'Souza, J. Moore, & G. Myers, editors, *HIV-1 Molecular Immunology Database*, volume 3, page Part III, Los Alamos, NM. Theoretical Biology and Biophysics, Los Alamos National Laboratory, 1997a.
- NOTE: This database.
- [Brander & Walker(1997b)] C. Brander & B. Walker. The HLA-class I restricted CTL response in HIV-1 infection: Identification of optimal epitopes. In B. Korber, C. Brander, B. Walker, R. Koup, B. Haynes, & J. Moore, editors, *HIV-1 Molecular Immunology Database*, volume 3, page Part III, Los Alamos, NM. Theoretical Biology and Biophysics, Los Alamos National Laboratory, 1997b.
- NOTE: This database.
- [Brander et al.(1998)] C. Brander, B. D. Walker, & B. Korber. Questionable HLA-A2 restriction of two HIV-1 Nef-derived CTL epitopes listed in the HIV Molecular Immunology Database. *AIDS Res Hum Retroviruses* **14**(11):923–4, 1998.
- NOTE: (Medline: 98349427).
- [Buseyne et al.(1993)] F. Buseyne, M. McChesney, F. Porrot, S. Kovarik, B. Guy, & Y. Riviere. Gag-specific cytotoxic T lymphocytes from human immunodeficiency virus type 1 infected individuals: gag epitopes are clustered in three regions of the p24 gag protein. *J Virol* **67**:694–702, 1993.
- NOTE: (Medline: 93124561) Using autologous Epstein-Barr virus transformed cells that were infected with vaccinia constructs carrying p18, p24, and p55 proteins of LA1, or truncations of p24, it was shown that epitopes within p24 were most commonly recognized in a set of cell lines derived from 29 infected subjects. The autologous transformed cells coated with synthetic peptides were used to identify several regions of p24 where CTL epitopes tended to cluster. HLA restriction was determined CTL responsive to four of the peptides. Among the four epitopes that had determined HLA specificities were the two peptides in the study that proved to stimulate CTL from the highest fraction of the cell lines: peptide p24(263-272) HLA-B27 and peptide p24(256-270) HLA-A33; these peptides were each able to stimulate CTL response from 14% of the cell lines.
- [Buseyne et al.(1997)] F. Buseyne, S. Stevanovic, H. Rammensee, & Y. Riviere. Characterization of an HIV-1 p24 gag epitope recognized by a CD8+ cytotoxic T-cell clone. *Immunol Lett* **55**(3):145–149, 1997.
- NOTE: (Medline: 97305622).
- [C. Wilson & Walker, Personal communication(1996)] D. R. C. Wilson, B. Wilkes & B. Walker, Personal communication. 1996. Defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.
- [Callan et al.(1998)] M. F. C. Callan, L. Tan, N. Annels, G. S. Ogg, J. D. K. W. C. A. O'Callaghan, N. Steven, A. J. McMichael, & A. B. Rickinson. Direct Visualization of Antigen-specific CD8+ T Cells during the Primary Immune Response to Epstein-Barr Virus in vivo. *J Exp Med* **187**:1395–1402, 1998.
- NOTE: (Medline: 98234421).
- [Cao et al.(1997)] H. Cao, P. Kanki, J. L. Sankale, A. Dieng-Sarr, G. P. Mazzara, S. Kalams, B. Korber, S. M'Boup, & B. D. Walker. CTL cross-reactivity among different HIV-1 clades: Implications for vaccine development. *J Virol* **71**:8615–8623, 1997.
- NOTE: (Medline: 98001384).

CTL References

[Carreno et al.(1992)] B. M. Carreno, S. Koenig, & J. E. C. W. E. Biddison. The peptide binding specificity of HLA class I molecules is largely allele-specific and non-overlapping. *Molecular Immunol* **29**:1131–1140, 1992.

NOTE: (Medline: 92357052) Peptide competition experiments for presentation of viral peptides restricted by HLA-A3 and HLA-B27 was performed to study the specificity of peptide binding to class I molecules. HIV-1 Nef (74-82) presentation by HLA-A3 was among the epitopes studied.

[Casement et al.(1995)] K. S. Casement, P. N. Nehete, R. B. Arlinghaus, & K. J. Sastry. Cross-reactive cytotoxic T lymphocytes induced by V3 loop synthetic peptides from different strains of human immunodeficiency virus type 1. *Virology* **211**:261–267, 1995.

NOTE: (Medline: 95373144) Seven diverse V3 peptides were found to induce CTL in immunized mice. All contained the H-2D^d binding motif G, P and R at positions 2, 3 and 5. Only a CTL, (no antibody response), was detected in immunized mice.

[Cease et al.(1987)] K. B. Cease, H. Margalit, J. L. Cornette, S. D. Putney, W. G. Robey, C. Ouyang, H. Z. Streicher, P. J. Fischinger, R. C. Gallo, C. DeLisi, et al. Helper T-cell antigenic site identification in the acquired immunodeficiency syndrome virus gp120 envelope protein and induction of immunity in mice to the native protein using a 16-residue synthetic peptide. *Proc Natl Acad Sci USA* **84**:4249–4254, 1987.

NOTE: (Medline: 87231983).

[Chen et al.(1990)] B. Chen, J. Rohrbard, & P. Parham. Apparent lack of MHC restriction in binding of class I HLA molecules to solid phase peptides. *J Exp Med* **172**:931–936, 1990.

NOTE: (Medline: 90354794) 64 viral antigenic peptides HLA-A,B,C heavy chains, and clathrin light chains were tested for binding to HLA-A2.1, Aw68.1, Aw69, B44, and B5. 15 of the peptides including T cell epitopes, gave significant binding.

[Cheynier et al.(1992)] R. Cheynier, P. Langlade-Demoyen, M. R. Marescot, S. B. S., G. Blondin, S. Wain-Hobson, C. Griscelli, E. Vilmer, & F. Plata. Cytotoxic T lymphocyte responses in the peripheral blood of children born to human immunodeficiency virus-1-infected mothers. *Eur J Immunol* **22**:2211–2217, 1992.

NOTE: (Medline: 92387221) CTL effectors that killed HLA-matched HIV-1-infected H9 target cells or doubly transfected P815-A2-env, gag or nef mouse tumor cells, which expressed the viral antigens in association with HLA-A1/A3 or HLA-A2, were isolated in children born to HIV-1-infected mothers. HIV-1-specific CTL were detected less than 2 months after birth, and declined with disease progression. CTL were detected in the PBMC of three children who subsequently became seronegative.

[Claverie et al.(1988)] J.-M. Claverie, P. Kourilsky, P. Langlade-Demoyen, A. Chalufour-Prochnicka, G. Dadaglio, F. Tekaiia, F. Plata, & K. Bougueret. T-immunogenic peptides are constituted of rare sequence patterns. Use in the identification of T epitopes in the human immunodeficiency virus gag protein. *Eur J Immunol* **18**:1547–1553, 1988.

NOTE: (Medline: 89052758) Based on what was known about epitope structure and amino acid frequencies in 1988, the authors predicted epitopes in the gag proteins. Four peptides that were predicted to contain epitopes were found to specifically stimulate an HLA-A2 restricted polyclonal CTL cell line, when presented by mouse P815 target cells that had been transfected with HLA-A2.

[Clerici et al.(1991)] M. Clerici, D. R. Lucey, R. A. Zajac, R. N. Boswell, H. M. Gebel, H. Takahashi, J. A. Berzofsky, & G. M. Shearer. Detection of cytotoxic T lymphocytes specific for synthetic peptides of gp160 in HIV-seropositive individuals. *J Immunol* **146**:2214–2219, 1991.

NOTE: (Medline: 91170774) Four peptides that could be used to stimulate helper T-cell function were also found to be reactive with MHC class I restricted CTL in infected individuals. 14 of 20 patients were responsive to at least one of the four peptides.

[Collins et al.(1998)] K. L. Collins, B. K. Chen, S. A. Kalams, B. D. Walker, & D. Baltimore. HIV-1 Nef protein protects infected primary cells against killing by cytotoxic T lymphocytes. *Nature* **391**:397–401, 1998.

NOTE: (Medline: 98111233).

[Coman et al.(1994)] F. Coman, F. Hlavac, J. Hoebelke, J. G. Guillet, & J. Choppin. A simple assay for detection of peptides promoting the assembly of HLA class I molecules. *Eur J Immunol* **24**:777–780, 1994.

NOTE: (Medline: 94170859) Peptides from influenza and HIV-1 tested for their ability to promote the assembly of HLA-A2 and HLA-B51 molecules in

CTL References

- [Culmann(1998)] B. Culmann. 1998.
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.
- [Corey et al.(1998)] L. Corey, M. J. McElrath, K. Weinhold, T. Matthews, D. Stablein, B. Graham, M. Keefer, D. Schwartz, G. Gorse, & the AIDS Vaccine Evaluation Group. Cytotoxic T cell and neutralizing antibody responses to human immunodeficiency virus type 1 envelope with a combination vaccine regimen. *J Infect Dis* **177**:301-9, 1998.
- NOTE: (Medline: 98125991).
- [Couillin et al.(1995)] I. Couillin, F. Connan, B. Culmann-Penciolelli, E. Gomard, J.-G. Guillet, & J. Choppin. HLA-dependent variations in human immunodeficiency virus Nef protein alter peptide/HLA binding. *Eur J Immunol.* **25**:728-732, 1995.
- NOTE: (Medline: 95220421) Viral sequences across this region were compared from 3 HLA-A11 positive and 10 negative donors. Substitutions that were found only in the 3 HLA-A11 donors did not promote HLA-A11 assembly. Substitutions that were found in both HLA-A11 positive and negative donors, however, did not markedly alter the reactivity of the peptides. This suggests that substitutions that result in loss of HLA-A11 occur mainly in HLA-A11 positive donors.
- [Couillin et al.(1994)] I. Couillin, B. Culmann-Penciolelli, E. Gomard, J. Choppin, J. Levy, J. G. Guillet, & S. Saragosti. Impaired cytotoxic T lymphocyte recognition due to genetic variations in the main immunogenic region of the human immunodeficiency virus 1 NEF protein. *J Exp Med* **180**:1129-34, 1994.
- NOTE: (Medline: 95220421) HIV-1 HLA-A11 and -B18 restricted epitopes were sequenced from donors who do and do not express the HLA-A11 and B18 molecule. Selective variations were only detected in virus isolated from individuals expressing the appropriate HLA type. Variant peptides with single substitutions within the minimal epitope did not always completely abrogate HLA binding, suggesting that multiple alterations within a particular epitope may need to accumulate during disease progression to allow viral escape.
- [Culmann et al.(1991)] B. Culmann, E. Gomard, M. Kiency, B. Guy, F. Dreyfus, A. Saimot, D. Sereni, D. Sicard, & J. Levy. Six epitopes with human cytotoxic CD8+ cells in the central region of the HIV-1 Nef protein. *J Immunol* **146**:1560-1565, 1991.
- NOTE: (Medline: 91132023) 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; TQGYFPQWQNWT, HLA B17, B37, NYTPGPGVRYPLT, HLA B7; and GVRVPLTFGWCVYKLVP, HLA B18.
- [Culmann et al.(1989)] B. Culmann, E. Gomard, M. P. Kiency, B. Guy, F. Dreyfus, & A. G. Saimot. An antigenic peptide of the HIV-1 NEF protein recognized by cytotoxic T lymphocytes of seropositive individuals in association with different HLA-B molecules. *Eur J Immunol* **19**:2383-2386, 1989.
- NOTE: (Medline: 90108082).
- [Culmann-Penciolelli et al.(1994)] B. Culmann-Penciolelli, S. Lamhamdi-Cherradi, I. Couillin, N. Guegan, J. P. Levy, J. G. Guillet, & E. Gomard. Identification of multirestricted immunodominant regions recognized by cytolytic T lymphocytes in the human immunodeficiency virus type 1 Nef protein (published erratum appears in J Virol 1995 Jan;69(1):618). *J Virol* **68**:7336-43, 1994.
- NOTE: (Medline: 95018646).
- [Dadaglio et al.(1991)] G. Dadaglio, A. Leroux, P. Langlade-Demoyen, E. M. Bahraoui, F. Traincard, R. Fisher, & F. Plata. Epitope recognition of conserved HIV envelope sequences by human cytotoxic T lymphocytes. *J Immunol* **147**:2302-2309, 1991.
- NOTE: (Medline: 92013025) Using synthetic peptides, six conserved epitopes on gp120 Env were identified, recognized by polyclonal human

