

REFERENCES

- 1.Cannon MJ, Stott EJ, Taylor G, Askonas BA. Clearance of persistent respiratory syncytial virus infections in immunodeficient mice following transfer of primed T cells. *Immunology* 1987;62:133-8.
- 2.Klavinskis LS, Whitton JL, Joly E, Oldstone MB. Vaccination and protection from a lethal viral infection: identification, incorporation, and use of a cytotoxic T lymphocyte glycoprotein epitope. *Virology* 1990;178:393-400.
- 3.Walter EA, Greenberg PD, Gilbert MJ, Finch RJ, Watanabe KS, Thomas ED, et al. Reconstitution of cellular immunity against cytomegalovirus in recipients of allogeneic bone marrow by transfer of T-cell clones from the donor. *N Engl J Med* 1995;333:1038-44.
- 4.Borrow P, Lewicki H, Hahn BH, Shaw GM, Oldstone MB. Virus-specific CD8+ cytotoxic T-lymphocyte activity associated with control of viremia in primary human immunodeficiency virus type 1 infection. *J Virol* 1994;68:6103-10.
- 5.Koup RA, Safrit JT, Cao Y, Andrews CA, McLeod G, Borkowsky W, et al. Temporal association of cellular immune responses with the initial control of viremia in primary human immunodeficiency virus type 1 syndrome. *J Virol* 1994;68:4650-5.

- 6.Ogg GS, Jin X, Bonhoeffer S, Dunbar PR, Nowak MA, Monard S, et al. Quantitation of HIV-1-specific cytotoxic T lymphocytes and plasma load of viral RNA. *Science* 1998;279:2103-6.
- 7.Moss PA, Rowland-Jones SL, Frodsham PM, McAdam S, Giangrande P, McMichael AJ, et al. Persistent high frequency of human immunodeficiency virus-specific cytotoxic T cells in peripheral blood of infected donors. *Proc Natl Acad Sci U S A* 1995;92:5773-7.
- 8.Harrer E, Harrer T, Buchbinder S, Mann DL, Feinberg M, Yilma T, et al. HIV-1-specific cytotoxic T lymphocyte response in healthy, long-term nonprogressing seropositive persons. *AIDS Res Hum Retroviruses* 1994;10 Suppl 2:S77-8.
- 9.Ferbas J, Kaplan AH, Hausner MA, Hultin LE, Matud JL, Liu Z, et al. Virus burden in long-term survivors of human immunodeficiency virus (HIV) infection is a determinant of anti-HIV CD8+ lymphocyte activity. *J Infect Dis* 1995;172:329-39.
- 10.Harrer T, Harrer E, Kalams SA, Elbeik T, Staprans SI, Feinberg MB, et al. Strong cytotoxic T cell and weak neutralizing antibody responses in a subset of persons with stable nonprogressing HIV type 1 infection. *AIDS Res Hum Retroviruses* 1996;12:585-92.

- 11.Klein MR, van Baalen CA, Holwerda AM, Kerkhof Garde SR, Bende RJ, Keet IP, et al. Kinetics of Gag-specific cytotoxic T lymphocyte responses during the clinical course of HIV-1 infection: a longitudinal analysis of rapid progressors and long-term asymptomatics. *J Exp Med* 1995;181:1365-72.
- 12.Goulder PJ, Phillips RE, Colbert RA, McAdam S, Ogg G, Nowak MA, et al. Late escape from an immunodominant cytotoxic T-lymphocyte response associated with progression to AIDS. *Nat Med* 1997;3:212-7.
- 13.Rinaldo C, Huang XL, Fan ZF, Ding M, Beltz L, Logar A, et al. High levels of anti-human immunodeficiency virus type 1 (HIV-1) memory cytotoxic T-lymphocyte activity and low viral load are associated with lack of disease in HIV-1-infected long-term nonprogressors. *J Virol* 1995;69:5838-42.
- 14.Rowland-Jones SL, Nixon DF, Aldhous MC, Gotch F, Ariyoshi K, Hallam N, et al. HIV-specific cytotoxic T-cell activity in an HIV-exposed but uninfected infant. *Lancet* 1993;341:860-1.
- 15.Bond KB, Sriwanthana B, Hodge TW, De Groot AS, Mastro TD, Young NL, et al. An HLA-directed molecular and bioinformatics approach identifies new HLA-A11 HIV-1 subtype E cytotoxic T lymphocyte epitopes in HIV-1-infected Thais. *AIDS Res Hum Retroviruses* 2001;17:703-17.

