

**UNIVERSITAT DE BARCELONA**

**FACULTAT DE MEDICINA**

DEPARTAMENT DE BIOLOGIA CEL·LULAR i

ANATOMIA PATOLÒGICA

***ESTUDI DE LA RESPOSTA IMMUNE EN  
PACIENTS INFECTATS PEL VIH-1 SOTMESOS  
A TERÀPIES IMMUNOMEDIADES***

Tesi Doctoral presentada per

**Anna López Plana**

Per optar al grau de

**Doctora en Farmàcia per la Universitat de Barcelona**

Directora de la tesi: Doctora Montserrat Plana Prades

Tutor: Doctor Carles Enrich Bastús

Barcelona, Novembre 2008

## **8. BIBLIOGRAFIA**



---

## 8. **BIBLIOGRAFIA**

- Addo M.M., R Draenert, A Rathod, C.L. Verrill, B.T. Davis, R.T. Gandhi, G.K. Robbins, N.O. Basqoz, D.R. Stone, D.E. Cohen, M.N. Johnston, T. Flynn, A.G. Wurcel, E.S. Rosenberg, M. Altfeld, and B.D. Walker. 2007. Fully differentiated HIV-1 specific CD8+ T effector cells are more frequently detectable in controlled than in progressive HIV-1 infection. *PLOS One* 2: e321.
- Akira S, Takeda K, Kaisho T. Toll-like receptors: critical proteins linking innate and acquired immunity. *Nat Immunol* 2001; 2(8): 675-680.
- Aladdin H, Ullum H, Dam NS, Espersen C, Mathiesen L, Katzenstein TL et al. Granulocyte colony-stimulating factor increases CD4+ T cell counts of human immunodeficiency virus-infected patients receiving stable, highly active antiretroviral therapy: results from a randomized, placebo-controlled trial. *J Infect Dis* 2000; 181(3):1148-1152.
- Alston B, Ellenberg JH, Standiford HC, Muth K, Martinez A, Greaves W et al. A multicenter, randomized, controlled trial of three preparations of low-dose oral alpha-interferon in HIV-infected patients with CD4+ counts between 50 and 350 cells/mm<sup>3</sup>. Division of AIDS Treatment Research Initiative (DATRI) 022 Study Group. *J Acquir Immune Defic Syndr* 1999; 22(4):348-357.
- Altfeld M, Rosenberg ES, Shankarappa R, Mukherjee JS, Hecht FM, Eldridge RL et al. Cellular immune responses and viral diversity in individuals treated during acute and early HIV-1 infection. *J Exp Med* 2001; 193(2):169-180.
- Altfeld M, van Lunzen J, Fram N, et al. Expansion of pre-existing, lymph node-localized CD8+ T-cells during supervised treatment interruptions in chronic HIV-1 infection. *J Clin Invest.* 2002;109:837–843.
- Amara RR, Villinger F, Altman JD, Lydy SL, O'Neil SP, Staprans SI et al. Control of a mucosal challenge and prevention of AIDS by a multiprotein DNA/MVA vaccine. *Science* 2001; 92(5514):69-74.

- 
- Andrieu JM, Lu W, Levy R. Sustained increases in CD4 cell counts in asymptomatic human immunodeficiency virus type 1-seropositive patients treated with prednisolone for 1 year. *J Infect Dis* 1995; 171(3):523-530.
  - Angel JB, Jacobson MA, Skolnik PR, Giordano M, Shapiro L, LeBeaut A et al. A multicenter, randomized, double-blind, placebo-controlled trial of recombinant human interleukin-10 in HIV-infected subjects. *AIDS* 2000; 14(16):2503-2508.
  - Appay V, Dunbar PR, Callan M, Klenerman P, Gillespie GM, Papagno L, Ogg GS, King A, Lechner F, Spina CA, Little S, Havlir DV, Richman DD, Gruener N, Pape G, Waters A, Easterbrook P, Salio M, Cerundolo V, McMichael AJ, Rowland-Jones SL. Memory CD8+ t cells vary in differentiation phenotype in different persistent virus infection. *Nat. Med.* 2002, 8(4): 379-385.
  - Appay V, Nixon DF, Donahoe SM, Gillespie GM, Dong T, King A et al. HIV-specific CD8(+) T cells produce antiviral cytokines but are impaired in cytolytic function. *J Exp Med* 2000; 192(1):63-75.
  - Appay V, Papagno L, Spina CA, Hansasuta P, King A, Jones L, Ogg GS, Little S, McMichael AJ, Richman DD, Rpwland-Jones SL. Dynamics of T cell responses in HIV infection. *J. Immunol.* 2002, 168: 3660-3666.
  - Arno A, Ruiz L, Juan M, Jou A, Balague M, Zayat MK et al. Efficacy of low-dose subcutaneous interleukin-2 to treat advanced human immunodeficiency virus type 1 in persons with  $\leq 250/\mu\text{L}$  CD4 T cells and undetectable plasma virus load. *J Infect Dis* 1999; 180(1):56-60.
  - Autran B, Carcelain G, Li TS, Blanc C, Mathez D, Tubiana R, *et al.*: Positive effects of combined antiretroviral therapy on CD4\_T cell homeostasis and function in advanced HIV disease [see comments]. *Science* 1997;277:112–116.
  - Autran B, Debre P, Walker B, Katlama C. Therapeutic vaccines against HIV need international partnerships. *Nat Rev Immunol* 2003; 3(6):503-508.
  - Autran B, Carcelain G, Combadiere B, Debre P. Therapeutic vaccines for chronic infections. *Science* 2004; 305 (5681): 205-208.