CTL References

- CTL in association with HLA-A2 class I. Conserved epitopes: RIQRGP-GRAFVTIGK, IIIB; LWVTVYVYGVPVWKEATTIIFCA; TTSYTLTSC-NTSVITQACPK; SVEINCTRPNNTTRKSI; PEIVTHS; KNCGGEFFY-CNS; LPCRIKQFINMWQEVGKAMY; VKIEPLGVAPTKAKRRVVQR. control: gag, YKRWIILGLNKVVRMYSPT, HLA B27.
- [Dai et al.(1992)] L. C. Dai, K. West, R. Littaua, K. Takahashi, & F. A. Emis. Mutation of human immunodeficiency virus type 1 at amino acid 585 on gp41 results in loss of killing by CD8⁺ A24-restricted cytotoxic T lymphocytes. *J Virol* **66**:3151–3154, 1992.
- NOTE: (Medline: 92219406) An A24-restricted CD8⁺ CTL gp41 epitope was localized: YLKDDQQLL, using a CTL clone from an HIV infected individual. Lys to (Arg or Gin) substitution in peptides used to pulse a target cell line eliminated killing.
- [De Groot et al.(1991)] A. S. De Groot, M. Clerici, A. Hosmalin, S. H. Hughes, D. Barnid, C. W. Hendrix, R. Houghten, G. M. Shearer, & J. A. Berzofsky. Human immunodeficiency virus reverse transcriptase T-helper epitopes identified in mice and humans: correlation with a cytotoxic T-cell epitope. *J Infect Dis* **164**:1058–1065, 1991.
- NOTE: (Medline: 92064980) This peptide stimulates both murine helper and cytotoxic T-cells and was able to stimulate IL-2 producing T-cells from 9 out of 17 HIV seropositive humans. RT epitope: CTMEKEGGKISKIGP.
- [De Maria et al.(1997)] A. De Maria, A. Ferraris, M. Guastella, S. Pilia, C. Cantoni, L. Polero, M. C. Mingari, D. Bassetti, A. S. Fauci, & L. Moretta. Expression of HLA class I-specific inhibitory natural killer cell. *Proc Natl Acad Sci USA* **94**:10285–8, 1997.
- NOTE: (Medline: 97439856).
- [Deml et al.(1997)] L. Deml, R. Schirrmbeck, J. Reimann, H. Wolf, & R. Wagner. Recombinant human immunodeficiency Pr55^{gag} virus-like particles presenting chimeric envelope glycoproteins induce cytotoxic T-cells and neutralizing antibodies. *Virology* **235**:26–39, 1997.
- NOTE: (Medline: 97445045).
- [DiBrino et al.(1993)] M. DiBrino, K. C. Parker, & J. S. et al. Endogenous peptides bound to HLA-A3 possess a specific combination of anchor residues
- that permit identification of potential antigenic peptides. *Proc Natl Acad Sci USA* **90**:1508–1512, 1993.
- NOTE: (Medline: 93165724).
- [DiBrino et al.(1994a)] M. DiBrino, K. C. Parker, D. H. Margulies, J. Shiloach, R. V. Turner, M. Garfield, W. E. B. WE, & J. E. Coligan. The HLA-B14 peptide binding site can accommodate peptides with different combinations of anchor residues. *J Biol Chem* **269**, 1994a.
- NOTE: (Medline: 95096094).
- [DiBrino et al.(1994b)] M. DiBrino, K. C. Parker, J. Shiloach, R. V. Turner, T. Tsuchida, M. Garfield, W. E. Biddison, & J. E. Coligan. Endogenous peptides with distinct amino acid anchor residue motifs bind to HLA-A1 and HLA-B8. *J Immunol* **152**, 1994b.
- NOTE: (Medline: 94110616).
- [Doe & Walker(1997)] B. Doe & C. M. Walker. HIV-1 p24 Gag-specific cytotoxic T-lymphocyte responses in mice. *AIDS* **10**:793–794, 1997.
- NOTE: Correspondence(Medline: 96399361).
- [Dong & et al.(1998)] T. Dong & et al. . *JCI* 1998.
- NOTE: In press.
- [Dong & Rowland-Jones(1998)] T. Dong & S. Rowland-Jones. 1998.
- NOTE: Personal communication.
- [Duarte et al.(1996)] E. A. Duarte, G. Eberl, & G. Corradin. Specific tolerization of active cytotoxic T lymphocyte responses in vivo with soluble peptides. *Cell. Immunol.* **169**:16–23, 1996.
- NOTE: (Medline: 96185988) Mice immunized with this peptide had an active CTL response that could be specifically tolerized with continued administration of soluble peptide; this was also observed with a malaria peptide. Suggests that soluble peptide may be useful for treatment of autoimmune disease.
- [Dupuis et al.(1995)] M. Dupuis, S. K. Kundu, & T. C. Merigan. Characterization of HLA-A*0201-restricted cytotoxic T-cell epitopes in conserved regions of the HIV type 1 gp160 protein. *J Immunol* **155**:2232–2239, 1995.

CTL References

- NOTE: (Medline: 95363191) Five HLA-A2 HIV-1 seropositive HIV-1 MN rec gp160 vaccinees had their CTL activity assessed using peptides known to bind with high affinity to HLA-A*0201. Four of the patients had specific CTL activity for a minimum of at least three epitopes, thus the response appears heterogeneous. One of the four peptides was confirmed to be HLA A2 restricted. Epitopes were highly conserved.
- [Durail et al.(1998)] D. Durail, J. Morvan, F. Letourneau, D. Schmitt, N. Guegan, M. Dalod, S. Saragosti, D. Sicard, J. P. Levy, & E. Gomard. Cross-reactions between the cytotoxic T-lymphocyte responses of human immunodeficiency virus-infected African and European patients. *J Virol* **72**:3547-53, 1998.
- NOTE: (Medline: 98216712).
- [Englehard et al.(1993)] V.H. Englehard, E. L. Huczko, & W.B. et al. Peptides bound to HLA-B7 determined by mass spectrometry. *J Cell Biochem Suppl* **1993** **17C**:56, 1993.
- NOTE: (Medline:).
- [Falk et al.(1994)] K. Falk, O. Rotzschke, & B. Grahavac. Allele-specific peptide motifs of HLA-C molecules. *Proc Natl Acad Sci USA* **90**:12005-12009, 1994.
- NOTE: (Medline: 94089758).
- [Falk et al.(1991)] K. Falk, O. Rotzschke, S. Stevanovic, G. Jung, & H. Rammensee. Allele-specific motifs revealed by sequencing of self-peptides eluted from MHC molecules. *Nature* **351**:290-296, 1991.
- NOTE: (Medline: 91238947).
- [Falk et al.(1995a)] K. Falk, O. Rotzschke, M. Takiguchi, V. Gnau, S. Stevanovic, G. Jung, & H. Rammensee. Peptide motifs of HLA-B38 and B39 molecules. *Immunogenetics* **41**:162-164, 1995a.
- NOTE: (Medline: 95104927).
- [Falk et al.(1995b)] K. Falk, O. Rotzschke, M. Takiguchi, V. Gnau, S. Stevanovic, G. Jung, & H. Rammensee. Peptide motifs of HLA-B58, B60, B61, and B62 molecules. *Immunogenetics* **41**:165-168, 1995b.
- NOTE: (Medline: 95104928).
- [Fan et al.(1997)] Z. Fan, X. L. Huang, L. Zheng, C. Wilson, L. Borowski, J. Liebmann, P. Gupta, J. Margolick, & C. Rinaldo. Cultured blood dendritic cells retain HIV-1 antigen-presenting capacity for memory CTL during progressive HIV-1 infection. *J Immunol* **159**:4973-82, 1997.
- NOTE: (Medline: 98031752).
- [Ferris et al.(1996)] R. L. Ferris, C. Buck, S. A. Hammond, A. S. Woods, R. J. Cotter, M. Takiguchi, Y. Igarashi, Y. Ichikawa, & R. F. Siliciano. Class I-restricted presentation of an HIV-1 gp41 epitope containing an N-linked glycosylation site. *J Immunol* **156**:834-840, 1996.
- NOTE: (Medline: 96133015) The class I processing pathway usually begins in the cytosol. Env proteins are co-translationally located in the endoplasmic reticulum, where they are glycosylated, and in general are not found in the cytosol. The N-linked glycosylation site was not occupied in the TAVP-WNASW naturally processed peptide presented by B*3501, and the non-glycosylated form was the form recognized by an env-specific CTL clone. This suggests that there may be limited failure of translocation, resulting in synthesis and degradation in the cytosol, and entry in the normal class I processing pathway.
- [Fomsgaard et al.(1998)] A. Fomsgaard, H. V. Nielsen, K. Bryder, C. Nielsen, R. Machuca, L. Bruun, J. Hansen, & S. Buus. Improved humoral and cellular immune responses against the gp120 V3 loop of HIV-1 following genetic immunization with a chimeric DNA vaccine encoding the V3 inserted into the hepatitis B surface antigen. *Scand J Immunol* **47**:289-95, 1998.
- NOTE: (Medline: 98260936).
- [Froebel et al.(1997)] K. S. Froebel, J. Y. Mok, M. C. Aldhous, M. P. Armitage, M. Arnott, L. M. Reynolds, J. F. Peutherer, & S. M. Burns. In vitro measurement of cytotoxic T cell activity does not predict clinical progression in pediatric HIV disease – two case studies. *Clin Exp Immunol* **110**:15-21, 1997.
- NOTE: (Medline: 98013192).
- [Garboczi et al.(1992)] D. N. Garboczi, D. T. Hung, & D. C. Wiley. HLA-A2-peptide complexes: refolding and crystallization of molecules expressed in Escherichia coli and complexed with single antigenic peptides. *Proc Natl Acad Sci USA* **89**:3429-3433, 1992.

CTL References

- NOTE: (Medline: 92228799).
- [Garcia et al.(1997)] S. Garcia, M. Fevrier, G. Dadaglio, H. Lecoeur, Y. Riviere, & M. Gougeon. Potential deleterious effect of anti-viral cytotoxic lymphocyte through the CD95 (FAS/APO-1)-mediated pathway during chronic HIV infection. *Immunol Lett* **57**:53–58, 1997.
- NOTE: (Medline: 97376315).
- [Goletz et al.(1997)] T. J. Goletz, K. R. Klimpel, N. Arora, S. H. Leppla, J. M. Keith, & J. A. Berzofsky. Targeting HIV proteins to the major histocompatibility complex class I processing pathway with a novel gp120-anthrax toxin fusion protein. *Proc Natl Acad Sci USA* **94**:12059–12064, 1997.
- NOTE: (Medline: 98004523).
- [Gotch et al.(1993)] F. Gotch, S. N. McAdam, & C. E. A. et al. Cytotoxic T-cells in HIV-2 seropositive grambians. identification of a virus specific MHC-restricted peptide epitope. *J Immunol* **151**:3361–3369, 1993.
- NOTE: (Medline: 93389165).
- [Gotch et al.(1990)] F. Gotch, D. Nixon, N. Alp, A. McMichael, & L. Bortysiewicz. High frequency of memory and effector gag specific cytotoxic T lymphocytes in HIV seropositive individuals. *Int Immunol* **2**:707, 1990.
- NOTE: (Medline: 91190784).
- [Goulder et al.(1996a)] P. Goulder, C. Conlon, K. McIntyre, & A. McMichael. Identification of a novel human leukogen antigen A26-restricted epitope in a conserved region of Gag. *AIDS* **10**(12):1441–1443, 1996a.
- NOTE: (Medline: 97057743) This paper is correspondence briefly describing the identification and characterization of an immuno-dominant A26-CTL epitope in an asymptomatic HIV+ individual.
- [Goulder et al.(1997)] P. Goulder, D. Price, M. Nowak, S. Rowland-Jones, R. Phillips, & A. McMichael. Co-evolution of human immunodeficiency virus and cytotoxic T-lymphocyte responses. *Immunol Rev* **159**:17–29, 1997.
- NOTE: (Medline: 98078460).
- [Goulder et al.(1997a)] P. Goulder, A. Sewell, D. Laloo, D. Price, J. Whealan, J. Evans, G. Taylor, G. Luzzi, P. Giangrande, R. Phillips, & A. J. McMichael. Patterns of immunodominance in hiv-1-specific cytotoxic T lymphocyte responses in two human histocompatibility leukocyte antigens (HLA)-identical siblings with hla-a*0201 are influenced by epitope mutation. *J Exp Med* **8**:1423–33, 1997a.
- NOTE: (Medline: 97272078).
- [Goulder et al.(1997b)] P. J. Goulder, M. Bunce, G. Luzzi, R. E. Phillips, & A. J. McMichael. Potential underestimation of HLA-C-restricted cytotoxic T-lymphocyte responses. *AIDS* **11**(15):1884–1886, 1997b.
- NOTE: (Medline: 98074190).
- [Goulder et al.(1997c)] P. J. Goulder, A. Edwards, R. E. Phillips, & A. J. McMichael. Identification of a novel HLA-B*3501-restricted cytotoxic T lymphocyte epitope using overlapping peptides. *AIDS* **11**(7):930–932, 1997c.
- NOTE: (Medline: 97333059).
- [Goulder et al.(1997d)] P. J. Goulder, A. Edwards, R. E. Phillips, & A. J. McMichael. Identification of a novel HLA-B*2705-restricted cytotoxic T lymphocyte epitope within a conserved region of HIV-1 Nef. *AIDS* **11**:536–538, 1997d.
- NOTE: (Medline: 97239113).
- [Goulder et al.(1996b)] P. J. R. Goulder, M. Bunce, P. Krausa, K. McIntyre, S. Crowley, B. Morgan, A. Edwards, P. Giangrande, R. E. Phillips, & A. J. McMichael. Novel, cross-restricted, conserved and immunodominant cytotoxic T lymphocyte epitopes in slow HIV type 1 infection. *AIDS Res and Hum Retroviruses* **12**:1691–1698, 1996b.
- NOTE: (Medline: 97118362) 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.
- [Goulder et al.(1997e)] P. J. R. Goulder, R. E. Phillips, R. A. Colbert, S. McAdam, G. Ogg, M. A. Nowak, P. Giangrande, G. Luzzi, B. Morgan, A. Edwards, A. McMichael, & S. Rowland-Jones. Late escape from an immunodominant cytotoxic T-lymphocyte response associated with progression to AIDS. *Nature Med* **3**:212–216, 1997e.