- 16.Threlkeld SC, Wentworth PA, Kalams SA, Wilkes BM, Ruhl DJ, Keogh E, et al. Degenerate and promiscuous recognition by CTL of peptides presented by the MHC class I A3-like superfamily: implications for vaccine development. *J Immunol* 1997;159:1648-57.
- 17.Connor R, Ho D, Kuritzkes D, Richman D. Human Immunodeficiency virus. In: Richman DD, Whitley RJ, Hayden FG, editors. *Clinical Virology*. New York: Churchill Livingstone Inc.; 1997. p. 707-716.
- 18.Siegal FP, Lopez C, Hammer GS, Brown AE, Kornfeld SJ, Gold J, et al. Severe acquired immunodeficiency in male homosexuals, manifested by chronic perianal ulcerative herpes simplex lesions. *N Engl J Med* 1981;305:1439-44.
- 19.Masur H, Michelis MA, Greene JB, Onorato I, Stouwe RA, Holzman RS, et al. An outbreak of community-acquired *Pneumocystis carinii* pneumonia: initial manifestation of cellular immune dysfunction. *N Engl J Med* 1981;305:1431-8.
- 20.Gottlieb MS, Schroff R, Schanker HM, Weisman JD, Fan PT, Wolf RA, et al. *Pneumocystis carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. *N Engl J Med* 1981;305:1425-31.

- 21.Barre-Sinoussi F, Chermann JC, Rey F, Nugeyre MT, Chamaret S, Gruest J, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 1983;220:868-71.
- 22.Henderson LE, Bowers MA, Sowder RC, 2nd, Serabyn SA, Johnson DG, Bess JW, Jr., et al. Gag proteins of the highly replicative MN strain of human immunodeficiency virus type 1: posttranslational modifications, proteolytic processings, and complete amino acid sequences. *J Virol* 1992;66:1856-65.
- 23.Gelderblom HR. Assembly and morphology of HIV: potential effect of structure on viral function. *Aids* 1991;5:617-37.
- 24.Bukrinsky MI, Haggerty S, Dempsey MP, Sharova N, Adzhubel A, Spitz L, et al. A nuclear localization signal within HIV-1 matrix protein that governs infection of non-dividing cells. *Nature* 1993;365:666-9.
- 25.Ehrlich LS, Agresta BE, Carter CA. Assembly of recombinant human immunodeficiency virus type 1 capsid protein in vitro. *J Virol* 1992;66:4874-83.
- 26.Berkowitz RD, Luban J, Goff SP. Specific binding of human immunodeficiency virus type 1 gag polyprotein and nucleocapsid protein to viral RNAs detected by RNA mobility shift assays. *J Virol* 1993;67:7190-200.

- 27.Darlix JL, Gabus C, Nugeyre MT, Clavel F, Barre-Sinoussi F. Cis elements and trans-acting factors involved in the RNA dimerization of the human immunodeficiency virus HIV-1. *J Mol Biol* 1990;216:689-99.
- 28.Marquet R, Baudin F, Gabus C, Darlix JL, Mougel M, Ehresmann C, et al. Dimerization of human immunodeficiency virus (type 1) RNA: stimulation by cations and possible mechanism. *Nucleic Acids Res* 1991;19:2349-57.
- 29.Farmerie WG, Loeb DD, Casavant NC, Hutchison CA, 3rd, Edgell MH, Swanstrom R. Expression and processing of the AIDS virus reverse transcriptase in Escherichia coli. *Science* 1987;236:305-8.
- 30.Debouck C, Gorniak JG, Strickler JE, Meek TD, Metcalf BW, Rosenberg M. Human immunodeficiency virus protease expressed in Escherichia coli exhibits autoprocessing and specific maturation of the gag precursor. *Proc Natl Acad Sci U S A* 1987;84:8903-6.
- 31.Kohl NE, Emini EA, Schleif WA, Davis LJ, Heimbach JC, Dixon RA, et al. Active human immunodeficiency virus protease is required for viral infectivity. *Proc Natl Acad Sci U S A* 1988;85:4686-90.
- 32.Loeb DD, Swanstrom R, Everitt L, Manchester M, Stamper SE, Hutchison CA, 3rd. Complete mutagenesis of the HIV-1 protease. *Nature* 1989;340:397-400.

- 33.Baltimore D. RNA-dependent DNA polymerase in virions of RNA tumour viruses.
Nature 1970;226:1209-11.
- 34.Temin HM. The DNA provirus hypothesis. Science 1976;192:1075-80.
- 35.Turner BG, Summers MF. Structural biology of HIV. J Mol Biol 1999;285:1-32.
- 36.Zaitseva M, Peden K, Golding H. HIV coreceptors: role of structure, posttranslational modifications, and internalization in viral-cell fusion and as targets for entry inhibitors. Biochim Biophys Acta 2003;1614:51-61.
- 37.Kuiken C, Foley B, Hahn B, Marx P, McCutchan F, Mellors JW, et al. Human Retroviruses and AIDS. New Maxico: Theoretical Biology and Biophysics; 1999.
- 38.Hua J, Blair W, Truant R, Cullen BR. Identification of regions in HIV-1 Nef required for efficient downregulation of cell surface CD4. Virology 1997;231:231-8.
- 39.Wiskerchen M, Cheng-Mayer C. HIV-1 Nef association with cellular serine kinase correlates with enhanced virion infectivity and efficient proviral DNA synthesis. Virology 1996;224:292-301.

