

## Bibliografia

1. Abe E, Miyaura C, Sakagami H, Takeda M, Konno K: Differentiation of mouse myeloid leukemia cells induced by 1 $\alpha$ ,25-dihydroxyvitamin D3. Proc. Natl. Acad. Sci. USA 78:4990–94, 1981.
2. Abe J, Nakamura K, Takita Y, Nakano T, Irie H, Nishii Y: Prevention of immunological disorders in MRL/l mice by a new synthetic analogue of vitamin D3: 22-oxa-1 $\alpha$ ,25-dihydroxyvitamin D3. J. Nutr. Sci. Vitaminol. 36:21–31, 1990.
3. Adam R, McMaster P, O'Grady JG, Castaing D, Klempnauer JL, Jamieson N, Neuhaus P, Lerut J, Salizzoni M, Pollard S, Muhlbacher F, Rogiers X, Garcia Valdecasas JC, Berenguer J, Jaeck D, Moreno Gonzalez E: Evolution of liver transplantation in Europe: report of the European Liver Transplant Registry. Liver Transpl 9:1231, 2003.
4. Adams JS, Gacad MA : Characterization of 1 $\alpha$ -hydroxylation of vitamin D3 sterols by cultured alveolar macrophages from patients with sarcoidosis. J. Exp. Med. 161:755–65, 1985.
5. Adorini L, Penna G, Casorati M, Davalli AM, Gregori S: Induction of transplantation tolerance by 1,25-dihydroxyvitamin D(3). Transplant Proc 33(1-2):58, 2001.
6. Alderson MR, R.J. Armitage, T.W. Tough, L. Strockbine, W.C. Fanslow and M.K. Spriggs, CD40 expression by human monocytes: regulation by cytokines and activation of monocytes by the ligand for CD40, J Exp Med 178 pp. 669–674, 1993.
7. Almerighi C, Bogdanos DP, Cholongitas V, Kraslova I, Meda F, Hussain M J, Burroughs A K, Vergani D; Immunomodulatory role of Vitamin D3 in

- primary biliary cirrhosis. Presentato all'Annual Meeting del BASL, Londra, UK, 7-9 September, 2005.
8. Barnes PF, Modlin RL, Bikle DD, Adams JS: Transpleural gradient of 1,25-dihydroxyvitamin D in tuberculosis pleuritis. *J. Clin. Invest.* 83:1527–32, 1989.
  9. Bar-Shavit Z, Noff D, Edelstein S, Meyer M, Shibolet S, Goldman R: 1,25-dihydroxyvitamin D<sub>3</sub> and the regulation of macrophage function. *Calcif. Tissue Int.* 33:673–76, 1981.
  10. Barrat FJ, D.J. Cua, A. Boonstra, D.F. Richards, C. Crain and H.F. Savelkoul: In vitro generation of interleukin 10-producing regulatory CD4+ T cells is induced by immunosuppressive drugs and inhibited by T Helper type 1 (Th1)-and Th2-inducing cytokines, *J Exp Med* 195 pp. 603–613, 2002.
  11. Bharat A, R.C. Fields, E.P. Trulock, G.A. Patterson and T. Mohanakumar, Induction of IL-10 suppressors in lung transplant patients by CD4+25+ regulatory T cells through CTLA-4 signaling, *J Immunol* 177 pp. 5631–5638, 2006.
  12. Becker BN, Hullett DA, O'Herrin JK, Malin G, Sollinger HW, DeLuca H: Vitamin D as immunomodulatory therapy for kidney transplantation. *Transplantation* 74(8):1204, 2002.
  13. Bemiss CJ, Mahon BD, Henry A, Weaver V, Cantorna MT: Interleukin-2 is one of the targets of 1,25-dihydroxyvitamin D<sub>3</sub> in the immune system. *Arch Biochem Biophys* 402(2):249, 2002.
  14. Bhalla AK: Hormones and the immune response. *Ann Rheum Dis* 48(1):1, 1989.