- 
- Banchereau J, Caux C, Davoust J, Lebecque S, Liu Y, Pulendran B et al. Immunobiology of dendritic cells. *Annu Rev Immunol.* 2000;18:767-811.
  - Banchereau J, Steinman RM. Dendritic cells and the control of immunity. *Nature.* 1998; 392:245-52.
  - Barao I, Ascensao JL. Human natural killer cells. *Arch Immunol Ther Exp* 1998; 46 (4): 213-229.
  - Barre-Sinoussi F et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 1983 May 20;220(4599):868-71.
  - Berard F, Blanco P, Davoust J, Neidhart-Berard EM, Nouri-Shirazi M, Taquet N et al. Cross-priming of naive CD8 T cells against melanoma antigens using dendritic cells loaded with killed allogeneic melanoma cells. *J Exp Med.* 2000;192:1535-44.
  - Bermejo M, Sánchez-Palomino S, Usán L, Alcamí J. Dynamics of HIV replication in lymphocytes and consequences in the efficacy of protease inhibitors. *J Med Virol* 2004; 73:502-7.
  - Bevan MJ, Braciale TJ. Why can't cytotoxic T cells handle HIV? *PNAS USA* 1995; 92(13):5765-5767
  - Blankson J, Gallant J, Quinn T, et al. Loss of HIV-1 specific immunity during treatment interruption in 2 chronically infected patients. *JAMA.* 2002;288:162–164.
  - Brites C, Gilbert MJ, Pedral-Sampaio D, Bahia F, Pedroso C, Alcantara AP et al. A randomized, placebo-controlled trial of granulocyte-macrophage colony-stimulating factor and nucleoside analogue therapy in AIDS. *J Infect Dis* 2000; 182(5):1531-1535.
  - Brodie SJ, Patterson BK, Lewinsohn DA, Diem K, Spach D, Greenberg PD et al. HIV-specific cytotoxic T lymphocytes traffic to lymph nodes and localize at sites of HIV replication and cell death. *J Clin Invest* 2000; 105:1407-1417.
  - Brodie SJ, Lewinsohn DA, Patterson BK, Jiyamapa D, Krieger J, Corey L et al. In vivo migration and function of transferred HIV-1-specific cytotoxic T cells. *Nat Med* 1999; 5(1):34-41.

- 
- Brossart P, Wirths S, Stuhler G, Reichardt VL, Kanz L, Brugger W. Induction of cytotoxic T-lymphocyte responses in vivo after vaccinations with peptide-pulsed dendritic cells. *Blood*. 2000;96:3102-8.
  - Buge SL, Murty L, Arora K, Kalyanaraman VS, Markham PD, Richardson ES et al. Factors associated with slow disease progression in macaques immunized with an adenovirus-simian immunodeficiency virus (SIV) envelope priming-gp120 boosting regimen and challenged vaginally with SIVmac251. *J Virol* 1999; 73(9):7430-7440.
  - Burton DR, Desrosiers RC, Doms RW et al. HIV vaccine design and the neutralizing antibody problem. *Nat Immunol* 2004; 5: 233-236.
  - Cambi A, Koopman M, Figdor CG. How C-type lectins detected pathogens. *Cell Microbiol* 2005; 7(4):481-488.
  - Cella M, Jarrossay D, Facchetti F, Alebardi O, Nakajima H, Lanzavecchia A et al. Plasmacytoid monocytes migrate to inflamed lymph nodes and produce large amounts of type I interferon. *Nat Med* 1999; 5(8): 919-923.
  - Cella M, Scheidegger D, Palmer-Lehmann K, Lane P, Lanzavecchia A, Alber G. Ligation of CD40 on dendritic cells triggers production of high levels of interleukin-12 and enhances T cell stimulatory capacity: T-T help via APC activation. *J Exp Med*. 1996;184:747-52.
  - Champagne P, Ogg GS, King AS, Knabenhans C, Ellefsen K, Nobile M, Pantaleo G. Skewed maturation of memory HIV-specific CD8 T lymphocytes. *Nature*. 2001, 410: 106-111.
  - Chehimi J, Campbell DE, Azzoni L, Bacheller D, Papasavvas E, Jerandi G et al. Persistent decreases in blood plasmacytoid dendritic cell number and function despite effective highly active antiretroviral therapy and increased blood myeloid dendritic cells in HIV-infected individuals. *J Immunol*. 2002;2002 May 1;168:4796-801.
  - Chun TW, Davey RT, Jr., Ostrowski M, Shawn JJ, Engel D, Mullins JI et al. Relationship between pre-existing viral reservoirs and the re-emergence of plasma viremia after discontinuation of highly active anti-retroviral therapy. *Nat Med* 2000; 6(7):757-761.
  - Chun TW, Engel D, Berry MM. Early establishment of a pool of latently infected, resting CD4+ T cells during primary HIV-1 infection. *PNAS USA* 1998; 95: 8869-8873.

- 
- Chun TW, Justement JS, Sanford C, Hallahan CW, Planta MA, Loutfy M et al. Relationship between the frequency of HIV-specific CD8+ T cells and the level of CD38+CD8+ T cells in untreated HIV-infected individuals. *Proc Natl Acad Sci U S A* 2004; 101(8):2464-2469.
  - Clark SJ, Saag MS, Decker WD. High titers of cytopathic virus in plasma of patients with symptomatic primary HIV-1 infection. *N Engl J Med* 1991; 324: 954-960.
  - 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 CD9+ T cells. *Science* 1995; 270:1811-1815.
  - Dallal RM, Lotze MT. The dendritic cell and human cancer vaccines. *Curr Opin Immunol*. 2000;12:583-88.
  - Danel C, Moh R, Minga A, Anzian A, Ba-Gomis O, Kanga C, Nzunetu G, Gabillard D, Rouet F, Sorho S, Chaix ML, Eholié S, Menan H, Sauvageot D, Bissagnene E, Salamon R, Anglaret X; Trivacan ANRS 1269 trial group. CD4-guided structured antiretroviral treatment interruption strategy in HIV-infected adults in west Africa (Trivacan ANRS 1269 trial): a randomised trial. *Lancet* 2006;367(9527):1981-9.
  - Day C, Walker BD. Progress in defining CD4 helper cell responses in chronic viral infections. *J Exp Med*. 2003;198:1773-77.
  - Deeks SG, Martin JN, Sinclair E, Harris J, Neilands TB, Maecker HT et al. Strong cell-mediated immune responses are associated with the maintenance of low-level viremia in antiretroviral-treated individuals with drug-resistant human immunodeficiency virus type 1. *J Infect Dis* 2004; 189(2):312-321.
  - Derdeyn CA, Silvestri G. Viral and host factors in the pathogenesis of HIV infection. *Curr Opin Immunol* 2005; 17(4):366-373.
  - Dhodapkar M.V., and R.M. Steinman. 2002. Antigen-bearing immature dendritic cells induce peptide-specific CD8+ regulatory T cells in vivo in humans. *Blood* 100: 174-7.