- 40.Kestler HW, 3rd, Ringler DJ, Mori K, Panicali DL, Sehgal PK, Daniel MD, et al. Importance of the nef gene for maintenance of high virus loads and for development of AIDS. *Cell* 1991;65:651-62.
- 41.Wyand MS, Manson KH, Garcia-Moll M, Montefiori D, Desrosiers RC. Vaccine protection by a triple deletion mutant of simian immunodeficiency virus. *J Virol* 1996;70:3724-33.
- 42.Kirchhoff F, Greenough TC, Brettler DB, Sullivan JL, Desrosiers RC. Brief report: absence of intact nef sequences in a long-term survivor with nonprogressive HIV-1 infection. *N Engl J Med* 1995;332:228-32.
- 43.Rhodes DI, Ashton L, Solomon A, Carr A, Cooper D, Kaldor J, et al. Characterization of three nef-defective human immunodeficiency virus type 1 strains associated with long-term nonprogression. Australian Long-Term Nonprogressor Study Group. *J Virol* 2000;74:10581-8.
- 44.Salvi R, Garbuglia AR, Di Caro A, Pulciani S, Montella F, Benedetto A. Grossly defective nef gene sequences in a human immunodeficiency virus type 1-seropositive long-term nonprogressor. *J Virol* 1998;72:3646-57.

45. Spina CA, Kwok TJ, Chow MY, Guatelli JC, Richman DD. The importance of nef in the induction of human immunodeficiency virus type 1 replication from primary quiescent CD4 lymphocytes. *J Exp Med* 1994;179:115-23.
46. Rhee SS, Marsh JW. Human immunodeficiency virus type 1 Nef-induced down-modulation of CD4 is due to rapid internalization and degradation of surface CD4. *J Virol* 1994;68:5156-63.
47. Yu Q, Landau N, Konig R. Vif and the Role of Antiviral Cytidine Deaminases in HIV-1 Replication. In: Leitner T, Foley B, Hahn B, Marx P, McCutchan F, Mellors J, et al., editors. *HIV Sequence Compendium 2003*. New Mexico: Theoretical Biology and Biophysics; 2003. p. 2-13.
48. Klimkait T, Strebel K, Hoggan MD, Martin MA, Orenstein JM. The human immunodeficiency virus type 1-specific protein vpu is required for efficient virus maturation and release. *J Virol* 1990;64:621-9.
49. Willey RL, Maldarelli F, Martin MA, Strebel K. Human immunodeficiency virus type 1 Vpu protein induces rapid degradation of CD4. *J Virol* 1992;66:7193-200.
50. Charneau P, Borman AM, Quillent C, Guetard D, Chamaret S, Cohen J, et al. Isolation and envelope sequence of a highly divergent HIV-1 isolate: definition of a new HIV-1 group. *Virology* 1994;205:247-53.

- 51.Simon F, Mauclere P, Roques P, Loussert-Ajaka I, Muller-Trutwin MC, Saragosti S, et al. Identification of a new human immunodeficiency virus type 1 distinct from group M and group O. *Nat Med* 1998;4:1032-7.
- 52.Carr JK, Salminen MO, Koch C, Gotte D, Artenstein AW, Hegerich PA, et al. Full-length sequence and mosaic structure of a human immunodeficiency virus type 1 isolate from Thailand. *J Virol* 1996;70:5935-43.
- 53.Tovanabutra S, Polonis V, De Souza M, Trichavaroj R, Chanbancherd P, Kim B, et al. First CRF01_AE/B recombinant of HIV-1 is found in Thailand. *Aids* 2001;15:1063-5.
- 54.Pantaleo G, Graziosi C, Fauci AS. New concepts in the immunopathogenesis of human immunodeficiency virus infection. *N Engl J Med* 1993;328:327-35.
- 55.Pantaleo G, Fauci AS. Immunopathogenesis of HIV infection. *Annu Rev Microbiol* 1996;50:825-54.
- 56.Fauci AS, Pantaleo G, Stanley S, Weissman D. Immunopathogenic mechanisms of HIV infection. *Ann Intern Med* 1996;124:654-63.

- 57.Flint SJ, Enquist LW, Krug RM, Racaniello VR, Skala AM. Multiple facets of Human Immunodeficiency Virus Pathogenicity. In: Virology: molecular biology pathogenesis and control. Washington, D.C.: ASM Press; 2000. p. 641-643.
- 58.Perelson AS, Neumann AU, Markowitz M, Leonard JM, Ho DD. HIV-1 dynamics in vivo: virion clearance rate, infected cell life-span, and viral generation time. *Science* 1996;271:1582-6.
- 59.Lehner T. Innate and adaptive mucosal immunity in protection against HIV infection. *Vaccine* 2003;21 Suppl 2:S68-76.
- 60.Lehner T, Mitchell E, Bergmeier L, Singh M, Spallek R, Cranage M, et al. The role of gammadelta T cells in generating antiviral factors and beta-chemokines in protection against mucosal simian immunodeficiency virus infection. *Eur J Immunol* 2000;30:2245-56.
- 61.Cocchi F, DeVico AL, Garzino-Demo A, Arya SK, Gallo RC, Lusso P. Identification of RANTES, MIP-1 alpha, and MIP-1 beta as the major HIV-suppressive factors produced by CD8+ T cells. In: *Science*; 1995. p. 1811-5.
- 62.Biron CA, Nguyen KB, Pien GC, Cousens LP, Salazar-Mather TP. Natural killer cells in antiviral defense: function and regulation by innate cytokines. *Annu Rev Immunol* 1999;17:189-220.