15. Bhalla AK, Amento EP, Clemens TL, Holick MF, Krane SM: Specific high-affinity receptors for 1,25-dihydroxyvitamin D<sub>3</sub> in human peripheral blood mononuclear cells: presence in monocytes and induction in T lymphocytes following activation. *J. Clin. Endocrinol. Metab.* 57:1308–10, 1983.
16. Bhalla AK, Amento EP, Krane SM: Differential effects of 1,25-dihydroxyvitamin D<sub>3</sub> on human lymphocytes and monocyte/macrophages: inhibition of interleukin-2 and augmentation of interleukin-1 production. *Cell Immunol* 98(2):311, 1986.
17. Bhalla AK, Amento EP, Serog B, Glimcher LH: 1,25-Dihydroxyvitamin D<sub>3</sub> inhibits antigen-induced T cell activation. *J Immunol* 133(4):1748, 1984.
18. Berer A, Skockl J, Majdic O, Wagner T, Kollars M: 1,25-dihydroxyvitamin D<sub>3</sub> inhibits dendritic cell differentiation and maturation in vitro. *Exp. Hematol.* 28:575–83, 2000.
19. Blazar BR, P.A. Taylor, A. Panoskaltsis-Mortari, J. Buhlman, J. Xu and R.A. Flavell, Blockade of CD40 ligand-CD40 interaction impairs T cell mediated alloreactivity by inhibiting mature donor T cell expansion and function after bone marrow transplantation, *J Immunol* 158 pp. 29–39, 1997.
20. Bolacchi F, M. Carbone, M. Capozzi, L. Ventura, M. Cepparulo and G. Rocchi: Effect of different activation stimuli on the cytokine response of human macrophages to CD40L, *Cytokine* 16 pp. 121–125, 2001.
21. Boonstra A, Barrat FJ, Crain C, Heath VL, Savelkoul HF, O'Garra A: 1alpha,25-Dihydroxyvitamin D<sub>3</sub> has a direct effect on naive CD4(+) T cells to enhance the development of Th2 cells. *J Immunol* 167(9):4974, 2001.
22. Bouillon R, Allewaert K, Xiang DX, Tan BK, van Baelen H: Vitamin D analogs with low affinity for the vitamin D binding protein: enhanced in vitro and decreased in vivo activity. *J. Bone Mineral Res.* 6:1051–57, 1991.

23. Branisteanu DD, Leenaerts P, van Damme B, Bouillon R: Partial prevention of active Heymann nephritis by 1 alpha, 25 dihydroxyvitamin D3. *Clin Exp Immunol* 94(3):412, 1993.
24. Branisteanu DD, Mathieu C, Bouillon R: Synergism between sirolimus and 1,25-dihydroxyvitamin D3 in vitro and in vivo. *J. Neuroimmunol.* 79:138–47 24, 1997.
25. Branisteanu DD, Waer M, Sobis H, Marcelis, Vandeputte M, Bouillon R: Prevention of murine experimental allergic encephalomyelitis: cooperative effects of cyclosporine and 1®,25 (OH)2 D3. *J. Neuroimmunol.* 61:151–60, 1995.
26. Brossart P, F. Grunebach, G. Stuhler, V.L. Reichardt, R. Mohle and L. Kanz: Generation of functional human dendritic cells from adherent peripheral blood monocytes by CD40 ligation in the absence of granulocyte-macrophage colony-stimulating factor, *Blood* 11 pp. 4238–4247, 1998.
27. Canning MO, Grotenhuis K, de Wit H, Ruwhof C, Drexhage HA: 1®,25-dihydroxyvitamin D3 (1,25(OH)2D3) hampers the maturation of fully active immature dendritic cells from monocytes. *Eur. J. Endocrinol.* 145:351–57, 2001.
28. Cantorna MT: Vitamin D and autoimmunity: is vitamin D status an environmental factor affecting autoimmune disease prevalence? *Proc Soc Exp Biol Med* 223(3):230, 2000.
29. Cantorna MT, Hayes CE, DeLuca HF: 1,25-Dihydroxyvitamin D3 reversibly blocks the progression of relapsing encephalomyelitis, a model of multiple sclerosis. *Proc Natl Acad Sci U S A* 93(15):7861, 1996.