CTL References

NOTE: (Medline: 97170968) The CTL response was studied in six HIV+ individuals who make a strong immunodominant response to the same B27 epitope. In two donors an escape mutation arose after close to 10 years of epitope stability, around the time of progression to AIDS.

[Goulder et al.(1997f)] P. J. R. Goulder, S. W. Reid, D. A. Price, C. A. O'Callaghan, A. J. McMichael, R. E. Phillips, & E. Y. Jones. Combined structural and immunological refinement of HIV-1 HLA-B8 restricted cytotoxic T lymphocyte epitopes. *Eur J Immunol* **27**:1515–1521, 1997.

NOTE: (Medline: 97353247).

[Griffiths et al.(1993)] J. Griffiths, S. J. Harris, G. T. Layton, E. L. Berrie, T. J. French, N. R. Burns, S. E. Adams, & A. J. Kingsman. Hybrid human immunodeficiency virus gag particles as an antigen carrier system: induction of cytotoxic T-cell and humoral responses by a gag:V3 fusion. *J Virol* **67**:3191–3198, 1993.

NOTE: (Medline: 91087316).

[Haas et al.(1997)] G. Haas, A. Hosmalin, F. Hadida, J. Duntze, P. Debre, & B. Autran. Dynamics of HIV variants and specific cytotoxic T-cell recognition in nonprogressors and progressors. *Immunol Lett* **57**:63–8, 1997.

NOTE: (Medline: 97376317).

[Haas et al.(1996)] G. Haas, U. Phlikat, P. Debre, M. Lucchiani, C. Kathama, Y. Dudoit, O. Bonduelle, M. Bauer, H. Ihlenfeldt, G. Jung, B. Maier, A. Meyrathans, & B. Autran. Dynamics of viral variants in HIV-1 Nef and specific cytotoxic T lymphocytes in vivo. *J Immunol* **157**:4212–4221, 1996.

NOTE: (Medline: 97047818).

[Haas et al.(1998)] G. Haas, A. Samri, E. Gomard, A. Hosmalin, J. Duntze, J. M. Bouley, H. G. Ihlenfeldt, C. Kathama, & B. Autran. Cytotoxic T cell responses to HIV-1 reverse transcriptase, integrase and protease. *AIDS* **12**(12):427–36, 1998.

NOTE: (Medline: 98394546).

[Hadida et al.(1995)] F. Hadida, G. Haas, G. Zimmermann, A. Hosmalin, R. Spohn, A. Samri, G. Jung, P. Debre, & B. Autran. CTL's from lymphoid organs recognize an optimal HLA-A2 restricted and HLA-B52 restricted

nonapeptide and several epitopes in the C-terminal region of HIV-1 Nef. *J Immunol* **154**:4174–4186, 1995.

NOTE: (Medline: 95221926) An *in vitro* limiting dilution analysis showed CTL recognition in the context of HLA B52 and A2.1, A2.2 and A2.4 in nanomolar concentrations. Molecular modeling suggests motifs important for peptide binding to the pocket of an HLA-A2.1 molecule.

[Hadida et al.(1992)] F. Hadida, A. Parrot, M. P. Klein, B. Sadat-Sowti, C. Mayaud, & P. Debre. Carboxyl-terminal and central regions of human immunodeficiency virus-1 NEF recognized by cytotoxic T lymphocytes from lymphoid organs. an *in vitro* limiting dilution analysis. *J Clin Invest* **89**:53–60, 1992.

NOTE: (Medline: 95221926) HIV-1 specific CTL can be detected in lymph nodes and spleens. The carboxyl-terminal domain of NEF is recognized by CTL in association with HLA-A1 and B8, with clonal frequencies of one CTL per 10^{-5} to 10^{-6} splenic lymphocytes.

[Hamajima et al.(1997)] K. Hamajima, J. Fukushima, H. Fukawa, 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.

NOTE: (Medline: 97288401).

[Hammond et al.(1995)] S. A. Hammond, R. P. Johnson, S. A. Kalams, B. D. Walker, M. Takiguchi, J. T. Safrit, R. A. Koup, & R. F. Siliciano. An epitope-selective transporter associated with antigen presentation TAP-1/2-independent pathway and a more general TAP-1/2-dependent antigen processing pathway allow recognition of the HIV-1 envelope glycoprotein by CD8+ CTL. *J Immunol* **154**:6140–6156, 1995.

NOTE: (Medline: 95271010) Two peptide processing pathways are utilized for MHC class I presentation of HIV-1 Env epitopes. The previously characterized TAP-1 and TAP-2 dependent pathway can generate all Env epitopes and uses Env protein mislocalized in the cytosol to produce peptides. The second, novel pathway uses a TAP-1/2 independent pathway, and allows a subset of MHC restricted epitopes to be processed in the endoplasmic reticulum or a Golgi compartment.

CTL References

- [Hammond et al.(1991)] S. A. Hammond, E. Obah, P. Stanhope, C. R. Monell, M. Strand, F. M. Robbins, W. B. Bias, R. W. Karr, S. Koenig, & R. F. Siliciano. Characterization of a conserved T-cell epitope in HIV-1 gp41 recognized by vaccine-induced human cytolytic T-cells. *J Immunol* **146**:1470–1477, 1991.
- NOTE: (Medline: 91132009) A HLA DPw4.2 human CTL epitope located in gp41 was described, recognized by CD4+ CTL clones that were induced in seronegative humans by immunization with recombinant gp160 BRU. gp41 CTL epitope: GIKQLQARILAVERYLKDQ.
- [Hanke et al.(1998a)] T. Hanke, T. J. Blanchard, J. Schneider, G. S. Ogg, R. Tan, M. Becker, S. C. Gilbert, A. V. Hill, G. L. Smith, & A. McMichael. Immunogenicities of intravenous and intramuscular administrations of modified vaccinia virus Ankara-based multi-CTL epitope vaccine for human immunodeficiency virus type 1 in mice. *J Gen Virol* **79**:83–90, 1998a.
- NOTE: (Medline: 98120825).
- [Hanke et al.(1998b)] T. Hanke, J. Schneider, S. G. Gilbert, A. V. S. Hill, & A. McMichael. DNA multi-CTL epitope vaccines for HIV and Plasmodium falciparum: Immunogenicity in mice. *Vaccine* **16**:426–435, 1998b.
- NOTE: (Medline: 98269949).
- [Harrer et al.(1996a)] E. Harrer, T. Harrer, P. Barbosa, M. Feinberg, R. P. Johnson, S. Buchbinder, & B. D. Walker. Recognition of the highly conserved YMDD region in the human immunodeficiency virus type 1 reverse transcriptase by HLA-A2-restricted cytotoxic T lymphocytes from an asymptomatic long-term nonprogresser. *J Inf Dis* **173**:476–479, 1996a.
- NOTE: (Medline: 96162113) The amino acid stretch YMDD is a critical functional domain of reverse transcriptase, and is highly conserved. This sequence is also part of an HLA-A2-restricted epitope. The substitution YMDD to YVDD confers drug resistance to FTC and dideoxyinosine, and also abolishes the CTL specific response.
- [Harrer et al.(1996b)] T. Harrer, E. Harrer, S. A. Kalams, P. Barbosa, A. Trocha, R. P. Johnson, T. Elbeik, M. B. Feinberg, S. P. Buchbinder, & B. D. Walker. Cytotoxic T lymphocytes in asymptomatic long-term nonprogressing HIV-1 infection. breadth and specificity of the response and relation to in vivo viral quasispecies in a person with prolonged infection and low viral load. *J Immunol* **156**:2616–2623, 1996b.
- NOTE: (Medline: 96180222).
- [Hickling et al.(1990)] J. K. Hickling, C. M. Fenton, K. Howland, S. G. Marsh, & J. B. Rothbard. Peptides recognized by class I restricted T-cells also bind to MHC class II molecules. *International Immunology* **2**:435–441, 1990.
- NOTE: (Medline: 91197875) Peptides shown to be presented in the context of MHC class I proteins by mouse or human CD8+ T lymphocytes could also bind to HLA-DR molecules on the surface of B lymphoblastoid cell lines (B-LCL). Four out of five class I restricted T cell determinants bound, including the HIV-1 gp120 epitope.
- [Hill et al.(1992)] A. V. Hill, J. Elvin, & A. C. W. et al. Characteristics of peptides eluted from HLA-B7. *Nature* **360**:434–439, 1992.
- NOTE: (Medline: 93078872).
- [Hosmalin et al.(1990)] A. Hosmalin, M. Clerici, R. Houghten, C. D. Pendleton, C. Flexner, D. R. Lucey, B. Moss, R. N. Germain, G. M. Shearer, & J. A. Berzofsky. An epitope in human immunodeficiency virus 1 reverse transcriptase recognized by both mouse and human cytotoxic T lymphocytes. *Proc Natl Acad Sci USA* **87**:2344–2348, 1990.
- NOTE: (Medline: 90192804).
- [Hunziker et al.(1998)] I. P. Hunziker, A. Cerny, & W. J. Pichler. Who is right? Or, how to judge the disagreement about HLA restriction of Nef peptides. *AIDS Res Hum Retroviruses* **14**:921–4, 1998.
- NOTE: (Medline: 98349426).
- [Ikeda-Moore et al.(1997)] Y. Ikeda-Moore, H. Tomiyama, K. Miwa, S. Oka, A. Iwamoto, Y. Kaneko, & M. Takiguchi. Identification and Characterization of Multiple HLA-A24-Restricted HIV-1 CTL Epitopes: Strong Epitopes Are Derived from V Regions of HIV-1. *J Immunology* **159**:6242–6252, 1997.
- NOTE: (Medline: 98209798).
- [Ishii et al.(1997)] N. Ishii, J. Fukushima, T. Kaneko, E. Okada, K. Tani, S. I. Tanaka, K. Hamajima, K. Q. Xin, S. Kawamoto, W. Koff, K. Nishioka, T. Yasuda, & K. Okuda. Cationic liposomes are a strong adjuvant for a DNA vaccine of human immunodeficiency virus type 1. *AIDS Res Hum Retroviruses* **13**:1421–8, 1997.

CTL References

NOTE: (Medline: 98022620).

[Jardetzky et al.(1991)] T. S. Jardetzky, W. S. Lane, R. A. Robinson, D. R. Madden, & D. C. Wiley. Identification of self peptides bound to purified HLA-B27. *Nature* **353**:326–9, 1991.

NOTE: (Medline: 92018188).

[Jassoy et al.(1993)] C. Jassoy, T. Harrer, T. Rosenthal, B. A. Navia, J. Worth, R. P. Johnson, & B. D. Walker. Human immunodeficiency virus type 1-specific cytotoxic T lymphocytes release gamma interferon, tumor necrosis factor alpha (TNF-alpha), and TNF-beta when they encounter their target antigens. *J Virol* **67**:2844–2852, 1993.

NOTE: (Medline: 93233253) In this study the ability of HIV-1-specific CTL clones derived from seropositive persons to release gamma interferon (IFN- γ), tumor necrosis factor alpha (TNF- α), and TNF- β upon contact with target cells presenting viral antigen was assessed. Epitopes: p17: KIRLRPG-GKKKYKLKHIVWASRELE, A3; gp41: VERYLKDQQL, B14 and A28, ERYLKDDQQL, B14; RT: AIFQSSMTKILEPFRKQNPDIVTYQ, A11; and Nef SQRRQDILDLWIYHTQGYFPDWQNY, B13.

[Jassoy et al.(1992)] C. Jassoy, R. P. Johnson, B. A. Navia, J. Worth, & B. D. Walker. Detection of a vigorous HIV-1 specific cytotoxic T lymphocyte response in cerebrospinal fluid from infected persons with AIDS dementia complex. *J Immunol* **149**:3113–3119, 1992.