- 
- D'Offizi G, Montesano C, Agrati C, Gioia C, Amicosante M, Topino S et al. Expansion of pre-terminally differentiated CD8 T cells in chronic HIV-positive patients presenting a rapid viral rebound during structured treatment interruption. *AIDS*. 2002;16:2431-38.
  - Donaghy H, Gazzard B, Gotch F, Patterson S. Dysfunction and infection of freshly isolated blood myeloid and plasmacytoid dendritic cells in patients infected with HIV-1. *Blood*. 2003;2003 Jun 1;101:4505-11.
  - Douek DC, Brenchley JM, Betts MR, Ambrozak DR, Hill BJ, Okamoto Y et al. HIV preferentially infects HIV-specific CD4+ T cells. *Nature* 2002; 417(6884):95-98.
  - Strategies for Management of Antiretroviral Therapy (SMART) Study Group, El-Sadr WM, Lundgren JD, Neaton JD, Gordin F, Abrams D, Arduino RC, Babiker A, Burman W, Clumeck N, Cohen CJ, Cohn D, Cooper D, Darbyshire J, Emery S, Fätkenheuer G, Gazzard B, Grund B, Hoy J, Klingman K, Losso M, Markowitz N, Neuhaus J, Phillips A, Rappoport C. CD4+ count-guided interruption of antiretroviral treatment. *New Engl J Med* 2006, 355(22):2283-96.
  - Engering A, Geijtenbeek TB, van Vliet SJ, Wijers M et al. The dendritic cell-specific adhesion receptor DC-SIGN internalizes antigen for presentation to T cells. *J Immunol* 2002; 168(5):2118-2126.
  - Fehervari Z, Sakaguchi S. CD4+ T regs and immune control. *J Clin Invest* 2004;114:1209-17.
  - Finzi D, Hermankova M, Pierson T, Carruth LM, Buck C, Chaisson RE et al. Identification of a reservoir for HIV-1 in patients on highly active antiretroviral therapy. *Science* 1997; 278 (5341): 1295-1300.
  - Fonteneauu JF, Larsson M, Beignon AS, Mckenna K, Dasilva I, Amara A, Liu YJ, Lifson JD, Littman DR, Bhardwaj N. Human immunodeficiency virus type 1 activates plasmacytoid dendritic cells and concomitantly induces the bystander maturation of myeloid dendritic cells. *J Virol* 2004; 78: 5223-32.
  - Fontenot J, Gavin M, Rudensky A. Foxp3 programs the development and function of CD4+CD25+ regulatory T cells. *Nat Immunol* 2003;4:330-6.

- 
- Gamberg J., L. Barrett, I. Bowmer, M. Howley, and M. Grant. 2004. Factors related to loss of HIV-specific cytotoxic T lymphocyte activity. *AIDS 18*: 597-604.
  - Garcia F, Plana M, Arnedo M, Brunet M, Castro P, Gil C et al. Effect of mycophenolate mofetil on immune response and plasma and lymphatic tissue viral load during and after interruption of highly active antiretroviral therapy for patients with chronic HIV infection: a randomized pilot study. *J Acquir Immune Defic Syndr* 2004; 36(3):823-830.
  - Garcia F, Plana M, Arnedo M, Ortiz GM, Miro JM, Lopalco L et al. A cytostatic drug improves control of HIV-1 replication during structured treatment interruptions: a randomized study. *AIDS* 2003; 17(1):43-51.
  - Garcia F, Plana M, Ortiz GM, Bonhoeffer S, Soriano A, Vidal C et al. The virological and immunological consequences of structured treatment interruptions in chronic HIV-1 infection. *AIDS* 2001; 15(9):F29-F40.
  - Garcia F, Plana M, Vidal C, Cruceta A, O'Brien WA, Pantaleo G et al. Dynamics of viral load rebound and immunological changes after stopping effective antiretroviral therapy. *AIDS* 1999; 13(11):F79-F86.
  - Gaynor R. Cellular transcription factors involved in the regulation of HIV-1 gene expression. *AIDS*. 1992 Apr;6(4):347-63. Review.
  - Geiger J, Hutchinson R, Hohenkirk L, McKenna E, Chang A, Mule J. Treatment of solid tumours in children with tumour-lysate-pulsed dendritic cells. *Lancet*. 2000;356:1163-65.
  - Geijtenbeek TB, Kwon DS, Torensma R, van Vliet SJ, van Duijnhoven GC, Middel J et al. DC-SIGN, a dendritic cell-specific HIV-1 binding protein that enhances trans-infection of T cells. *Cell* 2000; 100(5): 587-597.
  - Goldberg M.V., C.H. Maris, E.L. Hipkiss, A.S. Flies, L. Zhen, R.M. Tuder, J.F. Grosso, T.J. Harris, D. Getnet, K.A. Whartenby, D.G. Brockstedt, Tw.Jr. Dubensky, L. Chen, D.M. Pardoll, and C.G. Drake. 2007. Role of PD-1 and its ligand, B7-H1, in early fate decisions of CD8 T cells. *Blood 110*: 186-192.