30. Cantorna MT, Hayes CE, DeLuca HF: 1,25-Dihydroxycholecalciferol inhibits the progression of arthritis in murine models of human arthritis. *J Nutr* 128(1):68, 1998.
31. Cantorna MT, Hullett DA, Redaelli C, Brandt CR, Humpal-Winter J, Sollinger HW, Deluca HF: 1,25-Dihydroxyvitamin D3 prolongs graft survival without compromising host resistance to infection or bone mineral density. *Transplantation* 66(7):828, 1998.
32. Cantorna MT, Humpal-Winter J, DeLuca HF: Dietary calcium is a major factor in 1,25-dihydroxycholecalciferol suppression of experimental autoimmune encephalomyelitis in mice. *J Nutr* 129(11):1966, 1999.
33. Cantorna MT, Humpal-Winter J, DeLuca HF: In vivo up-regulation of interleukin-4 is one mechanism underlying the immunoregulatory effects of 1,25-dihydroxyvitamin D(3). *Arch Biochem Biophys* 377(1):135, 2000.
34. Cantorna MT, Mahon BD: Mounting evidence for vitamin D as an environmental factor affecting autoimmune disease prevalence. *Exp Biol Med (Maywood)* 229(11):1136, 2004.
35. Cantorna MT, Munsick C, Bemiss C, Mahon BD: 1,25-Dihydroxycholecalciferol prevents and ameliorates symptoms of experimental murine inflammatory bowel disease. *J Nutr* 130(11):2648, 2000.
36. Cantorna MT, Woodward WD, Hayes CE, DeLuca HF: 1,25-dihydroxyvitamin D3 is a positive regulator for the two anti-encephalitogenic cytokines TGF-beta 1 and IL-4. *J Immunol* 160(11):5314, 1998.

37. Cantorna MT, Zhu Y, Froicu M, Wittke A: Vitamin D status, 1,25-dihydroxyvitamin D<sub>3</sub>, and the immune system. *Am J Clin Nutr* 80(6 Suppl):1717S, 2004.
38. Carlberg C, Polly P: Gene regulation by vitamin D<sub>3</sub>. *Crit. Rev. Eukaryot. Gene Expr.* 8:19–42, 1998.
39. Carrington MN, Tharp-Hiltbold B, Knoth J, Ward FE: 1,25-Dihydroxyvitamin D<sub>3</sub> decreases expression of HLA class II molecules in a melanoma cell line. *J Immunol* 140(11):4013, 1988.
40. Casteels KM, Mathieu C, Waer M, Valckx D, Overbergh L: Prevention of type I diabetes in non-obese diabetic mice by late intervention with non-hypercalcemic analogs of 1,25-dihydroxyvitamin D<sub>3</sub> in combination with a short course of cyclosporine A. *Endocrinology* 139:95–102, 1998.
41. Casteels K, Waer M, Bouillon R, Depovere J, Vackx D: 1,25-dihydroxyvitamin D<sub>3</sub> restores sensitivity to cyclophosphamide-induced apoptosis in non-obese diabetic (NOD) mice and protects against diabetes. *Clin. Exp. Immunol.* 112:181–87, 1998.
42. Cerny A, Chisari FV: Pathogenesis of Chronic Hepatitis C: Immunological features of hepatic injury and viral persistence. *Hepatology* 30, 595-601, 1999.
43. Chang TL, C.M. Shea, S. Urioste, R.C. Thompson, W.H. Boom and A.K. Abbas, Heterogeneity of helper/inducer T lymphocytes III. Responses of IL-2- and IL-4-producing (Th1 and Th2) clones to antigens presented by different accessory cells, *J Immunol* 145 pp. 2803–2808, 1990.
44. Chaussabel D, F. Jacobs, J. de Jonge, M. de Veerman, Y. Carlier and K. Thielemans, CD40 ligation prevents trypanosoma cruzi infection through interleukin-12 upregulation, *Infect Immun* 67 pp. 1929–1934, 1999.