- 63.Goldsby RA, Kindt TJ, Osborne BA. Kuby Immunology. 4 ed. New York: W.H. Freeman And Company; 2000.
- 64.Brander C, Walker BD. T lymphocyte responses in HIV-1 infection: implications for vaccine development. *Curr Opin Immunol* 1999;11:451-9.
- 65.Goulder PJ, Rowland-Jones SL, McMichael AJ, Walker BD. Anti-HIV cellular immunity: recent advances towards vaccine design. *Aids* 1999;13 Suppl A:S121-36.
- 66.Townsend A, Bodmer H. Antigen recognition by class I-restricted T lymphocytes. *Annu Rev Immunol* 1989;7:601-24.
- 67.Draenert R, Le Gall S, Pfafferott KJ, Leslie AJ, Chetty P, Brander C, et al. Immune selection for altered antigen processing leads to cytotoxic T lymphocyte escape in chronic HIV-1 infection. *J Exp Med* 2004;199:905-15.
- 68.York IA, Rock KL. Antigen processing and presentation by the class I major histocompatibility complex. *Annu Rev Immunol* 1996;14:369-96.
- 69.Wange RL, Samelson LE. Complex complexes: signaling at the TCR. *Immunity* 1996;5:197-205.

70. Weiss A, Littman DR. Signal transduction by lymphocyte antigen receptors. *Cell* 1994;76:263-74.
71. Purbhoo MA, Sewell AK, Kleinerman P, Goulder PJ, Hilyard KL, Bell JI, et al. Copresentation of natural HIV-1 agonist and antagonist ligands fails to induce the T cell receptor signaling cascade. *Proc Natl Acad Sci U S A* 1998;95:4527-32.
72. Rammensee HG, Friede T, Stevanović S. MHC ligands and peptide motifs: first listing. *Immunogenetics* 1995;41:178-228.
73. Sewell AK, Price DA, Oxenius A, Kelleher AD, Phillips RE. Cytotoxic T lymphocyte responses to human immunodeficiency virus: control and escape. *Stem Cells* 2000;18:230-44.
74. Berke G. The CTL's kiss of death. *Cell* 1995;81:9-12.
75. Tschopp J, Hofmann K. Cytotoxic T cells: more weapons for new targets? *Trends Microbiol* 1996;4:91-4.
76. Su B, Bochan MR, Hanna WL, Froelich CJ, Brahmi Z. Human granzyme B is essential for DNA fragmentation of susceptible target cells. *Eur J Immunol* 1994;24:2073-80.

- 77.Kagi D, Ledermann B, Burki K, Seiler P, Odermatt B, Olsen KJ, et al. Cytotoxicity mediated by T cells and natural killer cells is greatly impaired in perforin-deficient mice. *Nature* 1994;369:31-7.
- 78.Kojima H, Shinohara N, Hanaoka S, Someya-Shirota Y, Takagaki Y, Ohno H, et al. Two distinct pathways of specific killing revealed by perforin mutant cytotoxic T lymphocytes. *Immunity* 1994;1:357-64.
- 79.Nagata S, Golstein P. The Fas death factor. *Science* 1995;267:1449-56.
- 80.van den Broek MF, Muller U, Huang S, Zinkernagel RM, Aguet M. Immune defence in mice lacking type I and/or type II interferon receptors. *Immunol Rev* 1995;148:5-18.
- 81.Hadida F, Vieillard V, Autran B, Clark-Lewis I, Baggolini M, Debre P. HIV-specific T cell cytotoxicity mediated by RANTES via the chemokine receptor CCR3. *J Exp Med* 1998;188:609-14.
- 82.Price DA, Klenerman P, Booth BL, Phillips RE, Sewell AK. Cytotoxic T lymphocytes, chemokines and antiviral immunity. *Immunol Today* 1999;20:212-6.