NOTE: (Medline: 93017933) CTL clones derived from CSF of individuals with AIDS dementia. HIV-1 specific CTL were detected in CSF from 5 out of 6 patients who were suffering from HIV-1 associated cognitive/motor complex disturbances.

[Johnson et al.(1994a)] R. P. Johnson, S. A. Hammond, A. Trocha, R. F. Siliciano, & B. D. Walker. Epitope specificity of MHC restricted cytotoxic T lymphocytes induced by candidate HIV-1 vaccine. *AIDS Research and Human Retroviruses* **10**, Supp 2:S73–S75, 1994a.

NOTE: (Medline: 95169519) Volunteers were immunized with recombinant vaccinia virus expressing HIV-1 gp160 (vac-env) and boosted with recombinant gp160 (rgp160). CTL clones were analyzed for HLA restriction and specificity. An immunodominant HLA-A3.1 restricted epitope was observed that showed very little sequence variation among B subtype sequences, (TVYVYGVPVWK). Naturally occurring variants of this peptide

were able to stimulate reactivity. Two additional CD8+ CTL epitopes from vaccinees were characterized, as well as two CD4+ CTL epitopes.

[Johnson et al.(1994b)] R. P. Johnson, S. A. Hammond, A. Trocha, R. F. Siliciano, & B. D. Walker. Induction of a major histocompatibility complex class I-restricted cytotoxic T-lymphocyte response to a highly conserved region of human immunodeficiency virus type 1 (HIV-1) gp120 in seronegative humans immunized with a candidate HIV-1 vaccine. *J Virol* **68**:3145–3153, 1994b.

NOTE: (Medline: 94202302) In two volunteers, immunization with a single strain of HIV-1 induced CD4+ and CD8+ CTL that are specific for multiple conserved regions of HIV-1 and would be expected to recognize a broad range of viral isolates. The immunodominant gp120 epitope, gp120-TVYYGVPVWK, elicited CD8+ HLA-A3.1 restricted CTL, and this epitope is highly conserved. CTL specific for this epitope could lyse target cells sensitized with all known natural sequence variants. Additionally, CD8+ HLA-B35 and CD8+ HLA-B18 restricted epitopes were defined as well as two CD4+ cytotoxic T-cell gp120 epitopes: ITQACPKVSFEPYPHYCA-PAGFAI and NNTLKVQIDSKLREQFG.

[Johnson et al.(1992)] R. P. Johnson, A. Trocha, T. M. Buchanan, & B. D. Walker. Identification of overlapping HLA class I-restricted cytotoxic T-cell epitopes in a conserved region of the human immunodeficiency virus type 1 envelope glycoprotein: definition of minimum epitopes and analysis of the effects of sequence variation. *J Exp Med* **175**:961–971, 1992.

NOTE: (Medline: 92202878) Fine mapping and mutational analysis of gp41 epitopes: ERYLKDDQQL, HLA B14 and YLKDDQQLL, HLA B8.

[Johnson et al.(1993)] R. P. Johnson, A. Trocha, T. M. Buchanan, & B. D. Walker. Recognition of a highly conserved region of human immunodeficiency virus type 1 gp120 by an HLA-Cw4-restricted cytotoxic T-lymphocyte clone. *J Virol* **67**:438–445, 1993.

NOTE: (Medline: 93100827) The epitope sequence FNCGGEFF stimulates CTL response; the natural variants FNCRGEFF (SF2), TNCRGEFL (ROD) and LNCGGEFF (NDK) do not serve as epitopes. This was the first report of an HIV antigen specific target cells restricted by an HLA-C molecule, Cw4.

[Johnson et al.(1991)] R. P. Johnson, A. Trocha, L. Yang, G. P. Mazzara, D. L. Panicali, T. M. Buchanan, & B. D. Walker. HIV-1 gag-specific cytotoxic T

CTL References

Lymphocytes recognize multiple highly conserved epitopes, fine specificity of the gag-specific response defined by using unstimulated peripheral blood mononuclear cells and cloned effector cells. *J Immunol* **147**:1512–1521, 1991.

NOTE: (Medline: 91349569) This study presented a detailed study of gag specific CTL from HIV-1 seropositive individuals. Seven p24 and two p17 epitopes were described, that were recognized by class I restricted CD3+CD8+ CTL. p17 epitopes: KIRLRPGGKKYKLKHWASRELE and GSEFLRSLYNTVATLYCVHQRIE; p24 epitopes: NPPIPVGEIYKRWIL-GLNKIV, VHQAIISPRTLNAWVKVVEEKAF, NAWVKVVEEKAFSPE-VIPMFSA, SALSEGATPQDLNTMLNTVGHH, GHQAAMQMLKETL-NEEAIAEWDR, and RAEQASQEVK.

[Johnson & Walker(1994)] R. P. Johnson & B. D. Walker. CTL in HIV-1 infection: Responses to structural proteins. *Curr Topics Microbiol Immunol* **189**:35–63, 1994.

NOTE: (Medline: 95008926) Review.

[Kalams et al.(1994)] S. Kalams, R. P. Johnson, A. K. Trocha, M. J. Dynan, H. S. Ngo, R. T. D'Aquila, J. T. Kurnick, & B. D. Walker. Longitudinal analysis of T-cell receptor (TCR) gene usage by HIV-1 envelope-specific cytotoxic T-lymphocyte clones reveals a limited TCR repertoire. *J Exp Med.* **179**:1261–1271, 1994.

NOTE: (Medline: 94194282) This paper presents an in depth longitudinal study of T-cell receptor gene usage to a well defined HLA B14 restricted gp41 epitope. Ten CTL clones were derived from a single individual over 31 months. T-cell receptor V-D-J sequencing was performed on PCR amplification products. All ten clones utilized $V\alpha 14$ and $V\beta 4$ genes; observed limited T-cell receptor diversity to an immunodominant epitope was suggested to facilitate immune escape. gp41 epitope: ERYLKDDQLL. An HLA B14 restricted RT epitope from this individual used $V\alpha 21$ and $V\beta 14$, showing use of these genes was not a feature of all HLA B14 restricted clones from this individual. RT epitope: AIYLAQJQDSGLEVNIVTDSQYALGI.

[Kalams et al.(1996)] S. A. Kalams, R. P. Johnson, M. J. Dynan, K. E. Hartman, T. Harrer, E. Harrer, A. K. Trocha, W. A. Blattner, S. P. Buchbinder, & B. D. Walker. T cell receptor usage and fine specificity of human immunodeficiency virus type 1 specific cytotoxic T lymphocyte clones: analysis

of quasispecies recognition reveals a dominant response directed against a minor in vivo variant. *J Exp Med* **183**:1699–1679, 1996.

NOTE: (Medline: 96261668).

[Kast et al.(1994)] W. M. Kast, R. M. Brandt, J. Sidney, J. W. Drijfhout, R. T. Kubo, H. M. Grey, C. J. Melief, & A. Sette. Role of HLA-A motifs in identification of potential CTL epitopes in human papillomavirus type 16 E6 and E7 proteins. *J Immunol* **152**:3904–3912, 1994.

NOTE: (Medline: 94194153) Binding affinities for five HLA-A alleles: HLA-A1 (A*0101), A2.1 (A*0201), A3 (A*0301), A11 (A*1101), and A24 (A*2401) was determined for all nonamer peptides of human papillomavirus type 16 E6 and E7. High affinity binding peptides allowed an assessment of binding-motifs.

[Kent et al.(1997)] S. J. Kent, P. D. Greenberg, M. C. Hoffman, R. E. Akridge, & M. J. McElrath. Antagonism of vaccine-induced HIV-1-specific CD4+ T cells by primary HIV-1 infection: potential mechanism of vaccine failure. *J Immunol* **158**:807–15, 1997.

NOTE: (Medline: 97146051) A vaccinia-gp160 vaccinee made a strong CD4+ T cell responses, including proliferative and cytolytic responses, but was infected anyway. The infecting virus had an escape mutant that could also serve as an antagonist.

[Kent et al.(1997)] S. J. Kent, A. Woodward, & A. Zhao. Human immunodeficiency virus type 1 (HIV-1)-specific T cell responses correlate with control of acute HIV-1 infection in macaques. *J Infect Dis* **176**:1188–97, 1997.

NOTE: (Medline: 98022676).

[Kim et al.(1997a)] D. T Kim, D. J. Mitchell, D. G. Brockstedt, L. Fong, G. P. Nolan, C. G. Fathman, E. G. Engleman, & J. B. Rothbard. Introduction of soluble proteins into the MHC class I pathway by conjugation to an HIV tat peptide. *J Immunol* **159** (4):1666–1668, 1997a.

NOTE: (Medline: 97400332) A vaccine based on the conjugation of OVA to a HIV Tat peptide that enhances protein uptake by APC cells stimulated MHC Class I-restricted T cell response *in vitro* and CTL generation *in vivo* in a murine system.

[Kim et al.(1997b)] J. J. Kim, V. Ayayavoo, M. L. Bagarazzi, M. A. Chattergoon, K. Dang, B. Wang, J. D. Boyer, & D. B. Weiner. In vivo engineering of a

CTL References

cellular immune response by coadministration of IL-12 expression vector with a DNA immunogen. *J Immunol* **158**:816-26, 1997b.

NOTE: (Medline: 97146052).

[Kim et al.(1997)] J. J. Kim, M. L. Bagarazzi, N. Trivedi, Y. Hu, K. Kazahaya, D. M. Wilson, R. Ciccarelli, M. A. Chattergoon, K. Dang, S. Mahalingam, A. A. Chaltan, M. G. Agadjanyan, J. D. Boyer, B. Wang, & D. B. Weiner. Engineering of *in vivo* immune responses to DNA immunization via codelivery of costimulatory molecule genes. *Nat Biotechnol* **15**:641-6, 1997.

NOTE: (Medline: 97362802).

[Klein et al.(1996)] M. R. Klein, J. Veenstra, A. M. Holwerda, M. T. Roos, I. Gow, G. Patou, R. A. Coutinho, F. De Wolf, & F. Miedema. Gag-specific immune responses after immunization with p17/p24:Ty virus-like particles in HIV type 1-seropositive individuals. *AIDS Res Hum Retroviruses* **13**:393-9, 1996.

NOTE: (Medline: 97229917).

[Klenerman et al.(1996)] P. Klenerman, G. Luzzi, K. McHytire, R. Phillips, & A. McMichael. Identification of a novel HLA-A25 restricted epitope in a conserved region of p24 gag (positions 71-80). *AIDS* **10**:348-350, 1996.

NOTE: (Medline: 97037037).

[Klenerman et al.(1995)] P. Klenerman, U.-C. Meier, R. E. Phillips, & A. J. McMichael. The effects of natural altered peptide ligands on the whole blood cytotoxic T lymphocyte response to human immunodeficiency virus. *Eur. J. Immunol.* **25**:1927-1931, 1995.

NOTE: (Medline: 95347391). This paper explores naturally occurring altered peptide ligands and their ability to sustain CTL, serve as antagonists to CTL specific for other variants, and to allow cell killing. The authors propose that a CTL response may be sustained *in vivo* that fails to recognize viral variants as they arise, proposing a mechanism for T-cell original antigenic sin.

[Klenerman et al.(1994)] P. Klenerman, S. Rowland-Jones, S. McAdam, J. Edwards, S. Daenke, D. Laloo, B. Koppe, W. Rosenberg, D. Boyd, A. Edwards, P. Giangrande, R. E. Phillips, & A. J. McMichael. Cytotoxic T-cell activity antagonized by naturally occurring HIV-1 Gag variants. *Nature* **369**:403-407, 1994.

NOTE:(Medline: 94255016) This paper documents that naturally occurring peptide variants can serve as antagonists, that is they can inhibit normal analysis 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.

[Kmiecik et al.(1998)] D. Kmiecik, T. J. Wasik, H. Tepler, J. Pientka, S. H. Hsu, H. Takahashi, K. Okumura, Y. Kaneko, & D. Kozbor. The effect of deletion of the V3 loop of gp120 on cytotoxic T cell responses and HIV gp120-mediated pathogenesis. *J Immunol* **160**:5676-83, 1998.

NOTE: (Medline: 98266211).

[Koenig et al.(1995)] S. Koenig, A. J. Conley, Y. A. Brewah, G. M. Jones, S. Leath, L. J. Boots, V. D. V. G. Pantaleo, J. F. Demarest, & C. Carter. Transfer of HIV-1-specific cytotoxic T lymphocytes to an AIDS patient leads to selection for mutant HIV variants and subsequent disease progression. *Nat Med* **1**(4):330-6, 1995.

NOTE: (Medline: 96071442).

[Koenig et al.(1990)] S. Koenig, T. R. Fuerst, L. V. Wood, R. M. Woods, J. A. Suzich, G. M. Jones, V. F. de la Cruz, R. T. Davey Jr., S. Venkatesan, B. Moss, W. E. Biddison, & A. S. Fauci. Mapping the fine specificity of a cytotoxic T-cell response to HIV-1 Nef protein. *J Immunol* **145**:127-135, 1990.