45. Chollet-Martin S, Depoix JP, Hvass U, Pansard Y, Vissuzaine C, Gougerot-Pocidalo MA: Raised plasma levels of tumor necrosis factor in heart allograft rejection. *Transplant Proc* 22:283, 1990.
46. Cippitelli M, Santoni A: Vitamin D3: a transcriptional modulator of the interferon-gamma gene. *Eur. J. Immunol.* 28: 3017–30, 1998.
47. Cippitelli M, Fionda C, Di Bona D, Di Rosa F, Lupo A, Piccoli M, Frati L, Santoni A: Negative regulation of CD95 ligand gene expression by vitamin D3 in T lymphocytes. *J Immunol* 168(3):1154, 2002.
48. Clavreul A, C.L. D'hellencourt, C. Montero-Menei, G. Potron and D. Couez, Vitamin D differentially regulates B7.1 and B7.2 expression on human peripheral blood monocytes, *Immunology* 95 (2) pp. 272–277, 1998.
49. Connor RI, Rigby WF: 1 alpha,25-dihydroxyvitamin D3 inhibits productive infection of human monocytes by HIV-1. *Biochem Biophys Res Commun* 176(2):852, 1991.
50. Dam TN, Kang S, Nickoloff BJ, Voorhees JJ: 1alpha,25-dihydroxycholecalciferol and cyclosporine suppress induction and promote resolution of psoriasis in human skin grafts transplanted on to SCID mice. *J Invest Dermatol* 113(6):1082, 1999.
51. D'Ambrosio D, Cipitelli M, Coccio G, Mazzeo D, Di Lucia P: Inhibition of IL-12 production by 1,25-dihydroxyvitaminD3: involvement of NF-B downregulation in transcriptional repression of the p40 gene. *J. Clin. Invest.* 101:252–62, 1998.
52. Delafuente JC: Immunosenescence. Clinical and pharmacologic considerations. *Med Clin North Am* 69(3):475, 1985.
53. De Luca HF, Cantorna MT: Vitamin D: its role and uses in immunology. *Faseb J* 15(14):2579, 2001.

54. Elst EF, Van Suijlekom-Smit LW, Oranje AP: Treatment of linear scleroderma with oral 1,25-dihydroxyvitamin D<sub>3</sub> (calcitriol) in seven children. *Pediatr Dermatol* 16(1):53, 1999.
55. The EURODIAB substudy 2 study group: Vitamin D supplement in early childhood and risk for type I (insulindependent) diabetes mellitus. *Diabetologia* 42:51–54, 1999.
56. Fournier C, Gepner P, Sadouk M, Charreire J: In vivo beneficial effects of cyclosporin A and 1,25-dihydroxyvitamin D<sub>3</sub> on the induction of experimental autoimmune thyroiditis. *Clin Immunol Immunopathol* 54(1):53, 1990.
57. Froicu M, Weaver V, Wynn TA, McDowell MA, Welsh JE, Cantorna MT: A crucial role for the vitamin D receptor in experimental inflammatory bowel diseases. *Mol Endocrinol* 17(12):2386, 2003.
58. Foy TM, A. Aruffo, J. Bajorath, J.E. Buhlmann and R.J. Noelle, Immune regulation by CD40 and its ligand gp39, *Annu Rev Immunol* 14 pp. 591–617, 1996.
59. Gajewski TF, M. Pinnas, T. Wong and F.W. Fitch, Murine Th1 and Th2 clones proliferate optimally in response to distinct antigen-presenting cell populations, *J Immunol* 146 pp. 1750–1758, 1991.
60. Golshayan D, Buhler L, Lechler RI, Pascual M From current immunosuppressive strategies to clinical tolerance of allografts. *Transpl Int* 20:12, 2007.
61. Gorczynski RM, Adams RB, Levy GA, Chung SW: Correlation of peripheral blood lymphocyte and intragraft cytokine mRNA expression with rejection in orthotopic liver transplantation. *Surgery* 120:496, 1996.