- 
- Granelli-Piperno A, Golebiowska A, Trumphyeller C, Siegal FP, Steinman RM. HIV-1-infected monocyte-derived dendritic cells do not undergo maturation but can elicit IL-10 production and T cell regulation. *Proc Natl Acad Sci U S A.* 2004;101:7669-74.
  - 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(3):1780-1788.
  - Grossman Z, Meier-Schellersheim M, Sousa AE, Victorino RM, Paul WE. CD4+ T-cell depletion in HIV infection: are we closer to understanding the cause? *Nat Med* 2002; 8(4):319-323.
  - Harari A, Petitpierre S, Vallelian F, Pantaleo G. Skewed representation of functionally distinct populations of virus-specific CD4 T cells in HIV-1-infected subjects with progressive disease: changes after antiretroviral therapy. *Blood.* 2004, 103(3): 966- 972.
  - Harari A, Vallelian F, Meylan PR, Pantaleo G. Functional heterogeneity of memory CD4 T cell responses in different conditions of antigen exposure and persistence. *J Immunol* 2005; 174(2):1037-1045.
  - Hazenberg MD, Hamann D, et al. T cell depletion in HIV infection : how CD4+ T cells go out of stock. *Nat Immunol* 2000; 1:285-9.
  - Hel Z, Nacsa J, Trynieszewska E, Tsai WP, Parks RW, Montefiori DC et al. Containment of simian immunodeficiency virus infection in vaccinated macaques: correlation with the magnitude of virus-specific pre- and postchallenge CD4+ and CD8+ T cell responses. *J Immunol.* 2002;169:4778-87.
  - Hellinger JA, Iwane MK, Smith JJ, Fleishman AN, Torres RA, Schrader S et al. A randomized study of the safety and antiretroviral activity of hydroxyurea combined with didanosine in persons infected with human immunodeficiency virus type 1. American Foundation for AIDS Research Community-Based Clinical Trials Network. *J Infect Dis* 2000; 181(2):540-547.
  - Henrard DR, Phillips JF, Muenz LR. Natural history of HIV-1 cell-free viremia. *JAMA* 1995; 274, 554-558.

- 
- Ho DD, Neumann AU, Perelson AS, Chen W, Leonard JM, Markowitz M. Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection. *Nature* 1995; 373:123-6.
  
  - Hori S, Sakaguchi S. Foxp3: a critical regulator of the development and function of regulatory T cells. *Microbes Infect* 2004;6:745-51.
  
  - Ide F, Nakamura T, Tomizawa M, Kawana-Tachikawa A et al, Peptide-loaded dendritic-cell vaccination followed by treatment interruption for chronic HIV-1 infection: a phase 1 trial. *J Med Virol* 2006; 78(6): 711-718
  
  - Iyasere C, Tilton JC, Johnson AJ, Younes AJ, Yassine-Diab B, Sekaly RP, Kwok WW, Migueles SA, Laborico AC, Shupert WL, Hallahan CW, Davey RT, Dybul M, Vogel S, Metcalf J, Connors M. Diminished proliferation of human immunodeficiency virus-specific CD4+ T cells is associated with diminished interleukin-2 (IL-2) production and is recovered by exogenous IL-2. *J. Virol.* 2003, 77(20): 10900-10909.
  
  - Jacobson JM, Greenspan JS, Spritzler J, Ketter N, Fahey JL, Jackson JB et al. Thalidomide for the treatment of oral aphthous ulcers in patients with human immunodeficiency virus infection. National Institute of Allergy and Infectious Diseases AIDS Clinical Trials Group. *N Engl J Med* 1997; 336(21):1487-1493.
  
  - Jacobson MA, Hardy D, Connick E, Watson J, DeBruin M. Phase 1 trial of a single dose of recombinant human interleukin-12 in human immunodeficiency virus-infected patients with 100-500 CD4 cells/microL. *J Infect Dis* 2000; 182(4):1070-1076.
  
  - Jacobson EL, Pilaro F, Smith KA. Rational interleukin 2 therapy for HIV positive individuals: daily low doses enhance immune function without toxicity. *Proc Natl Acad Sci USA* 1996; 93(19):10405-10410.
  
  - Jamieson B.D., O.O. Yang , L. Hultin , M.A. Hausner , P. Hultin , J. Matud , K. Kunstman, S. Killian , J. Altman , K. Kommander , B. Korber , J. Giorgi , and S. Wolinsky. 2003. Epitope escape mutation and decay of human immunodeficiency virus type 1-specific CTL responses. *J. Immunol.* 171: 5372-9.

- 
- Janeway Ca, Jr., Dinzani U, Portoles P, Rath S, Reich EP, Rojo J et al. Cross-linking and conformational change in T-cell receptors: role in activation and in repertoire selection. *Cold Spring Harb Symp Quant Biol* 1989; 54 Pt 2:657-666.
  
  - Janeway CA, Jr., Medzhitop R. Innate immune recognition. *Annu Rev Immunol* 2002; 20:197-216.
  
  - Janssen EM, Lemmens EE, Wolfe T, Christen U, von Herrath MG, Schoenberger SP. CD4+ T cells are required for secondary expansion and memory in CD8+ T lymphocytes. *Nature*. 2003, Feb.
  
  - Kanai T, Thomas EK, Yasutomi Y, Letvin NL. IL-15 stimulates the expansion of AIDS virus-specific CTL. *J Immunol* 1996; 157(8):3681-3687.
  
  - Kinloch-de Loes S, Hoen B, Smith DE, Autran B, Lampe FC, Phillips AN et al. Impact of therapeutic immunization on HIV-1 viremia after discontinuation of antiretroviral therapy initiated during acute infection. *J Infect Dis* 2005; 192(4):607-617.
  
  - Kinter A.L., M. Hennessey, A. Bell, S. Kern, Y. Lin, M. Daucher, M. Planta, M. McGlaughlin, R. Jackson, S.F Ziegler and A.S. Fauci. 2004. CD25(+)CD4(+) regulatory T cells from the peripheral blood of asymptomatic HIV-infected individuals regulate CD4(+) and CD8(+) HIV-specific T cell immune responses in vitro and are associated with favorable clinical markers of disease status. *J. Exp. Med.* 200:331-43.
  
  - Kobayashi N, Takata H, Yokota S, and Takiguchi M: Down-regulation of CXCR4 expression on human CD8\_ T cells during peripheral differentiation. *Eur J Immunol* 2004;34:3370–3378.
  
  - Koup RA, Saag MS, Yang LC, Clark SJ, Kappes JC, Luk KC et al. Temporal association of cellular immune responses wwith the initial control of viremia in primary human immunodeficiency virus type 1 syndrome. *J Virol* 1994; 68:4650-4655.
  
  - Kovacs JA, Vogel S, Albert JM, Falloon J, Davey RT, Jr., Walker RE et al. Controlled trial of interleukin-2 infusions in patients infected with the human immunodeficiency virus. *N Engl J Med* 1996; 335(18):1350-1356.