NOTE: (Medline: 90293448) A 10 residue peptide that triggers CTL in association with the HLA A3.1 molecule was studied. Human cell transfectants were used to map a critical residue in the HLA A3.1 molecule for recognition, amino acid 152, which is present on the alpha-2 helix in HLA-A3.1 and is modified in the HLA A3.2 A3 allele.

[Konya et al.(1997)] J. Konya, G. Stuber, A. Bjorndal, E. M. Fenyo, & J. Dillmer. Primary induction of human cytotoxic lymphocytes against a synthetic peptide of the human immunodeficiency virus type 1 protease. *J Gen Virol* **78**:2217-2224, 1997.

NOTE: (Medline: 97437476).

[Kundu et al.(1998)] S. K. Kundu, E. Engleman, C. Benike, M. H. Shapero, M. Dupuis, W. C. van Schooten, M. Eibl, & T. C. Merigan. A pilot clinical

CTL References

- trial of HIV antigen-pulsed allogeneic and autologous dendritic cell therapy in HIV-infected patients. *AIDS Res Hum Retroviruses* **14**:551–60, 1998.
- NOTE: (Medline: 98252383).
- [Kurane & West(1998)] I. Kurane & K. West. 1998.
- NOTE: Personal communication.
- [Lalvani et al.(1997)] A. Lalvani, T. Dong, G. Ogg, A. A. Patham, H. Newell, A. V. Hill, A. J. McMichael, & S. Rowland-Jones. Optimization of a peptide-based protocol employing IL-7 for in vitro restimulation of human cytotoxic T lymphocyte precursors. *J Immunol Methods* **210**:65–77, 1997.
- NOTE: (Medline: 98161691).
- [Lapham et al.(1996)] C. Lapham, B. Golding, J. Inman, R. Blackburn, J. M. Ischewitz, P. Highet, & H. Golding. *Brucella abortus* conjugated with a peptide derived from the V3 loop of human immunodeficiency virus (HIV) type 1 induces HIV-specific cytotoxic T-cell responses in normal and in CD4+ cell-depleted BALB/c mice. *J Virol*. **70**:3084–3092, 1996.
- NOTE: (Medline: 96186738).
- [Layton et al.(1993)] G. T. Layton, S. J. Harris, A. J. Gearing, M. Hill-Perkins, J. S. Cole, J. C. Griffiths, N. R. Burns, A. J. Kingsman, & S. E. Adams. Induction of HIV-specific cytotoxic T lymphocytes in vivo with hybrid HIV-1 V3:Ty-virus-like particles. *J Immunol* **151**:1097–1107, 1993.
- NOTE: (Medline: 95271010) V3-Ty-Virus-like particles can induce type specific CTL in mice in the absence of adjuvant.
- [Leggatt et al.(1997)] G. R. Leggatt, M. A. Alexander-Miller, A. Kumar, S. L. Hoffman, & J. A. Berzofsky. Cytotoxic T lymphocyte (CTL) adherence assay (CAA): a non-radioactive assay for murine CTL recognition of peptide-MHC class I complexes. *J Immunol Methods* **201**:1–10, 1997.
- NOTE: (Medline: 97184603) This paper describes a novel assay, the CTL adhesion assay (CAA), and uses an HIV epitope in a murine system as a model system. CAA is a rapid, simple screening method for identifying cytolytic epitopes for a given CTL line, and may also identify peptides that cause T cell activation and adherence but not cytolytic activity.
- [Legrand et al.(1997)] E. Legrand, I. Pellegrin, D. Neau, J. L. Pellegrin, J. M. Ragnaud, M. Dupon, B. Guillenain, & H. J. Fleury. Course of specific T lymphocyte cytotoxicity, plasma and cellular viral loads, and neutralizing antibody titers in 17 recently seroconverted HIV type 1-infected patients. *AIDS Res Hum Retroviruses* **13**:1383–94, 1997.
- NOTE: (Medline: 98022616).
- [Levin et al.(1997)] N. L. Letvin, D. C. Montefiori, Y. Yasutomi, H. C. Perry, M. E. Davies, C. Lekutis, M. Alroy, D. C. Freed, C. I. Lord, L. K. Handt, M. A. Liu, & J. W. Shiver. Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination. *Proc Natl Acad Sci USA* **94**:9378–83, 1997.
- NOTE: (Medline: 97404403).
- [Lieberman(1998)] J. Lieberman. . . *JCI* 1998.
- NOTE: Personal communication.
- [Lieberman et al.(1997)] J. Lieberman, J. A. Fabry, D. M. Fong, & G. R. Parkinson 3rd. Recognition of a small number of diverse epitopes dominates the cytotoxic T lymphocytes response to HIV type 1 in an infected individual. *AIDS Res Hum Retroviruses* **13**:383–92, 1997.
- NOTE: (Medline: 97229916).
- [Lieberman et al.(1992)] J. Lieberman, J. A. Fabry, M. Kuo, P. Earl, B. Moss, & P. R. Skolnik. Cytotoxic T lymphocytes from HIV-1 seropositive individuals recognize immunodominant epitopes in gp160 and reverse transcriptase. *J Immunol* **148**:2738–2747, 1992.
- NOTE: (Medline: 92242898) This paper does not use T-cell clones to map epitopes, but rather T-cell lines from HIV infected donors. 20 amino acid peptides were used of map the region of the reactive epitopes. HLA restriction was not tested for all epitopes.
- [Lieberman et al.(1995)] J. Lieberman, J. A. Fabry, P. Shankar, L. Beckett, & P. R. Skolnik. *In vivo* expansion of HIV type 1-specific cytolytic T cells from HIV type 1-seropositive subjects. *AIDS Res Hum Retroviruses* **11**:257–271, 1995.
- NOTE: (Medline: 95260535) Potent HIV-specific CTL lines were developed through culture of non-specific stimulation of T cell lines with autologous antigen presenting cells preincubated with HIV-1 peptides.

CTL References

- [Lieberman et al.(1997)] J. Lieberman, P. R. Skolnik, G. R. Parkerson 3rd, J. A. Fabry, B. Landry, J. Bethel, & J. Kagan. Safety of autologous, ex vivo-expanded human immunodeficiency virus (HIV)-specific cytotoxic T-lymphocyte infusion in HIV-infected patients. *Blood* **90**:2196–206, 1997.
- NOTE: (Medline: 97454395).
- [Littaua et al.(1991)] R. A. Littaua, M. B. A. Oldstone, A. Takeda, C. De-bouck, J. T. Wong, C. U. Tuazon, B. Moss, F. Kievis, & F. A. Ennis. An HLA-C-Restricted CD8+ cytotoxic T-Lymphocyte clone recognizes a highly conserved epitope on human immunodeficiency virus type 1 gag. *J Virol* **65**:4051–4056, 1991.
- NOTE: (Medline: 91303653) Fine mapping of gag p24 epitope with HLA-C restriction: QAIISPR, HLA, Cw3.
- [Lubaki et al.(1997)] N. M. Lubaki, S. C. Ray, B. Dhruba, T. C. Quinn, R. F. Siliciano, & R. C. Bollinger. Characterization of a polyclonal cytolytic T lymphocyte response to human immunodeficiency virus in persons without clinical progression. *J Infect Dis* **6**:1360–7, 1997.
- NOTE: (Medline: 97323979) Five individuals were studied who survived HIV infection in good health for over 5 years. A broad polyclonal response was found to multiple proteins.
- [Lubeck et al.(1997)] M. D. Lubeck, R. Natuk, M. Myagkikh, N. Kalyan, K. Aldrich, F. Sinangil, S. Alipanah, S. C. S. Murthy, P. K. Chanda, S. M. Nigida Jr., P. D. Markham, S. Zolla-Pazner, K. Steimer, M. Wade, M. S. Reitz Jr., L. O. Arthur, S. Mizutani, A. Davis, P. P. Hung, R. C. Gallo, J. Eichberg, & M. Robert-Guroff. Long-term protection of chimpanzees against high-dose HIV-1 challenge induced by immunization. *Nature Med* **3 No 6**:651–58, 1997.
- NOTE: (Medline: 97319589).
- [Luo et al.(1998)] L. Luo, Y. Li, J.-S. Chang, S. Y. Cho, T. Y. Kim, M. J. Choi, H. S. Cheong, H. J. Kim, H. J. Ahn, M. K. Min, B. H. Chun, S. M. Jung, S. G. Woo, S. Y. Park, & C. Y. Kang. Induction of V3-specific cytotoxic T lymphocyte responses by HIV gag particles carrying multiple immunodominant V3 epitopes of gp120. *Virology* **240**:316–25, 1998.
- NOTE: (Medline: 98118457).
- [Macatonia et al.(1991)] S. E. Macatonia, S. Patterson, & S. C. Knight. Primary proliferative and cytotoxic T-cell responses to HIV induced in vitro by human dendritic cells. *Immunology* **74**(3):399–406, 1991.
- NOTE: (Medline: 92120708) A primary CTL response in cells from uninfected donors was detected by using a system where peptide was presented by human dendritic cells.
- [MacGregor et al.(1998)] R. R. MacGregor, J. D. Boyer, K. E. Ugen, K. E. Lacy, S. J. Gluckman, M. L. Bagarazzi, M. A. Chattergoon, Y. Baime , T. J. Higgins, R. B. Ciccarelli, L. R. Coney, R. S. Ginsberg, & D. B. Weiner. First human trial of a DNA-based vaccine for treatment of human immunodeficiency virus type 1 infection: safety and host response . *J Infect Dis* **178**:92–100, 1998.
- NOTE: (Medline: 98314535).
- [McAdam et al.(1998)] S. McAdam, P. Kaleebu, P. Krausa, P. Goulder, N. French, B. Collin, T. Blanchard, J. Whitworth, A. McMichael, & F. Gotch. Cross-clade recognition of p55 by cytotoxic T lymphocytes in HIV-1 infection. *AIDS* **12**:571–9, 1998.
- NOTE: (Medline: 98242898).
- [McAdam et al.(1995)] S. McAdam, P. Klennerman, L. Tussey, S. Rowland-Jones, D. Laloo, R. Phillips, A. Edwards, P. Giangrande, A. L. Brown, & F. Gotch. Immunogenic HIV variant peptides that bind to HLA-B8 can fail to stimulate cytotoxic T lymphocyte responses. *J Immunol* **155**:2729–36, 1995.
- NOTE: (Medline: 95378698).
- [McMichael & O'Callaghan(1998)] A. J. McMichael & C. A. O'Callaghan. A New Look at T Cells. *J Exp Med* **187**(9):1367–1371, 1998.
- NOTE: (Medline: 98234418) Review.
- [McMichael & Walker(1994)] A. J. McMichael & B. D. Walker. Cytotoxic T lymphocytes epitopes: implications for HIV vaccine. *AIDS* **8S**:S155–S173, 1994.
- NOTE: (Medline: no entry) Comprehensive review summarizing CTL epitopes that have known HLA type and are fine mapped to indicate epitope boundaries. Anchor residues are indicated when known for different HLA

CTL References

restricted epitopes. Includes a summary of the published literature, as well as much work that was in press or submitted for publication.

[Meter et al.(1995)] U. Meier, P. Klennerman, P. Griffin, W. James, B. Koppe, B. Larder, R. E. Phillips, A. J. McMichael, & R. E. Phillips. Cytotoxic T lymphocyte lysis inhibited by viable HIV mutants. *Science* **270**:1360-1362, 1995.

NOTE: (Medline: 96085065) HIV bearing mutations in epitope allowed transactive inhibition of specific CTL mediated lysis. Therefore, mutations in epitopes may not only allow escape from specific CTL, but enhance the ability of wildtype virus to persist.

[Meyerhans et al.(1991)] A. Meyerhans, G. Dadaglio, J. P. Vartanian, P. Langlade-Demoyen, R. Frank, B. Asjo, F. Plata, & S. Wain-Hobson. *In vivo* persistence of an HIV-1-encoded HLA-B27-restricted cytotoxic T lymphocyte epitope despite specific *in vitro* reactivity. *Eur J Immunol* **21**:2637-2640, 1991.

NOTE: (Medline: 92008181) This study looked for the presence of CTL escape mutants *in vivo* in proviral DNA from an infected individual who had CTL activity; in 8 and 14 months escape mutants had not accumulated.

[Moss et al.(1995)] P. A. H. Moss, S. L. Rowland-Jones, P. M. Frodsham, S. McAdam, P. Giangrande, A. McMichael, & J. I. Bell. Persistent high frequency of human immunodeficiency virus-specific cytotoxic T cells in peripheral blood of infected donors. *Proc Nat Acad Sci USA* **92**:5773-5777, 1995.

NOTE: (Medline: 95320157).

[Musey et al.(1997)] L. Musey, Y. Hu, L. Eckert, M. Christensen, T. Karchmer, & M. J. McElrath. HIV-1 induces cytotoxic T lymphocytes in the cervix of infected women. *J Exp Med* **185**:293-303, 1997.