- 83.Price DA, Sewell AK, Dong T, Tan R, Goulder PJ, Rowland-Jones SL, et al. Antigen-specific release of beta-chemokines by anti-HIV-1 cytotoxic T lymphocytes. *Curr Biol* 1998;8:355-8.
- 84.Wagner L, Yang OO, Garcia-Zepeda EA, Ge Y, Kalams SA, Walker BD, et al. Beta-chemokines are released from HIV-1-specific cytolytic T-cell granules complexed to proteoglycans. *Nature* 1998;391:908-11.
- 85.Cocchi F, DeVico AL, Garzino-Demo A, Arya SK, Gallo RC, Lusso P. Identification of RANTES, MIP-1 alpha, and MIP-1 beta as the major HIV-suppressive factors produced by CD8+ T cells. *Science* 1995;270:1811-5.
- 86.Cocchi F, DeVico AL, Garzino-Demo A, Cara A, Gallo RC, Lusso P. The V3 domain of the HIV-1 gp120 envelope glycoprotein is critical for chemokine-mediated blockade of infection. *Nat Med* 1996;2:1244-7.
- 87.Yang OO, Walker BD. CD8+ cells in human immunodeficiency virus type I pathogenesis: cytolytic and noncytolytic inhibition of viral replication. *Adv Immunol* 1997;66:273-311.
- 88.Levy JA, Mackewicz CE, Barker E. Controlling HIV pathogenesis: the role of the noncytotoxic anti-HIV response of CD8+ T cells. *Immunol Today* 1996;17:217-24.

- 89.Sidney J, del Guercio MF, Southwood S, Engelhard VH, Appella E, Rammensee HG, et al. Several HLA alleles share overlapping peptide specificities. *J Immunol* 1995;154:247-59.
- 90.McMichael A, Hanke T. The quest for an AIDS vaccine: is the CD8+ T-cell approach feasible? *Nat Rev Immunol* 2002;2:283-91.
- 91.Clayton J, Lonjon C, Whittle D. Allele and haplotype frequencies for HLA loci in various ethnic group. In: Charron D, editor. In HLA Volume I genetic diversity of HLA functional and medical implication. Paris: EDK Medical and Scientific International; 1997. p. 665-820.
- 92.Yap KL, Ada GL, McKenzie IF. Transfer of specific cytotoxic T lymphocytes protects mice inoculated with influenza virus. *Nature* 1978;273:238-9.
- 93.Sethi KK, Omata Y, Schneweis KE. Protection of mice from fatal herpes simplex virus type 1 infection by adoptive transfer of cloned virus-specific and H-2-restricted cytotoxic T lymphocytes. *J Gen Virol* 1983;64 (Pt 2):443-7.
- 94.Jin X, Bauer DE, Tuttleton SE, Lewin S, Gettie A, Blanchard J, et al. Dramatic rise in plasma viremia after CD8(+) T cell depletion in simian immunodeficiency virus-infected macaques. *J Exp Med* 1999;189:991-8.

- 95.Schmitz JE, Kuroda MJ, Santra S, Sasheville VG, Simon MA, Lifton MA, et al.
Control of viremia in simian immunodeficiency virus infection by CD8+
lymphocytes. Science 1999;283:857-60.
- 96.Papadopoulos EB, Ladanyi M, Emanuel D, Mackinnon S, Boulad F, Carabasi MH, et
al. Infusions of donor leukocytes to treat Epstein-Barr virus-associated
lymphoproliferative disorders after allogeneic bone marrow transplantation. N
Engl J Med 1994;330:1185-91.
- 97.Heslop HE, Brenner MK, Rooney CM. Donor T cells to treat EBV-associated
lymphoma. N Engl J Med 1994;331:679-80.
- 98.Heslop HE, Ng CY, Li C, Smith CA, Loftin SK, Krance RA, et al. Long-term
restoration of immunity against Epstein-Barr virus infection by adoptive transfer
of gene-modified virus-specific T lymphocytes. Nat Med 1996;2:551-5.
- 99.Riddell SR, Watanabe KS, Goodrich JM, Li CR, Agha ME, Greenberg PD.
Restoration of viral immunity in immunodeficient humans by the adoptive transfer
of T cell clones. Science 1992;257:238-41.
- 100.Gray CM, Lawrence J, Schapiro JM, Altman JD, Winters MA, Crompton M, et al.
Frequency of class I HLA-restricted anti-HIV CD8+ T cells in individuals

receiving highly active antiretroviral therapy (HAART). *J Immunol* 1999;162:1780-8.

101. Greenough TC, Brettler DB, Somasundaran M, Panicali DL, Sullivan JL. Human immunodeficiency virus type 1-specific cytotoxic T lymphocytes (CTL), virus load, and CD4 T cell loss: evidence supporting a protective role for CTL in vivo. *J Infect Dis* 1997;176:118-25.

102. Clerici M, Shearer GM. Correlates of protection in HIV infection and the progression of HIV infection to AIDS. *Immunol Lett* 1996;51:69-73.

103. Haynes BF, Pantaleo G, Fauci AS. Toward an understanding of the correlates of protective immunity to HIV infection. *Science* 1996;271:324-8.

104. Rowland-Jones SL, McMichael A. Immune responses in HIV-exposed seronegatives: have they repelled the virus? *Curr Opin Immunol* 1995;7:448-55.

105. Looney DJ. Immune responses to human immunodeficiency virus type 1 in exposed but uninfected individuals: protection or chance? *J Clin Invest* 1994;93:920.

106. Langlade-Demoyen P, Ngo-Giang-Huong N, Ferchal F, Oksenhendler E. Human immunodeficiency virus (HIV) nef-specific cytotoxic T lymphocytes in noninfected heterosexual contact of HIV-infected patients. *J Clin Invest* 1994;93:1293-7.