- 
- Kulkosky J, Nunnari G, Otero M, Calarota S, Dornadula G, Zhang H et al. Intensification and stimulation therapy for human immunodeficiency virus type 1 reservoirs in infected persons receiving virally suppressive highly active antiretroviral therapy. *J Infect Dis* 2002; 186(10):1403-1411.
  
  - Kuritzkes DR, Jacobson J, Powderly WG, Godofsky E, DeJesus E, Haas F et al. Antiretroviral activity of the anti-CD4 monoclonal antibody TNX-355 in patients infected with HIV type 1. *J Infect Dis* 2004; 189(2):286-291.
  
  - Kwon DS, Gregorio G, Bitton N, Hendrickson WA, Littman DR. DC-SIGN-mediated internalization of HIV is required for trans-enhancement of T cell infection. *Immunity*. 2002;2002 Jan;16:135-44.
  
  - Lapenta C, Santini S, Logozzi M, Spada M, Andreotti M, Pucchio T et al. Potent immune responses against HIV-1 and protection from virus challenge in hu-PBL-SCID mice immunized with inactivated virus-pulsed dendritic cells generated in the presence of IFN-alpha. *J Exp Med*. 2003;198:361-67.
  
  - Larsson M, Fonteneau J, Bhardwaj N. Cross-presentation of cell-associated antigens by dendritic cells. *Curr Top Microbiol Immunol*. 2003;276:261-75.
  
  - Letvin NL, Walker BD. Immunopathogenesis and immunotherapy in AIDS virus infections. *Nat Med*. 2003;9:861-66.
  
  - Levine BL, Bernstein WB, Aronson NE, Schlienger K, Cotte J, Perfetto S et al. Adoptive transfer of costimulated CD4+ T cells induces expansion of peripheral T cells and decreased CCR5 expression in HIV infection. *Nat Med* 2002; 8(1):47-53.
  
  - Levy Y, Gahery-Segard H, Durier C, Lascaux AS, Goujard C, Meiffredy V et al. Immunological and virological efficacy of a therapeutic immunization combined with interleukin-2 in chronically HIV-1 infected patients. *AIDS* 2005; 19(3):279-286.
  
  - Levy J, Youvan T, Lee ML. Passive hyperimmune plasma therapy in the treatment of acquired immunodeficiency syndrome: results of a 12-month multicenter double-blind controlled trial. *Blood* 1994; 84:2130-2135.

- 
- Lichterfeld M, Kaufmann DE, Yu XG, Muy SK, Addo M, Johnston MN et al. Loss of HIV-1-specific CD8+ T cell proliferation after acute HIV-1 infection and restoration by vaccine-induced HIV-1-specific CD4+ T cells. *J Exp Med* 2004; 200(6):701-712.
  - Lieberman-Blum SS, Fung HB, Bandres JC. Maraviroc: a CCR5-receptor antagonist for the treatment of HIV-1 infection. *Clin Ther.* 2008 Jul;30(7):1228-50.
  - Lisziewicz J, Bakare N, Lori F. Therapeutic vaccination for future management of HIV/AIDS. *Vaccine* 2003; 21(7-8):620-623.
  - Liu YJ. Dendritic cell subsets and lineages and their functions in innate and adaptive immunity. *Cell* 2001; 106(3): 259-262.
  - López M, V. Soriano, S. Lozano, P. Martínez, J. Sempere, J. González-Lahoz, and J. Benito. 2006. Impact of Gag sequence variability on level, phenotype, and function of anti-HIV Gag-specific CD8+ cytotoxic T lymphocytes in untreated chronically HIV-infected patients. *AIDS Res. Hum. Retroviruses* 22: 884-92.
  - Lori F, Lewis MG, Xu J, Varga G, Zinn DE, Jr., Crabbs C et al. Control of SIV rebound through structured treatment interruptions during early infection. *Science* 2000; 290(5496):1591-1593.
  - Lu W, Arraes L, Ferreira W, Andrieu JM. Therapeutic dendritic-cell vaccine for chronic HIV-1 infection. *Nat Med.* 2004;10:1359-65.
  - Lu W, Wu X, Lu Y, Guo W, Andrieu JM. Therapeutic dendritic-cell vaccine for simian AIDS. *Nat Med.* 2003;2003 Jan;9:27-32.
  - MacGregor RR, Ginsberg R, Ugen KE, Baine Y, Kang CU, Tu XM et al. T-cell responses induced in normal volunteers immunized with a DNA-based vaccine containing HIV-1 env and rev. *AIDS* 2002; 16(16):2137-2143.
  - Mackall CL, Fleisher TA, Brown MR, Andrich MP, Chen CC, Feuerstein IM et al. Age, thymopoiesis, and CD4+ T-lymphocyte regeneration after intensive chemotherapy. *N Engl J Med* 1995; 332(3):143-149.
  - Mackall CL, Hakim FT, Gress RE. T-cell regeneration: all repertoires are not created equal. *Immunol Today* 1997; 18(5):245-251.

- 
- Marin M, Rose KM, Kozak SL, Kabat D. HIV-1 Vif protein binds the editing enzyme APOBEC3G and induces its degradation. *Nat Med* 2003; 9:1398-403.
  - McConkey SJ, Reece WH, Moorthy VS, Webster D, Dunachie S, Butcher G et al. Enhanced T-cell immunogenicity of plasmid DNA vaccines boosted by recombinant modified vaccinia virus Ankara in humans. *Nat Med* 2003; 9(6):729-735.
  - McKinnon L.R., T. Blake Ball, C. Wachihi, P.J. McLaren, J.L.M. Waruk, X. Mao, S. Ramdahin, A. Omu Anzala, J. Kamene, M. Luo, K.R. Fowke and Francis A. Plummer. 2007. Epitope cross-reactivity frequently differs between central and effector memory HIV-specific CD8+ T cells. *J. Immunol* 178: 3750-3756.
  - Metzner K, Jin X, Gettie A, Bauer DE, Di Mascio M, et al. Effects of in vivo CD8(+) T cell depletion on virus replication in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine. *J Exp Med.* 2000;191:1921-31.
  - Migueles SA, Laborico AC, Shupert WL, Sabbaghian MS, Rabin R, Hallahan CW, Van Baarle D, Kostense S, Miedema F, McLaughlin M, Ehler L, Metcalf J, Liu S, Connors M. HIV-specific CD8+ T cell proliferation is coupled to perforin expression and is maintained in nonprogressors. *Nat. Immunol.* 2002.
  - Mitsuyasu RT, Anton PA, Deeks SG, Scadden DT, Connick E, Downs MT et al. Prolonged survival and tissue trafficking following adoptive transfer of CD4zeta gene-modified autologous CD4(+) and CD8(+) T cells in human immunodeficiency virus-infected subjects. *Blood* 2000; 96(3):785-793.
  - Nabel GJ, Sullivan J. Antibodies and Resistance to Natural HIV Infection. *N Eng J Med* 2000; 343: 17-19.
  - Napolitano LA, Lo JC, Gotway MB, Mulligan K, Barbour JD, Schmidt D et al. Increased thymic mass and circulating naive CD4 T cells in HIV-1-infected adults treated with growth hormone. *AIDS* 2002; 16(8):1103-1111.
  - Nestle FO, Alijagic S, Gilliet M, Sun Y, Grabbe S, Dummer R et al. Vaccination of melanoma patients with peptide- or tumor lysate-pulsed dendritic cells. *Nat Med.* 1998; 4:328-32.