NOTE: (Medline: 97169071) Mononuclear cells in cytobrush specimens from the cervical samples were stimulated with antigen. Eight women with CD4 positive counts $\geq 500 \text{ cells}/\mu\text{l}$ had HIV-1 specific CTL, but only 4/11 with counts $< 500 \text{ cells}/\mu\text{l}$ had HIV-1 specific CTL responses.

[Nakamura et al.(1997)] Y. Nakamura, M. Kameoka, M. Tobiume, M. Kaya, K. Ohki, T. Yamada, & K. Ikuta. A chain section containing epitopes for cytotoxic T, B and helper T cells within a highly conserved region found in

the human immunodeficiency virus type 1 gag protein. *Vaccine* **5**:489-96, 1997.

NOTE: (Medline: 97304244).

[Nehete et al.(1995)] P. N. Nehete, K. S. Casement, R. B. Arlinghus, & K. J. Sastry. Studies on *in vivo* induction of HIV-1 Envelope-specific cytotoxic T lymphocytes by synthetic peptides from the V3 loop region of HIV-1 IIIB gp120. *Cellular Immunology* **160**:217-223, 1995.

NOTE: (Medline: 95236465).

[Newman et al.(1997)] M. J. Newman, J. Wu, B. H. Gardner, C. A. Anderson, C. R. Kensil, J. Recchia, R. T. Coughlin, & M. F. Powell. Induction of cross-reactive cytotoxic T-lymphocyte responses specific for HIV-1 gp120 using saponin adjuvant (QS-21) supplemented subunit vaccine formulations. *Vaccine* **15**:1001-1007, 1997.

NOTE: (Medline: 97405277).

[Nietfeld et al.(1995)] W. Nietfeld, M. Bauer, M. Fevrier, R. Maier, B. Holzwarth, R. Frank, B. Maier, Y. Riviere, & A. Meyerhans. Sequence constraints and recognition by CTL of an HLA-B27-restricted HIV-1 gag epitope. *J Immunol* **154**:2188-2197, 1995.

NOTE: (Medline: 95173425) Single point mutations were introduced into this epitope in the viral strain LAI, and the ability comparable peptides to sensitize target strains were tested. The change of anchor residue R 264 to (L or G), results in infectious virus, and corresponding peptide has reduced binding affinities for HLA-B27. The change of G 267 to K or E abrogated infectivity, and the peptide bound to HLA-B27, but did not serve as a target; thus nonrecognition of peptides derived from quasispecies analysis of a small region might not really be associated with an escape mutant, but rather a non-viable mutant.

[Nixon & McMichael(1991a)] D. Nixon & A. J. McMichael. Cytotoxic T-cell recognition of HIV proteins and peptides. *AIDS* **5**:1049-1059, 1991a.

NOTE: (Medline: 92029720).

[Nixon et al.(1988)] D. Nixon, A. Townsend, J. Elvin, C. Rizza, J. Gallaway, & A. McMichael. HIV-1 gag-specific cytotoxic T lymphocytes defined with recombinant vaccinia virus and synthetic peptides. *Nature* **336**:484-487, 1988.

CTL References

- NOTE: (Medline: 89057146) p24 KRWIILGLNLKIVRMY.
- [Nixon et al.(1990)] D. F. Nixon, S. Huet, J. Rothbard, M. Kienvy M. Delchambre, C. Thiria, C. R. Rizza, F. M. Gotch, & A. J. McMichael. An HIV-1 and HIV-2 cross-reactive cytotoxic T-cell epitope. *AIDS* **4**:841–845, 1990.
- NOTE: (Medline: 91069449) An HLA-B27 specific CTL clone from an HIV-1 infected individual that reacts with the Gag SF2 epitope KRWIILGLNLKIVRMY also cross-reacts with the HIV-2 ROD analog RRWIQIGLQLQKSVRMY. The CTL also reacts with HIV-1 ELI KR-WIIVGLNLKIVRMY and SIVnm142 RRWIQIGLQLQKSVRMY, but only at very high concentration of peptide with SIVk6w78 RRWIQIQLRLQKSVRMY. The binding of the SIVk6w78 peptide to HLA-B27 does not seem to be reduced, so the authors suggest that the reduced ability to stimulate is in this case due to T-cell receptor interaction.
- [Nixon & McMichael(1991b)] D. F. Nixon & A. J. McMichael. Cytotoxic T-cell recognition of HIV proteins and peptides. *AIDS* **5**:1049, 1991b.
- NOTE: (Medline: 92029720) p17: LRPGGKKYKLKHIV, HLA B8 and p24: VQANANPDCKTILKAL, HLA B8.
- [Nowak et al.(1995)] M. A. Nowak, R. M. May, R. E. Phillips, S. Rowland-Jones, D. G. Lalloo, S. McAdam, P. Klennerman, B. Koppe, K. Sigmund, C. R. M. Bangham, & A. J. McMichael. Antigenic oscillations and shifting immunodominance in HIV-1 infections. *Nature* **375**:606–611, 1995.
- NOTE: (Medline: 95312083) This paper presents longitudinal studies of epitope variation and corresponding CTL responses in two patients. A mathematical model was created to provide a framework to explain the observed shifts in epitope and CTLp frequencies. For discussion, see also: J. M. Coffin, *Nature* **375**:534–535 (1995).
- [Ogg et al.(1998a)] G. S. Ogg, T. Dong, P. Hansasuta, L. Dorrell, J. Clarke, R. Coker, G. Luzzi, C. Conlon, A. P. McMichael, & S. Rowland-Jones. Four novel cytotoxic T-lymphocyte epitopes in the highly conserved major homology region of HIV-1 Gag, restricted through B*4402, B*1801, A*2601, B*70. *AIDS* **12**:1561–3, 1998a.
- NOTE: (Medline: 98394568).
- [Ogg et al.(1998b)] G. S. Ogg, X. Jin, S. Bonhoeffer, P. R. Dunbar, M. A. Nowak, S. Monard, J. P. Segal, Y. Cao, S. L. Rowland-Jones, V. Cerundolo,
- A. Hurley, M. Markowitz, D. D. Ho, D. F. Nixon, & A. J. McMichael. Quantitation of HIV-1-specific cytotoxic T lymphocytes and plasma load of viral RNA. *Science* **279**:2103–6, 1998b.
- NOTE: (Medline: 98182444).
- [Okuda et al.(1997)] K. Okuda, K. O. Xin, T. Tsuji, H. Bukawa, S. Tanaka, W. C. Koff, K. Tani, K. Okuda, K. Honma, S. Kawamoto, K. Hamajima, & J. Fukushima. DNA vaccination followed by macromolecular multicomponent peptide vaccination against HIV-1 induces strong antigen-specific immunity. *Vaccine* **15**:1049–56, 1997.
- NOTE: (Medline: 97414189).
- [Pantaleo et al.(1997)] G. Pantaleo, H. Soudeyns, J. F. Demarest, M. Vaccarezza, C. Graziosi, S. Paolucci, M. B. Daucher, O. J. Cohen, F. Denis, W. E. Biddison, R. P. Sekaly, & A. S. Fauci. Accumulation of human immunodeficiency virus-specific cytotoxic T lymphocytes away from the predominant site of virus replication during primary infection. *Eur J Immunol* **27**:3166–73, 1997.
- NOTE: (Medline: 98124449).
- [Parker et al.(1994)] K. C. Parker, M. A. Bednarek, & J. E. Coligan. Scheme for ranking potential HLA-A2 binding peptides based on independent binding of individual peptide side-chains. *J Immunol* **152**, 1994.
- NOTE: (Medline: 94075819) The authors conclude that peptide amino acid side-chain binding to the HLA-A2 molecule is independent of the sequence of the peptide, and developed a table of coefficients that can be used to help predict peptide binding to HLA-A2.
- [Parker et al.(1992)] K. C. Parker, M. A. Bednarek, L. K. Hull, U. Utz, B. C. H. J. Zweerink, W. E. Biddison, & J. E. Coligan. Sequence motifs important for peptide binding to the human MHC class I molecule, HLA-A2. *J Immunol* **149**, 1992.
- NOTE: (Medline: 93056532).
- [Phillips et al.(1991)] R. E. Phillips, S. Rowland-Jones, D. F. Nixon, F. M. Gotch, J. P. Edwards, A. O. Ogunesi, J. G. Elvin, J. A. Rothbard, C. R. Bangham, C. R. Rizza, & A. J. McMichael. Human immunodeficiency virus genetic variation that can escape cytotoxic T-cell recognition. *Nature* **354**:453–459, 1991.

CTL References

- NOTE: (Medline: 92086044) Fluctuations in the specificity of cytotoxic T-cells for HIV were correlated with variability in proviral gag (DNA) epitope sequences.
- [Pinto et al.(1995)] L. A. Pinto, J. Sullivan, J. A. Berzofsky, M. Clerici, H. A. Kessler, A. L. Landay, & G. M. Shearer. Env-specific cytotoxic T lymphocyte responses in HIV seronegative health care workers occupationally exposed to HIV-contaminated body fluids. *J. Clin. Invest.* **96**:867-876, 1995.
- NOTE: (Medline: 95362849).
- [Pogue et al.(1995)] R. R. Pogue, J. Eron, J. A. Frelinger, & M. Matsui. Amino-terminal alteration of the HLA-A*0201-restricted human immunodeficiency virus pol peptide increases complex stability and in vitro immunogenicity. *Proc Natl Acad Sci USA* **92**:8166-8170, 1995.
- NOTE: (Medline: 95396758) In this mutational study a substitution of 476 I to Y did not increase affinity but did increase complex stability with HLA-A*0201. The altered peptide (Y) provided a greater stimulation of wildtype pol-specific CTL response relative to the wildtype peptide (I), in three different seropositive individuals.
- [Porgador et al.(1997)] A. Porgador, H. F. Stats, B. Faiole, E. Gilboa, & T. J. Parker. 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.
- NOTE: (Medline: 97146054).
- [Price et al.(1997)] D. A. Price, P. J. Goulder, P. Klennerman, 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.
- NOTE: (Medline: 97203157).
- [Price et al.(1995)] P. Price, R. P. Johnson, D. T. Scadden, C. Jassoy, T. Rosenthal, S. Kalams, & B. D. Walker. Cytotoxic CD8+ T lymphocytes reactive with human immunodeficiency virus-1 produce granulocyte/macrophage colony-stimulating factor and variable amounts of interleukins 2, 3, and 4 following stimulation with the cognate epitope. *Clinical Immunology and Immunopathology* **74**:100-106, 1995.
- NOTE: (Medline: 95087232) Cytokine 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.
- [Rammensee et al.(1995)] H.-G. Rammensee, T. Friede, & S. Stevanovic. Mhc ligands and peptide motifs: first listing. *Immunogenetics* **41**:178-228, 1995.
- NOTE: (Medline: 95197186).
- [Rammensee, Personal communication.(1997)] H.-G. Rammensee, Personal communication. MHC ligands and peptide motifs: second listing . *in press* 1997.
- [Ray et al.(1998)] S. C. Ray, N. Lubaki, B. R. Dhruva, R. F. Siliciano, & R. C. Bollinger. Autologous strain-specific cytolytic T lymphocyte responses directed against human immunodeficiency virus type 1 Env. *AIDS Res Hum Retroviruses* **14**:3-13, 1998.
- NOTE: (Medline: 98113991).
- [Reid et al.(1996)] S. Reid, S. McAdam, K. Smith, P. Klennerman, C. O'Callaghan, K. Harlos, B. Jakobsen, A. McMichael, J. Bell, D. Stuart, & E. Jones. Antagonist HIV-1 gag peptides induce structural changes in HLA B8. *J Exp Med* **184**:2279-2286, 1996.
- NOTE: (Medline: 97130420).
- [Robertson et al.(1993)] M. N. Robertson, F. Buseyne, O. Schwartz, & Y. Riviere. Efficient antigen presentation to cytotoxic T lymphocytes by cells transduced with a retroviral vector expressing the HIV-1 Nef protein. *AIDS Res and Hum Retroviruses* **9**:1217-1223, 1993.
- NOTE: (Medline: 94190626) This paper presents a retroviral vector system for antigen presentation to CTLs. As part of the controls to test their system, they study the response to specific Nef peptides, which contain the dominant CTL epitopes in Nef in their study subject.
- [Rowland-Jones(1995)] S. Rowland-Jones. 1995.
- NOTE: Personal communication.