- 107.Lee CH, Saksela K, Mirza UA, Chait BT, Kuriyan J. Crystal structure of the conserved core of HIV-1 Nef complexed with a Src family SH3 domain. *Cell* 1996;85:931-42.
- 108.Cohen GB, Gandhi RT, Davis DM, Mandelboim O, Chen BK, Strominger JL, et al. The selective downregulation of class I major histocompatibility complex proteins by HIV-1 protects HIV-infected cells from NK cells. *Immunity* 1999;10:661-71.
- 109.Xu XN, Screamton GR, Gotch FM, Dong T, Tan R, Almond N, et al. Evasion of cytotoxic T lymphocyte (CTL) responses by nef-dependent induction of Fas ligand (CD95L) expression on simian immunodeficiency virus-infected cells. *J Exp Med* 1997;186:7-16.
- 110.Xu XN, Laffert B, Screamton GR, Kraft M, Wolf D, Kolanus W, et al. Induction of Fas ligand expression by HIV involves the interaction of Nef with the T cell receptor zeta chain. *J Exp Med* 1999;189:1489-96.
- 111.Seeger M, Ferrell K, Frank R, Dubiel W. HIV-1 tat inhibits the 20 S proteasome and its 11 S regulator-mediated activation. *J Biol Chem* 1997;272:8145-8.
- 112.Sewell AK, Price DA, Teisserenc H, Booth BL, Jr., Gileadi U, Flavin FM, et al. IFN-gamma exposes a cryptic cytotoxic T lymphocyte epitope in HIV-1 reverse transcriptase. *J Immunol* 1999;162:7075-9.

- 113.Gould KG, Bangham CR. Virus variation, escape from cytotoxic T lymphocytes and human retroviral persistence. *Semin Cell Dev Biol* 1998;9:321-8.
- 114.Phillips RE, Rowland-Jones S, Nixon DF, Gotch FM, Edwards JP, Ogunlesi AO, et al. Human immunodeficiency virus genetic variation that can escape cytotoxic T cell recognition. *Nature* 1991;354:453-9.
- 115.Borrow P, Lewicki H, Wei X, Horwitz MS, Peffer N, Meyers H, et al. Antiviral pressure exerted by HIV-1-specific cytotoxic T lymphocytes (CTLs) during primary infection demonstrated by rapid selection of CTL escape virus. *Nat Med* 1997;3:205-11.
- 116.Price DA, Goulder PJ, Klenerman P, Sewell AK, Easterbrook PJ, Troop M, et al. Positive selection of HIV-1 cytotoxic T lymphocyte escape variants during primary infection. *Proc Natl Acad Sci U S A* 1997;94:1890-5.
- 117.Ossendorp F, Eggers M, Neisig A, Ruppert T, Groettrup M, Sijts A, et al. A single residue exchange within a viral CTL epitope alters proteasome-mediated degradation resulting in lack of antigen presentation. *Immunity* 1996;5:115-24.
- 118.Uebel S, Kraas W, Kienle S, Wiesmuller KH, Jung G, Tampe R. Recognition principle of the TAP transporter disclosed by combinatorial peptide libraries. *Proc Natl Acad Sci U S A* 1997;94:8976-81.

- 119.Neisig A, Roelse J, Sijts AJ, Ossendorp F, Feltkamp MC, Kast WM, et al. Major differences in transporter associated with antigen presentation (TAP)-dependent translocation of MHC class I-presentable peptides and the effect of flanking sequences. *J Immunol* 1995;154:1273-9.
- 120.Couillin I, Connan F, Culmann-Penciolelli B, Gomard E, Guillet JG, Choppin J. HLA-dependent variations in human immunodeficiency virus Nef protein alter peptide/HLA binding. *Eur J Immunol* 1995;25:728-32.
- 121.Couillin I, Culmann-Penciolelli B, Gomard E, Choppin J, Levy JP, Guillet JG, et al. 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* 1994;180:1129-34.
- 122.Klenerman P, Meier UC, Phillips RE, McMichael AJ. The effects of natural altered peptide ligands on the whole blood cytotoxic T lymphocyte response to human immunodeficiency virus. *Eur J Immunol* 1995;25:1927-31.
- 123.Klenerman P, Rowland-Jones S, McAdam S, Edwards J, Daenke S, Laloo D, et al. Cytotoxic T-cell activity antagonized by naturally occurring HIV-1 Gag variants. *Nature* 1994;369:403-7.