- 
- Nishimura Y, Igarashi T, Haigwood NL, Sadjadpour R, Donau OK, Buckler C et al. Transfer of neutralizing IgG to macaques 6 h but not 24 h after SHIV infection confers sterilizing protection: implications for HIV-1 vaccine development. *Proc Natl Acad Sci U S A*. 2003;100:15131-36.
  - Norris PJ, Moffett HF, Yang OO, Kaufmann DE, Clark MJ, Addo MM et al. Beyond help: direct effector functions of human immunodeficiency virus type 1-specific CD4+ T cells. *J Virol* 2004; 78(16):8844-8851.
  - Nuvor SV, Van der SM, Rowland-Jones S, Whittle H, Jaye A. Natural Killer cell function is well preserved in asymptomatic human immunodeficiency virus type 2 infection but similar to that HIV-1 infection when CD4 T-cell counts fall. *J Virol* 2006; 80(5): 2529-2538.
  - Ogg GS, Jin X, Bonhoeffer S, Moss P, Nowak MA, Monrad S et al. Decay kinetics of human immunodeficiency virus-specific effector cytotoxic T lymphocytes after combination antiretroviral therapy. *J Virol* 1999; 73(1):797-800.
  - Ortiz GM, Wellons M, Brancato J, et al. Structured antiretroviral treatment interruptions in chronically HIV-1-infected subjects. *Proc Natl Acad Sci U S A*. 2001;98:13288–13293.
  - Ortiz GM, Nixon DF, Trkola A, Binley J, Jin X, Bonhoeffer S et al. HIV-1-specific immune responses in subjects who temporarily contain virus replication after discontinuation of highly active antiretroviral therapy. *J Clin Invest* 1999; 104(6):R13-R18.
  - Oxenius A, Price DA, Gunthard HF, Dawson SJ, Fagard C, Perrin L et al. Stimulation of HIV-specific cellular immunity by structured treatment interruption fails to enhance viral control in chronic HIV infection. *Proc Natl Acad Sci U S A* 2002; 99(21):13747-13752.
  - Oxenius A, Price DA, Easterbrook PJ, O'Callaghan CA, Kelleher AD, Whelan JA et al. Early highly active antiretroviral therapy for acute HIV-1 infection preserves immune function of CD8+ and CD4+ T lymphocytes. *Proc Natl Acad Sci U S A* 2000; 97(7):3382-3387.

- 
- Pakker NG, Notermans DW, de Boer RJ, Roos MT, de Wolf F, Hill A, *et al.*: Biphasic kinetics of peripheral blood T cells after triple combination therapy in HIV-1 infection: A composite of redistribution and proliferation. *Nat Med* 1998;4:208–214.
  
  - Palmer BE, Wilson CC. Effects of sustained HIV-1 plasma viremia on HIV-1 gag-specific CD4+ T cell maturation and function. *J. Immunol.* 2004, 172: 3337-3347.
  
  - Pantaleo G, Grazioni C, Fauci AS. New concepts in the immunopathology of human immunodeficiency virus infection. *N Engl J Med* 1993; 330:327-335.
  
  - Pappasavvas E, Thiel B, Pistilli M, Mackiewicz A, Farabaugh M, Moore EC, Gallo C, Gross R, Foulkes A, Mounzer K, *et al.* Differential modulation of whole blood naive and memory CD4+ and CD8+ T-cell subsets by viral replication during therapy interruption in chronically HIV-1 infected patients. Abstract 63. 10th CROI, Boston, MA. February 10-14, 2003.
  
  - Parren PW, Marx PA, Hessel AJ, Luckay A, Harouse J, Cheng-Mayer C *et al.* Antibody protects macaques against vaginal challenge with a pathogenic R5 simian/human immunodeficiency virus at serum levels giving complete neutralization in vitro. *J Virol* 2001; 75(17):8340-8347.
  
  - Patterson BK, Carlo DJ, Kaplan MH, Marecki M, Pawha S, Moss RB. Cell-associated HIV-1 messenger RNA and DNA in T-helper cell and monocytes in asymptomatic HIV-1-infected subjects on HAART plus an inactivated HIV-1 immunogen. *AIDS* 1999; 13(13):1607-1611.
  
  - Peliska JA, Benkovic SJ. Mechanism of DNA strand transfer reactions catalyzed by HIV-1 reverse transcriptase. *Science.* 1992 Nov 13;258(5085):1112-8.
  
  - 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(5255):1582-1586.
  
  - Petrovas C., J.P. Casazza, J.M. Brenchley, D.A. Price, E. Gostick, W.C. Adams, M.L. Precopio, T. Shacker, M. Roederer, D.C. Douek, and R.A. Koup. 2006. PD-1 is a regulator of virus-specific CD8+ T cell survival in HIV infection. *J. Exp. Med.* 203: 2281-92.