CTL References

- [Rowland-Jones et al.(1998)] S. Rowland-Jones, T. Dong, P. Krausa, J. Sutton, H. Newell, K. Ariyoshi, F. Gotch, S. Sabally, T. Corrah, J. Kimani, K. Mac-Donald, F. Plummer, J. Ndinya-Achola, H. Whittle, & A. McMichael. The role of cytotoxic T-cells in HIV infection. *Dev Biol Stand* **92**:209–14, 1998.
- NOTE: (Medline: 98214896) 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.
- [Rowland-Jones et al.(1997)] S. Rowland-Jones, R. Tan, & A. McMichael. Role of cellular immunity in protection against HIV infection. In *Adv Immunol*, volume 65, pages 277–346. Academic Press, 1997.
- NOTE: Review (Medline: 97381156) An comprehensive, excellent review of CTL immunity.
- [Rowland-Jones et al.(1993a)] S. L. Rowland-Jones, D. F. Nixon, M. C. Aldous, 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.
- NOTE: (Medline: 93218363).
- [Rowland-Jones et al.(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.
- NOTE: (Medline: 93345604) Individual fails to present HLA-B8-restricted influenza epitope, but can present an HLA-B8-restricted HIV-1 gag epitope.
- [Rowland-Jones et al.(1995)] S. L. Rowland-Jones, J. Sutton, K. Ariyoshi, T. Dong, 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.
- [Safrit et al.(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.
- NOTE: (Medline: 94125027) 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 RLRLDLL-LIVTR, 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 VLSIVNVRQGYSPLSFQTH. Autologous viral sequences from seroconversion were recognized by the CTL clones, but not the HIV-1 strain MN.
- [Safrit et al.(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.
- NOTE: (Medline: 95015873) 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, RPNNNTIRKSI, 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.
- [Sastry et al.(1992)] K. J. Sastry, P. N. Nehete, S. Venkatnarayanan, J. Morkowski, C. D. Platoucas, & R. B. Arlinghaus. Rapid in vivo induction of HIV-specific CD8+ cytotoxic T lymphocytes by a 15-amino acid

CTL References

- unmodified free peptide from the immunodominant V3-loop of gp120. *Virology* **188**:502–509, 1992.
- NOTE: (Medline: 92263753).
- [Selby et al.(1997)] M. J. Selby, B. Doe, & C. M. Walker. Virus-specific cytotoxic T-lymphocyte activity elicited by coinmunization with human immunodeficiency virus type 1 genes regulated by the bacteriophage T7 promoter and T7 RNA polymerase protein. *J Virol* **71**:7827–7831, 1997.
- NOTE: (Medline: 97456556).
- [Sewell et al.(1997)] A. K. Sewell, G. C. Harcourt, P. J. Goulder, D. A. Price, & R. E. Phillips. Antagonism of cytotoxic T lymphocyte-mediated lysis by natural HIV-1 altered peptide ligands requires simultaneous presentation of agonist and antagonist peptides. *Eur J Immunol* **27**:2323–9, 1997.
- NOTE: (Medline: 98000983).
- [Shankar et al.(1996)] P. Shankar, J. A. Fabry, D. M. Fong, & J. Lieberman. Three regions of HIV-1 gp160 contain clusters of immunodominant CTL epitopes. *Immunol Lett* **52**:23–30, 1996.
- NOTE: (Medline: 97031490).
- [Shiga et al.(1996)] H. Shiga, T. Shioda, H. Tomiyama, Y. Takamiya, S. Oka, S. Kimura, Y. Yamaguchi, T. Gjojoubori, H. G. Ramnath, K. Miwa, & M. Takiguchi. Identification of multiple HIV-1 cytotoxic T-cell epitopes presented by human leukocyte antigen B35 molecule. *AIDS* **10**:1075–1083, 1996.
- NOTE: (Medline: 97028610).
- [Shirai et al.(1997)] M. Shirai, S. Kozlowski, D. H. Margulies, & J. A. Berzofsky. Degenerate MHC restriction reveals the contribution of class I MHC molecules in determining the fine specificity of CTL recognition of an immunodominant determinant of HIV-1 gp160 V3 loop. *J Immunol* **158**:3181–8, 1997.
- NOTE: (Medline: 97240759).
- [Shirai et al.(1996)] M. Shirai, K. Kurokohchi, C. D. Pendleton, T. Arichi, L. F. Boyd, H. Takahashi, D. H. Margulies, & J. A. Berzofsky. Reciprocal cytotoxic T lymphocytes cross-reactivity interactions between two major epitopes within HIV-1 gp160. *J Immunol* **157**:4399–4411, 1996.
- NOTE: (Medline: 9613245).
- [Shirai et al.(1992)] M. Shirai, C. D. Pendleton, & J. A. Berzofsky. Broad recognition of cytotoxic T cell epitopes from the HIV-1 envelope protein with multiple class I histocompatibility molecules. *J Immunol* **148**:1657–1667, 1992.
- NOTE: (Medline: 92176620) This paper explored the possibility that defined epitopes from HIV-1 Env might be presented by multiple class I genes to CTLs using a murine system, isolating CTL from mice immunized with gp160 expressing recombinant vaccinia virus. The CTL epitope at the tip of the V3 loop (P18) was found to be presented by class I MHC molecules from four of ten haplotypes tested. Peptides that had previously been defined as helper T cell determinants (T1 in gp120, and HP53 (also called TH4.3)) were also able to stimulate CTL from mice with multiple haplotypes.
- [Shirai et al.(1993)] M. Shirai, M. S. Vacchio, R. J. Hodges, & J. A. Berzofsky. Preferential V beta usage by cytotoxic T cells cross-reactive between two epitopes of HIV-1 gp160 and degenerate in class I MHC restriction. *J Immunol* **151**:2283–2295, 1993.
- NOTE: (Medline: 93346775).
- [Shiver et al.(1997)] J. W. Shiver, M. E. Davies, Y. Yasutomi, H. C. Perry, D. C. Freed, N. L. Letvin, & M. A. Liu. Anti-HIV env immunities elicited by nucleic acid vaccines. *Vaccine* **15**:884–7, 1997.
- NOTE: (Medline: 97378942).
- [Siliciano et al.(1988)] R. Siliciano, T. Lawton, C. Knall, R. Karr, P. Berman, T. Gregory, & E. Reinherz. Analysis of host-virus interactions in AIDS with anti-gp120 T-cell clones: Effect of HIV sequence variation and a mechanism for CD4+ cell depletion. *Cell* **54**:561–575, 1988.
- NOTE: (Medline: 88295131) This article demonstrated that a class II HLA-DR4 restricted response can be stimulated by CD4 uptake of gp120, suggesting a mechanism for T-cell depletion in vivo. This peptide containing the epitope was also able to stimulate a class I restricted, CD8+ CTL response.
- [Sipsas et al.(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.

CTL References

[Smith et al.(1996)] K. J. Smith, S. W. Reid, D. I. Stuart, A. J. McMichael, E. Y. Jones, & J. I. Bell. An altered position of the alpha 2 helix of MHC class I is revealed by the crystal structure of HLA-B*3501. *Immunity* **4**:203-213, 1996.

NOTE: (Medline: 96209671) The crystal structure of HLA-B*3501 complexed with Nef epitope VPLRPMTY was determined at 2 angstrom resolution, revealing details about binding such as the structural basis for the tyrosine specificity of the F pocket.

[Soudeyns & Pantaleo(1997)] H. Soudeyns & G. Pantaleo. New mechanisms of viral persistence in primary human immunodeficiency virus (HIV) infection. *J Biol Regul Homeost Agents* **11**:37-9, 1997.

NOTE: (Medline: 98079354) Review.

[Steinle et al.(1996)] A. Steinle, K. Flak, O. Rötzschke, V. Gnau, S. Stevanovic, G. Jung, D. J. Schedel, & H. G. Rammensee. Motif of HLA-B*3503 peptide ligands. *Immunogenetics* **43**:105-107, 1996.

NOTE: (Medline: 96128264).

[Stuhler & Schlossman(1997)] G. Stuhler & S. F. Schlossman. Antigen organization regulates cluster formation and induction of cytotoxic T lymphocytes by helper T cell subsets. *Proc Natl Acad Sci USA* **94**:622-627, 1997.

NOTE: (Medline: 97165072) Generation of cytolytic activity requires a three-cell type cluster consisting of APC's, Helper, and CTL's, and co-expression of helper and CTL epitopes on the same APC.

[Sutton et al.(1993)] J. Sutton, S. Rowland-Jones, W. Rosenberg, D. Nixon, F. Gotch, X. Gao, N. Murray, A. Spoonas, P. Driscoll, M. Smith, A. Willis, & A. McMichael. A sequence pattern for peptides presented to cytotoxic T lymphocytes by HLA B8 revealed by analysis of epitopes and eluted peptides. *Eur J Immunol* **23**:447-453, 1993.

NOTE: (Medline: 93170395).

[Takahashi et al.(1988)] H. Takahashi, J. Cohen, A. Hosmalin, K. B. Cease, R. Houghten, J. L. Cornette, C. DeLisi, B. Moss, R. N. Germain, & J. A. Berzofsky. An immunodominant epitope of the human immunodeficiency virus envelope glycoprotein gp160 recognized by class I major histocompatibility complex molecule-restricted murine cytotoxic T lymphocytes. *Proc Natl Acad Sci USA* **85**:3105-3109, 1988.

NOTE: (Medline: 88203649) Mice were infected with a recombinant vaccinia virus expressing the HIV gp160 envelope gene, and the primed lymphocytes were restimulated *in vitro* with a transfected histocompatible cell line expressing the same gene. H-2^d mice respond predominantly to a single immunodominant site represented by a 15-residue synthetic peptide.

[Takahashi et al.(1989a)] H. Takahashi, R. Houghten, S. D. Putney, D. H. Margulies, B. Moss, R. N. Germain, & J. A. Berzofsky. Structural requirements for class I MHC molecule-mediated antigen presentation and cytotoxic T-cell recognition of an immunodominant determinant of the human immunodeficiency virus envelope protein. *J Exp Med* **170**:2023-2035, 1989a.

NOTE: (Medline: 90063467) Murine BALBc CTL Class I D^d cells elicited by HIV-1 IIB peptide: RIQRGPGRAFVTIGK.

[Takahashi et al.(1989b)] H. Takahashi, S. Merri, S. D. Putney, R. Houghten, B. Moss, R. N. Germain, & J. A. Berzofsky. A single amino acid interchange yields reciprocal CTL specificities for HIV-1 gp160. *Science* **246**:118-121, 1989b.

NOTE: (Medline: 89388278) Murine BALBc CTL Class I D^d epitope elicited by HIV-1 IIB and MN gp160 vaccinia construct, stimulated with peptides: RIQRGPGRAFVTIGK, IIB and RIHQGPGRAFYTTKN, MN. These two peptides were non-cross reactive. Val/Tyr exchange was sufficient to interchange the specificities of the two peptides.

[Takahashi et al.(1996)] H. Takahashi, Y. Nakagawa, G. R. Leggatt, Y. Ishida, T. Saito, K. Yokomuro, & J. A. Berzofsky. Inactivation of human immunodeficiency virus (HIV-1) envelope-specific CD8⁺ cytotoxic T lymphocytes by free antigenic peptide: a self-veto mechanism?. *J Exp Med* **183**:879-889, 1996.

NOTE: (Medline: 96228309).

[Takahashi et al.(1992)] H. Takahashi, Y. Nakagawa, C. D. Pendleton, R. Houghten, K. Yokomuro, R. N. Germain, & J. A. Berzofsky. Induction

CTL References

of broadly cross-reactive cytotoxic T-cells recognizing and HIV-1 envelope determinant. *Science* **255**:333–336, 1992.

NOTE: (Medline: 92196580) Murine BALBc CTL Class I epitope elicited by HIV-1 RF, IIIB and MN gp160 vaccinia construct, stimulated with peptides: SITKGPGRVIVYATGQ, RF; RIQRGPGRAFVIGK, IIIB; and RIGPGRAFYITKN, MN.

[Takahashi et al.(1993)] H. Takahashi, Y. Nakagawa, K. Yokomuro, & J. A. Berzofsky. Induction of CD8+ cytotoxic T lymphocytes by immunization with syngeneic irradiated HIV-1 envelope derived peptide-pulsed dendritic cells. *Internat Immunol* **5**:849–857, 1993.

NOTE: (Medline: 94001802).

[Takahashi et al.(1991)] K. Takahashi, L. Dai, T. R. Fuerst, W. E. Biddison, P. L. Earl, B. Moss, & F. A. Ennis. Specific lysis of human immunodeficiency virus type 1-infected cells by a HLA-A3.1-restricted CD8+ cytotoxic T-lymphocyte clone that recognizes a conserved peptide sequence within the gp41 subunit of the envelope protein. *Proc Natl Acad Sci USA* **88**:10277–10281, 1991.

NOTE: (Medline: 92052253) gp41 epitope: RLRLDLLLIVTR, HLA A3.1 (NL43). Synthetic peptides of RF and CDC4 were recognized by CTL clone despite non-conservative Thr to (Val or Ala) change, but an MN peptide with four natural substitutions was not recognized.