- 124.Fukada K, Chujo Y, Tomiyama H, Miwa K, Kaneko Y, Oka S, et al. HLA-A*1101-restricted cytotoxic T lymphocyte recognition of HIV-1 Pol protein. Aids 1999;13:1413-4.
- 125.Kaul R, Rowland-Jones SL, Kimani J, Dong T, Yang HB, Kiama P, et al. Late seroconversion in HIV-resistant Nairobi prostitutes despite pre-existing HIV-specific CD8+ responses. J Clin Invest 2001;107:341-9.
- 126.Subbarao S, Vanichseni S, Hu DJ, Kitayaporn D, Choopanya K, Raktham S, et al. Genetic characterization of incident HIV type 1 subtype E and B strains from a prospective cohort of injecting drug users in Bangkok, Thailand. In: AIDS Res Hum Retroviruses; 2000. p. 699-707.
- 127.Buseyne F, McChesney M, Porrot F, Kovarik S, Guy B, Riviere Y. Gag-specific cytotoxic T lymphocytes from human immunodeficiency virus type 1-infected individuals: Gag epitopes are clustered in three regions of the p24gag protein. J Virol 1993;67:694-702.
- 128.Frahm N, Korber BT, Adams CM, Szinger JJ, Draenert R, Addo MM, et al. Consistent cytotoxic-T-lymphocyte targeting of immunodominant regions in human immunodeficiency virus across multiple ethnicities. J Virol 2004;78:2187-200.

- 129.Dalod M, Dupuis M, Deschemin JC, Goujard C, Deveau C, Meyer L, et al. Weak anti-HIV CD8(+) T-cell effector activity in HIV primary infection. *J Clin Invest* 1999;104:1431-9.
- 130.Larsson M, Jin X, Ramratnam B, Ogg GS, Engelmayer J, Demoitie MA, et al. A recombinant vaccinia virus based ELISPOT assay detects high frequencies of Pol-specific CD8 T cells in HIV-1-positive individuals. *Aids* 1999;13:767-77.
- 131.Novitsky V, Cao H, Rybak N, Gilbert P, McLane MF, Gaolekwe S, et al. Magnitude and frequency of cytotoxic T-lymphocyte responses: identification of immunodominant regions of human immunodeficiency virus type 1 subtype C. *J Virol* 2002;76:10155-68.
- 132.Musey L, Hughes J, Schacker T, Shea T, Corey L, McElrath MJ. Cytotoxic-T-cell responses, viral load, and disease progression in early human immunodeficiency virus type 1 infection. *N Engl J Med* 1997;337:1267-74.
- 133.Goulder PJ, Addo MM, Altfeld MA, Rosenberg ES, Tang Y, Govender U, et al. Rapid definition of five novel HLA-A*3002-restricted human immunodeficiency virus-specific cytotoxic T-lymphocyte epitopes by elispot and intracellular cytokine staining assays. *J Virol* 2001;75:1339-47.

134.Migueles SA, Connors M. Frequency and function of HIV-specific CD8(+) T cells.

In: Immunol Lett; 2001. p. 141-50.

135.Propato A, Schiaffella E, Vicenzi E, Francavilla V, Baloni L, Paroli M, et al.

Spreading of HIV-specific CD8+ T-cell repertoire in long-term nonprogressors
and its role in the control of viral load and disease activity. Hum Immunol
2001;62:561-76.

136.Goulder PJ, Sewell AK, Laloo DG, Price DA, Whelan JA, Evans J, et al. 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 1997;185:1423-33.

137.Yokomaku Y, Miura H, Tomiyama H, Kawana-Tachikawa A, Takiguchi M, Kojima
A, et al. Impaired processing and presentation of cytotoxic-T-lymphocyte (CTL)
epitopes are major escape mechanisms from CTL immune pressure in human
immunodeficiency virus type 1 infection. J Virol 2004;78:1324-32.

138.Ruppert J, Sidney J, Celis E, Kubo RT, Grey HM, Sette A. Prominent role of
secondary anchor residues in peptide binding to HLA-A2.1 molecules. Cell
1993;74:929-37.

- 139.MeintJies PL, Rodrigo AG. Evolution of relative synonymous codon usage in Human Immunodeficiency virus type-1. In: the second conference on Asia-Pacific Bioinformatics Conference; 2004; New Zeland: Australian Computer Society, Inc.; 2004. p. 277-282.
- 140.Deacon NJ, Tsykin A, Solomon A, Smith K, Ludford-Menting M, Hooker DJ, et al. Genomic structure of an attenuated quasi species of HIV-1 from a blood transfusion donor and recipients. Science 1995;270:988-91.
- 141.Mariani R, Kirchhoff F, Greenough TC, Sullivan JL, Desrosiers RC, Skowronski J. High frequency of defective nef alleles in a long-term survivor with nonprogressive human immunodeficiency virus type 1 infection. J Virol 1996;70:7752-64.
- 142.Saksela K, Cheng G, Baltimore D. Proline-rich (PxxP) motifs in HIV-1 Nef bind to SH3 domains of a subset of Src kinases and are required for the enhanced growth of Nef+ viruses but not for down-regulation of CD4. Embo J 1995;14:484-91.