- 
- Phan G.K., C.E. Touloukian, J.C. Yang, N.P. Restifo, R.M. Sherry, P. Hwu, S.L. Topalian, D.J. Schwartzentruber, C. A. Seipp, L.J. Freezer, K.E. Morton, S. A. Mavroukakis, D. E. White, and S.A. Rosenberg. 2003. Immunization of patients with metastatic melanoma using both class-I and class-II-restricted peptides from melanoma-associated antigens. *J. Immunotherapy* 26(4): 349-356.
  
  - Pitcher C, Quittner C, Peterson D, Connors M, Koup RA, Maino VC et al. HIV-1 specific CD4+ T cells are detectable in most individuals with active HIV-1 infection, but decline with prolonged viral suppression. *Nat Med* 1999; 5:518-525.
  
  - Plana M, Garcia F, Gallart MT, Miro JM, and Gatell JM. Lack of T-cell proliferative response to HIV-1 antigens after one year of HAART in very early HIV-1 disease. *Lancet*. 1998; 352:1194-95.
  
  - Plana M, García F, Gallart MT, Tortajada C. Soriano A, Palou E, et al. Immunological benefits of antiretroviral therapy in very early stages of asymptomatic chronic HIV-1 infection. *AIDS* 2000; 14: 1921-1933.
  
  - Pulendran B, Palucka K, Banchereau J. Sensing pathogens and tuning immune responses. *Science* 2001; 293 (5528): 253-256.
  
  - de Quiros JC, Shupert WL, McNeil AC, Gea-Banacloche JC, Flanigan M, Savage A et al. Resistance to replication of human immunodeficiency virus challenge in SCID-Hu mice engrafted with peripheral blood mononuclear cells of nonprogressors is mediated by CD8(+) T cells and associated with a proliferative response to p24 antigen. *J Virol*. 2000;74:2023-28.
  
  - Ramsdell F. Foxp3 and natural regulatory T cells: key to a cell lineage? *Immunity* 2003;19:165-8.
  
  - Richman DD, Wrin T, Little SJ, Petropoulos CJ. Rapid evolution of the neutralizing antibody response to HIV type 1 infection. *PNAS USA*, 2003: 4144-9.
  
  - Ridge JP, Di RF, Matzinger P. A conditioned dendritic cell can be a temporal bridge between a CD4+ T-helper and a T-killer cell. *Nature* 1998; 393(6684):474-478.
  
  - Rizzardi GP, Vaccarezza M, Capiluppi B, Tambussi G, Lazzarin A, Pantaleo G. Cyclosporin A in combination with HAART in primary HIV-1 infection. *J Biol Regul Homeost Agents* 2000; 14(1):79-81.

- 
- Robbins GK, Addo MM, Troung H, Rathod A, Habeeb K, Davis B et al. Augmentation of HIV-1-specific T helper cell responses in chronic HIV-1 infection by therapeutic immunization. *AIDS* 2003; 17(8):1121-1126.
  
  - Rosenberg ES, Altfeld M, Poon SH, Phillips MN, Wilkes BM, Eldridge RL et al. Immune control of HIV-1 after early treatment of acute infection. *Nature* 2000; 407(6803):523-526.
  
  - Ruiz L, Ribera E, Bonjoch A, Romeu J, Martinez-Picado J, Paredes R et al. Role of structured treatment interruption before a 5-drug salvage antiretroviral regimen: the Retrogene Study. *J Infect Dis* 2003; 188(7):977-985.
  
  - Ruiz L, Carcelain G, Martinez-Picado J, Frost S, Marfil S, Paredes R et al. HIV dynamics and T-cell immunity after three structured treatment interruptions in chronic HIV-1 infection. *AIDS* 2001; 15(9):F19-F27.
  
  - Sallusto F, Cella M, Danieli C, Lanzavecchia A. Dendritic cells use macropinocytosis and the mannose receptor to concentrate macromolecules in the major histocompatibility complex class II compartment: downregulation by cytokines and bacterial products. *J Exp Med*. 1995;182:389-4
  
  - Sallusto F, Lanzavecchia A. Efficient presentation of soluble antigen by cultured human dendritic cells is maintained by granulocyte/macrophage colony-stimulating factor plus interleukin 4 and downregulated by tumor necrosis factor alpha. *J Exp Med*. 1994;179:1109-18.
  
  - Sauce D., J.R. Almeida, M. Larsen, L. Haro, B. Nutran, G.J. Freeman, and V. Apia. 2007. PD-1 expression on human CD8 T cells depends on both state of differentiation and activation status. *AIDS*. 21: 2005-2013.
  
  - Schmitz JE, Kuroda MJ, Santra S. Control of viremia in simian immunodeficiency virus infection by CD8+ lymphocytes. *Science* 1999; 283: 857-860.
  
  - Seddiki N, Santner-Nanan B, Martinson J, et al. Expression of interleukin (IL)-2 and IL-7 receptors discriminates between human regulatory and activated T cells. *J Exp Med* 2006;203:1693-1700.
  
  - Schadendorf D, Nestle FO. Autologous dendritic cells for treatment of advanced cancer--an update. *Recent Results Cancer Res*. 2001;158:236-48.