[Takeshita et al.(1995)] T. Takeshita, H. Takahashi, S. Kozlowski, J. D. Ahlers, C. D. Pendleton, R. L. Moore, Y. Nakagawa, K. Yokomuro, B. S. Fox, D. H. Margulies, & J. A. Berzofsky. Molecular analysis of the same HIV peptide functionally binding to both a class I and a class II MHC molecule. *J Immunol* **154**:1973–1986, 1995.

NOTE: (Medline: 95138543) Of RGPGRAFVII, the upper case amino acids iGPgRaFvII are critical for binding, consistent with H-2D d motif XGPX(RKH)XXX(X)(LIF). Stimulation of the HLA class II I-A d required a longer peptide, IQRGPGRAFVII or RIQRGPGRAFVII, and rIqrGP-gRaFvII were essential for binding to the Class II molecule.

[Threlkeld et al.(1997)] S. C. Threlkeld, P. A. Wentworth, S. A. Kalams, B. M. Wilkes, D. J. Ruhl, E. Kepph, J. Sidney, S. Southwood, B. D. Walker, & A. Sette. Degenerate and promiscuous recognition by CTL of peptides

presented by the MHC class IA3-like superfamily. *J Immunol* **159** (4):1648–1657, 1997.

NOTE: (Medline: 97400330) Similarities in peptide binding across A3-like superfamily results in similar peptide-MHC complex structures engaged by T-cell receptors.

[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.

NOTE: (Medline: 97217373).

[Tomiyama et al.(1997)] H. Tomiyama, K. Miwa, H. Shiga, Y. I. Moore, S. Oka, A. Iwamoto, Y. Kaneko, & M. Takiguchi. Evidence of presentation of multiple HIV-1 cytotoxic T lymphocyte epitopes by HLA-B*3501 molecules that are associated with the accelerated progression of AIDS. *J Immunol* **158**:5026–34, 1997.

NOTE: (Medline: 97289618).

[Trickett et al.(1998)] A. E. Trickett, M. Kelly, B. A. Cameron, A. Lloyd, R. A. French, & J. M. Dwyer. A preliminary study to determine the effect of an infusion of cryopreserved autologous lymphocytes on immunocompetence and viral load in HIV-infected patients. *J Acquir Immune Defic Syndr Hum Retrovir* **17**:129–36, 1998.

NOTE: (Medline: 98132355).

[Tsomides et al.(1994)] T. J. Tsomides, A. Aldovini, R. P. Johnson, B. D. Walker, R. A. Young, & H. N. Eisen. Naturally processed viral peptides recognized by cytotoxic T lymphocytes on cells chronically infected by human immunodeficiency virus type 1. *J Exp Med* **180**:1283–1293, 1994.

NOTE: (Medline: 95016420) Naturally processed peptides can be purified from trifluoroacetic acid lysates of HIV-1 infected cells. A gag and RT epitope were compared; both synthetic peptides are optimally active in CTL assays. The naturally processed gag peptide was more abundant than the RT peptide in HIV-1 infected HLA-A2 positive cells, and the gag specific CTL more effective, suggesting surface density of peptides may influence efficiency of CTL killing.

CTL References

- [Tsonides et al.(1991)] T. J. Tsonides, B. D. Walker, & H. N. Eisen. An optimal viral peptide recognized by CD8+ T-cells binds very tightly to the restricting class I major histocompatibility complex protein on intact cells but not to the purified class I protein. *Proc Natl Acad Sci USA* **88**:11276–11280, 1991.
- NOTE: (Medline: 92107932).
- [van Baalen et al.(1993)] C. A. van Baalen, M. R. Klein, A. M. Geretti, R. I. P. M. Keet, F. Miedema, C. A. C. M. van Els, & A. D. M. E. Osterhaus. Selective *in vitro* expansion of HLA class I-restricted HIV-1 Gag-specific CD8+ T-cells: cytotoxic T-lymphocyte epitopes and precursor frequencies. *AIDS* **7**:781–786, 1993.
- NOTE: (Medline: 93371704) Gag specific epitopes and precursor frequencies were studied in seven individuals; for CTLs from one individual, fine mapping was done using peptides. PFA-fixed rVV-Gag-infected B-LCL cells were used as stimulator cells of bulk PBMC cultures to determine precursor frequencies and identify epitopes.
- [van Baalen et al.(1996)] C. A. van Baalen, M. R. Klein, R. C. Huisman, M. E. Dinges, S. R. Kerkhof Garde, A. M. Geretti, R. Gruters, C. A. van Els, F. Miedema, & A. D. Osterhaus. Fine-specificity of cytotoxic T-lymphocytes which recognize conserved epitopes of the gag protein of human immunodeficiency virus type 1. *J Gen Virol* **77**:1659–1665, 1996.
- NOTE: (Medline: 96332502).
- [van Baalen et al.(1997)] C. A. van Baalen, O. Pontesilli, R. C. Huisman, A. M. Geretti, M. R. Klein, F. de Wolf, F. Miedema, R. A. Gruters, & A. D. M. E. Osterhaus. Human immunodeficiency virus type 1 Rev- and Tat-specific cytotoxic T-lymphocyte frequencies inversely correlate with rapid progression to AIDS. *J Gen Virol* **78**:1913–1918, 1997.
- NOTE: (Medline: 97410272) CTLp frequencies to Rev and Tat were inversely correlated with rapid progression to AIDS, but not Gag, RT or Nef. 3/7 long term non-progressors and 0/5 progressors were positive for HLA B57, so it was again found to be associated with long term survival.
- [van der Burg et al.(1997)] S. H. van der Burg, M. R. Klein, O. Pontesilli, A. M. Holwerda, J. Drijfhout, W. M. Kast, F. Miedema, & C. J. M. Melief. HIV-1 reverse transcriptase-specific CTL against conserved epitopes do not protect against progression to AIDS. *J Immunol* **159**:3648–3654, 1997.
- NOTE: (Medline: 97461484).
- [van der Burg et al.(1995)] S. H. van der Burg, M. R. Klein, C. J. Van de Velde, W. M. Kast, F. Miedema, & C. J. Melief. Induction of a primary human cytotoxic T lymphocyte response against a novel conserved epitope in a functional sequence of HIV-1 reverse transcriptase. *AIDS* **9**:121–127, 1995.
- NOTE: (Medline: 95234243).
- [van der Burg et al.(1996)] S. H. van der Burg, M. J. W. Visseren, R. M. P. Brandt, W. M. Kast, & C. J. M. Melief. Immunogenicity of peptides bound to MHC class I molecules depends on the MHC-peptide complex stability. *J Immunol* **156**:3308–3314, 1996.
- NOTE: (Medline: 96194537) Peptide-MHC dissociation rate is highly correlated with immunogenicity. In this study, HLA-A*0201 restricted epitopes from HPV, HBV and HIV were studied, some in the context of immunogenicity in peptide immunized HLA-A*0201/K^b transgenic mice.
- [Van der Ryst et al.(1998)] E. Van der Ryst, T Nakasone, A. Habel, A. Venet, E. Gomard, R. Altmeyer, M. Girard, & A. M. Bornman. Study of the immunogenicity of different recombinant Mengo viruses expressing HIV1 and SV40 epitopes. *Res Virol* **149**:5–20, 1998.
- NOTE: (Medline: 98222345) Mengo virus did not prove to be a good background for eliciting a strong CTL response to HIV or SV40 protein fragments, in Rhesus macaques or mice.
- [Wagner et al.(1998a)] L. Wagner, O. O. Yang, E. A. Zepeda, Y. Ge, S. A. Kalams, B. D. Walker, M. S. Pasternack, & A. D. Luster. Beta-chemokines are released from HIV-1-specific cytolytic T-cell granules complexed to proteoglycans. *Nature* **391**:908–11, 1998a.
- NOTE: (Medline: 98154733).
- [Wagner et al.(1998b)] R. Wagner, V. J. Teeuwsen, L. Deml, F. Notka, A. G. Haaksma, S. S. Jhaghjoorsingh, H. Niphuis, H. Wolf, & J. L. Heeney. Cytotoxic 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.
- NOTE: (Medline: 98277073) A VLP is a non-infectious virus like particle self-assembled from HIV Pr55 gag. Macaques were immunized with

CTL References

- 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 intravenous challenge with SHIV chimeric chal-lenge 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.
- [Walker et al.(1989)] B. D. Walker, C. Flexner, K. Birch-Limberger, L. Fisher, T. J. Paradis, A. Aldovini, R. Young, B. Moss, & R. T. Schooley. Long-term culture and fine specificity of human cytotoxic T-lymphocyte clones reactive with human immunodeficiency virus type 1. *Proc Natl Acad Sci USA* **86**:9514–9518, 1989.
- NOTE: (Medline: 90083298) Seven HIV-1 reverse transcriptase-specific cytotoxic T-lymphocyte (CTL) clones from the peripheral blood of two seropositive subjects were generated. Five different HLA restricted CTL epitopes were identified by peptide mapping.
- [Walter et al (1997)] J. B. Walter, C. Brander, M. Mammen, D. N. Garbozzi, S. A. Kalams, G. M. Whiteside, B. D. Walker, & H. N. Eisen. Stimulation of human cytotoxic T cells with hiv-1-derived peptides presented by recombinant HLA-A2 peptide complexes. *Int Immunol* **9**:451–9, 1997.
- NOTE: (Medline: 97244174) HLA-A2 heavy chain and beta 2-microglobulin refolded in the presence of peptides became susceptible to lysis by HLA-A2-restricted cytotoxic T lymphocyte (CTL) clones specific for the peptides. Recombinant HLA-A2 peptide complexes covalently immobilized on microspheres stimulated the development of HLA-A2 peptide-specific CTL.
- [Wilson et al.(1997)] C. C. Wilson, S. A. Kalams, B. M. Wilkes, D. J. Ruhl, F. Gao, B. H. Hahn, I. C. Hanson, K. Luzuriaga, S. Wolinsky, R. Koup, S. P. Buchbinder, R. P. Johnson, & B. D. Walker. Overlapping epitopes in human immunodeficiency virus type 1 gp120 presented by HLA A, B, and C molecules: effects of viral variation on cytotoxic T-lymphocyte recognition. *J Virol* **71**:1256–64, 1997.
- NOTE: (Medline: 97151113) CTL clones were isolated from four individuals that interact with the same 25 amino-acid peptide using three different HLA presenting molecules.
- [Wilson et al.(1998)] J. D. Wilson, G. S. Ogg, R. L. Allen, P. J. Goulder, A. Kelleher, A. K. Sewell, C. A. O'Callaghan, S. L. Rowland-Jones, M. F. Callan, & A. J. McMichael. Oligoclonal expansions of CD8(+) T cells in chronic HIV infection are antigen specific. *J Exp Med* **188**(4):785–90, 1998.
- NOTE: (Medline: 98372770).
- [Wolinsky et al.(1996)] S. M. Wolinsky, B. T. M. Korber, A. U. Neumann, M. Daniels, K. J. Kuntzman, A. J. Whetsell, M. R. Furtado, Y. Chao, D. D. Ho, J. T. Safrit, & R. A. Koup. Adaptive evolution of human immunodeficiency virus-type 1 during the natural course of infection. *Science* **272**:537–542, 1996.
- NOTE: (Medline: 96194668) In a longitudinal study of six patients, epitope variation occurred only when there was a notable CTLp frequency and the individual had the appropriate HLA type.
- [Yang et al.(1996)] O. O. Yang, S. A. Kalams, M. Rosenzweig, A. Trocha, N. Jones, M. Koziel, B. D. Walker, & R. P. Johnson. Efficient Lysis of Human Immunodeficiency Virus Type 1-infected cells by cytotoxic T lymphocytes. *J Virol* **70**:5799–5806, 1996.
- NOTE: (Medline: 96323090).
- [Yang et al.(1997)] O. O. Yang, S. A. Kalams, A. Trocha, H. Cao, A. Luster, R. P. Johnson, & B. D. Walker. Suppression of human immunodeficiency virus type 1 replication by CD8+ cells: evidence for HLA class I-restricted triggering of cytolytic and noncytolytic mechanisms. *J Virol* **71**:3120–8, 1997.
- NOTE: (Medline: 97213986).
- [Yang et al.(1997)] O. O. Yang, A. C. Tran, S. A. Kalams, R. P. Johnson, M. R. Roberts, & B. D. Walker. Lysis of HIV-1-infected cells and inhibition of viral replication by universal receptor T cells. *Proc Natl Acad Sci USA* **94**:11478–83, 1997.
- NOTE: (Medline: 97470992).

CTL References

[Zerhouni et al.(1997)] B. Zerhouni, K. Sanhadji, & J. L. Touraine. Loss of T-cell cytotoxic responses in the course of HIV-1 infection. *Thymus* **24**:203-19, 1997.

NOTE: (Medline: 98154335).

[Zhang et al.(1993)] Q. Zhang, R. Gavioli, G. Klein, & M. G. Masucci. An HLA-A11-specific motif in nonamer peptides derived from viral and cellular proteins. *Proc Natl Acad Sci USA* **90**:2217-2221, 1993.

NOTE: (Medline: 93211933).