APPENDIX

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APPENDIX A

Reagent, Materials, and Instruments

A. Media and Reagents

Absolute ethanol	(Merck, Germany)
Agarose (ultrapure)	(Merck, Germany)
Alkaline phosphatase substrate	(Bio Rad Labs., Hercules, CA)
Anti-IFN- γ mAb 1-D1K	(Mabtech, Stockholm, Sweden)
Anti-IFN- γ mAb 7-B6-1	(Mabtech, Stockholm, Sweden)
DMSO	(Sigma, UK)
dNTPs	(Invitrogen, U.S.A.)
EDTA	(Amresco, U.S.A.)
Ethydium bromide	(Amresco, U.S.A.)
Fetal Bovine Serum	(Bio Whittaker, Maryland, USA)
Glutamine	(Sigma, UK)
Isoprep	(Robbins Scientific, Norway)
PBS	(Sigma, UK)
Penicillin	(General Drugs House, Thailand)
RPMI medium 1640	(GIBCO, USA)
Streptavidin-alkaline phosphatase conjugate	(Mabtech, Stockholm, Sweden)
Peptide	(Minotope, Australia)
Trypan blue	(Sigma, UK)

B. Materials

Centrifuge tube	(Corning, U.S.A.)
Disposable serological pipette	(Costar, U.S.A.)
ELISpot plate	(Millipore, U.S.A.)
Filter Tip	(Sorenson, U.S.A.)

Microcentrifuge tube	(Sorenson, U.S.A.)
Tissue culture plate	(IWAKI, Japan)

C. Instruments

Autoclave (model-SS-325)	(Tomy, Japan)
Chemi doc	(Bio-Rad, U.S.A.)
CO ₂ Incubator	(Thermo Forma, U.S.A.)
DNA thermocycle system	(Hybaid, U.S.A.)
Electrophoresis chamber	(CBS, U.S.A.)
Microcentrifuge	(Fotodyne, U.S.A.)
Mixer-Vertex-Genic	(Scientific industries, U.S.A.)
Power supply (Model 1000/500)	(Bio-Rad, U.S.A.)
Refrigerator	(Toshiba, Japan)
Spectrophotometer (SmartSpect™ 3000)	(Bio-Rad, U.S.A.)
Vertical electrophoresis chamber	(CBS, U.S.A.)
Water bath	(Julabo, Germany)

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APPENDIX B

REAGENTS PREPARATION

Reagents for molecular analysis

1. TE buffer (Tris/EDTA)

Tris, PH 7.4	10	mM
EDTA, pH 8.0	1	mM

2. 10 mg/ml Ethidium bromide

Ethidium bromide	1.0	g
Distilled water	100	ml

Mix the solution and store in the dark at 4°C.

3. 1.5% Agarose gel

Agarose	0.525	g
1x TBE	35	ml

Dissolve by heating in microwave oven and occasional mix until no granules of agarose are visible.

Reagents for CTL analysis

1. Ficoll-Hypaque solution (ready to use)

2. RPMI medium 1640 (ready to use)

3. Penicillin 10,000 Units/ml

3.1 Stock penicillin 100,000 Units/ml

Penicillin G 1,000,000 Units per ampoule was reconstituted with sterile DW 10 ml and mixed

a. Working penicillin 10,000 Units/ml

Stock penicillin 100,000 Units/ml	1	ml
RPMI1640	9	ml

4. Streptomycin 10,000 µg/ml

4.1 Stock streptomycin 100,000 µg/ml

Streptomycin 1 gm was reconstituted with sterile DW 10 ml and mixed

4.2 Working streptomycin 10,000 Units/ml

Stock streptomycin 100,000 Units/ml	1	ml
RPMI1640	9	ml

5. Reagent for culture

4.1 R10

RPMI1640+100 Units/ml Streptomycin	90	ml
Fetal Bovine Serum (FBS)	10	ml

4.2 R20

RPMI1640+100 Units/ml Streptomycin	80	ml
Fetal Bovine Serum (FBS)	20	ml

6. Cyclosporin A 1 µg/ml

5.1 Stock CSA 1 mg/ml

CSA 50 mg/ml	100	µl
Normal Saline Sterile	4900	µl

5.2 Stock CSA 10^{-4} g/ml

Stock CSA 1 mg/ml	100	µl
R20	900	µl

5.3 CSA 1 µg/ml

Stock CSA 10 ⁻⁴ g/ml	100	µl
R20	900	µl

7. Peptide preparation**6.1 Stock peptide 1 mg/ml**

Peptide	1	mg
1% DMSO in PBS	1	ml

6.2 Peptide 200 µg/ml

Stock peptide 1 mg/ml	200	µl
Sterile PBS	800	µl

APPENDIX C

AMINO ACID

1. Abbreviation for amino acids

A	alanine	L	leucine
R	arginine	K	lysine
N	asparagine	M	methionine
D	aspartic acid	F	phenylalanine
C	cysteine	P	praline
Q	glutamine	S	serine
E	glutamine	T	threonine
G	glycine	W	tryptophan
H	histidine	Y	tyrosine
I	isoleucine	V	valine

BIOGRAPHY

Miss Sasiporn Ruangdachsuwan was born on July 23, 1980 in Chachoengsao province, Thailand. She previously graduated with the Bachelor degree of Science in Microbiology from Burapha University in 2001 and then attends to particulate in Medical Microbiology program, Graduate School, Chulalongkorn University for her master degree.



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