- 
- Shedlock DJ, Shen H. Requirement for CD4 T cell help in generating functional CD8 T cell memory. *Science*. 2003;300:337-39.
  - Sun JC, Bevan MJ. Defective CD8 T cell memory following acute infection without CD4 T cell help. *Science*. 2003;300:339-42.
  - Tan R, Xu X, Ogg GS, Hansasuta P, Dong T, Rostron T et al. Rapid death of adoptively transferred T cells in acquired immunodeficiency syndrome. *Blood* 1999; 93(5):1506-1510.
  - Temesgen Z, Siraj DS. Raltegravir: first in class HIV integrase inhibitor. *Ther Clin Risk Manag*. 2008 Apr;4(2):493-500.
  - Thiebaut R, Pellegrin I, Chene G, Viallard JF, Fleury H, Moreau JF et al. Immunological markers after long-term treatment interruption in chronically HIV-1 infected patients with CD4 cell count above 400 x 10<sup>6</sup> cells/l. *AIDS* 2005; 19(1):53-61.
  - Trabattoni D, Piconi S, Biasin M, Rizzardini G, Migliorino M, Seminari E, Boasso A, Piacentini L, Villa ML, Maserati R, Clerici M. Granule-dependent mechanisms of lysis are defective in CD8 T cells of HIV-infected, antiretroviral therapy-treated individuals. *AIDS*. 2004, 18: 859-869.
  - Truong MJ, Darcissac EC, Hermann E, Dewulf J, Capron A, Bahr GM. Interleukin-16 inhibits human immunodeficiency virus type 1 entry and replication in macrophages and in dendritic cells. *J Virol* 1999; 73(8):7008-7013.
  - Turville SG, Cameron PU, Handley A, Lin G, Pohlmann S, Doms RW et al. Diversity of receptors binding HIV on dendritic cell subsets. *Nat Immunol* 2002; 3(10):975-983.
  - Vaccari M., C.J. Trindade, D. Venzon, M. Zanetti, and G. Franchini. 2005. Vaccine-induced CD8<sup>+</sup> central memory T cells in protection from simian AIDS. *J. Immunol.* 175: 3502-7.
  - Valladeau J, Dezutter-Dambuyant C, Saeland S. Langerin/CD207 sheds light on formation of Birbeck granules and their possible function in Langerhans cells. *Immunol Res* 2003; 28: 93-107.
  - Van KY, Geijtenbeek TB. DC-SIGN: escape mechanism for pathogens. *Nat Rev Immunol* 2003;3(9):697-709.

- 
- Van Baarle D, Kostense S, van Oers MH, Hamann D, Miedema F. Failing immune control as a result of impaired CD8+ T-cell maturation: CD27 might provide a clue. *Trends Immunol.* 2002, 23: 586-591.
  
  - Van Lier RA, Ten Berge IJ, Gamadia LE. Human CD8+ T-cell differentiation in response to viruses. *Nat. Rev. Immunol.* 2003, 3: 1-8.
  
  - Veazey RS, DeMaria M, Chalifoux LV, Shvetz DE, Pauley DR, Knight HL et al. Gastrointestinal tract as a major site of CD4+ T cell depletion and viral replication in SIV infection. *Science* 1998; 280 (5362): 427-431.
  
  - Walker M, Kasproicz D, Gersuk V, et al. Induction of FoxP3 and acquisition of T regulatory activity by stimulated human CD4+CD25- T cells. *J Clin Invest* 2003;112:1437-43.
  
  - Wei X, Decker JM, Wang S et al. Antibody neutralization and escape by HIV-1. *Nature* 2003; 422: 307-312.
  
  - Wei X, Ghosh SK, Taylor ME, Johnson VA, Emini EA, Deutsch P et al. Viral dynamics in human immunodeficiency virus type 1 infection. *Nature* 1995; 373(6510):117-122.
  
  - Wherry EJ, Ahmed R. Memory CD8 T-cell differentiation during viral infection. *J. Virol.* 2004, 78(11): 5535-5545.
  
  - Whitcomb JM, Kumar R, Hughes SH. Sequence of the circle junction of human immunodeficiency virus type 1: implications for reverse transcription and integration. *J Virol.* 1990 Oct;64(10):4903-6.
  
  - Williams M.A., and M.J. Bevan. 2007. Effector and memory CTL differentiation. *Annu. Rev. Immunol.* 25: 171-92.
  
  - Wu L, KewalRamani VN. Dendritic-cell interactions with HIV: infection and viral dissemination. *Nat Rev Immunol* 2006; 6(11):859-868.
  
  - Yerly S, Perneger TV, Vora S, Hirschel B, Perrin L. Decay of cell-associated HIV-1 DNA correlates with residual replication in patients treated during acute HIV-1 infection. *AIDS* 2000; 14(18):2805-2812.

- 
- Yoshida A, Tanaka R, Murakami T, Takahashi Y, Koyanagi Y, Nakamura M et al. Induction of protective immune responses against R5 Human Immunodeficiency virus type 1 (HIV-1) infection in hu-PBL-SCID mice by intraesplenic immunization with HIV-1 pulsed dendritic cells: possible involvement of a novel factor of human CD4+ T-cell origin. *J Virol.* 2003;77:8719-28.
  - Younes SA, Yassine-Diab B, Dumont AR, Boulassel MR, Grossman Z, Routy JP, Sekaly RP. HIV-1 viremia prevents the establishment of interleukin 2-producing HIV-specific memory CD4+ T cells endowed with proliferative capacity. *J. Exp. Med.* 2003, 198(12): 1909-1922.
  - Yu XG, Addo MM, Rosenberg AS, et al. Consistent patterns in the development and immunodominance of human immunodeficiency virus type I (HIV-1)-specific CD8+ T-cell responses following acute HIV-1 infection. *J Virol.* 2002;76:8690–8701.
  - Yue FY, Kovacs CM, Dimayuga RC, Parks P, Ostrowski MA. HIV-1-specific memory CD4+ T cells are phenotypically less mature than cytomegalovirus-specific memory CD4+ T cells. *J. Immunol.* 2004, 172: 2476-2486.
  - Zhang ZQ, Notermans DW, Sedgewick G, Cavert W, Wietgreffe S, Zupancic M et al. Kinetics of CD4+ T cell repopulation of lymphoid tissues after treatment of HIV-1 infection. *Proc Natl Acad Sci U S A* 1998; 95(3):1154-1159.
  - Zhang L, Ramratnam B, Tenner-Racz K, He Y, Vesanen M, Lewin S et al. Quantifying residual HIV-1 replication in patients receiving combination antiretroviral therapy. *N Engl J Med* 1999; 340(21):1605-1613.
  - Zhang d, Shankar P, Xu Z, Harmish B, Chen G, lange C, Lee SJ, Valdez H, Lederman MM, Lieberman J. Most antiviral CD8 T cells during chronic viral infection do not express high levels of perforin and are not directly cytotoxic. *Blood.* 2003, 101(1): 226-235.
  - Zhang JY, Zhang Z, Wang X, Fu JL, Yao J, Jiao Y, Chen L, Zhang H, Wei J, Jin L, Shi M, Gao GF, Wu H, Wang FS. PD-1 up-regulation is correlated with HIV-specific memory CD8+ T-cell exhaustion in typical progressors but not in long-term nonprogressors. *Blood* 2007; 1;109(11):4671-8.