62. Goules A, A.G. Tzioufas, M.N. Manousakis, K.A. Kirou, M.K. Crow and J.G.E. Routsias, Levated levels of soluble CD40 ligand (sCD40L) in serum of patients with systemic autoimmune diseases, *J Autoimmun* 26 pp. 165–171, 2006.
63. Gregori S, Casorati M, Amuchastegui S, Smiroldo S, Davalli A, Adorini L: Transplantation tolerance by 1,25-dihydroxyvitamin D(3)-induced costimulation blockade. *Transplant Proc* 33(1-2):219, 2001.
64. Gregori S, Casorati M, Amuchastegui S, Smiroldo S, Davalli AM, Adorini L: Regulatory T cells induced by 1 alpha,25-dihydroxyvitamin D3 and mycophenolate mofetil treatment mediate transplantation tolerance. *J Immunol* 167(4):1945, 2001.
65. Gregori S, Giarratana N, Smiroldo S, Uskokovic M, Adorini L: A 1alpha,25-dihydroxyvitamin D(3) analog enhances regulatory T-cells and arrests autoimmune diabetes in NOD mice. *Diabetes* 51(5):1367, 2002.
66. Grewal IS and R.A. Flavell, The CD40 ligand: at the centre of the immune universe?, *Immunol Res* 16, pp. 59–70, 1997.
67. Griffin MD, Lutz W, Phan VA, Bachman LA, McKean DJ, Kumar R: Potent inhibition of dendritic cell differentiation and maturation by vitamin D analogs. *Biochem. Biophys. Res. Comm.* 270:701–8, 2000.
68. Griffin MD, Lutz W, Phan VA, Bachman LA, McKean DJ, Kumar R: Dendritic cell modulation by 1®,25 dihydroxyvitamin D3 and its analogs: a vitamin D receptor-dependent pathway that promotes a persistent state of immaturity in vitro and in vivo. *Proc. Natl. Acad. Sci. USA* 98:6800–5, . 2001.
69. Guerkov RE, Targoni OS, Kreher CR, Boehm BO, Herrera MT, Tary-Lehmann M, Lehmann PV, Schwander SK: Detection of low-frequency

- antigen-specific IL-10-producing CD4(+) T cells via ELISPOT in PBMC: cognate vs. nonspecific production of the cytokine. *J Immunol Methods* 279(1-2):111, 2003.
70. Guillonneau C, V. Aubry, K. Renaudin, C. Séveno, C. Usal and K. Tezuka, Inhibition of chronic rejection and development of tolerogenic T cells after ICOS-ICOSL and CD40-CD40L co-stimulation blockade, *Transplantation* 80 pp. 546–554, 2005.
71. Gysemans C, Van Etten E, Overbergh L, Verstuyf A, Waer M: Treatment of autoimmune diabetes recurrencecin non-obese diabetic mice by mouse interferon- $\beta$  in combination with an analogue of 1®,25-dihydroxyvitamin D3. *Clin. Exp. Immunol.* 128:213–20, 2002.
72. Heath WR, Kurts C, Miller JFAP, Carbone FR: Cross-tolerance: a pathway for inducing tolerance to peripheral tissue antigens. *J. Exp. Med.* 187:1549–53, 1998.
73. Hollenbaugh D, H.D. Ochs, R.J. Noelle, J.A. Ledbetter and A. Aruffo, The role of CD40 and its ligand in the regulation of the immune response, *Immunol Rev* 138 pp. 23–37, 1994.
74. Hullett DA, Cantorna MT, Redaelli C, Humpal-Winter J, Hayes CE, Sollinger HW, Deluca HF: Prolongation of allograft survival by 1,25-dihydroxyvitamin D3. *Transplantation* 66(7):824, 1998.
75. Hypponen E, Laara E, Reunanen A, Jarvelin MR, Virtanen SM: Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. *Lancet* 358:1500, 2001.
76. Iho S, Takahashi T, Kura F, Sugiyama H, Hoshino T: The effect of 1,25-dihydroxyvitamin D3 on in vitro immunoglobulin production in human B cells. *J Immunol* 136(12):4427, 1986.

77. Imagawa DK, Millis JM, Olthoff KM, Derus LJ, Chia D, Sugich LR, Ozawa M, Dempsey RA, Iwaki Y, Levy PJ: The role of tumor necrosis factor in allograft rejection. I. Evidence that elevated levels of tumor necrosis factor-alpha predict rejection following orthotopic liver transplantation. *Transplantation* 50:219, 1990.
78. Jensen J, M. Krakauer and F. Sellebjerg, Increased T cell expression of CD154 (CD40-ligand) in multiple sclerosis, *Eur J Neurol* 8 pp. 321–328, 2001.
79. Johnsson C, Binderup L, Tufveson G: Vitamin D analogues for immunosuppression: a comparison between various routes of administration. *Transplant Proc* 27(6):3538, 1995.
80. Johnsson C, Binderup L, Tufveson G: The effects of combined treatment with the novel vitamin D analogue MC 1288 and cyclosporine A on cardiac allograft survival. *Transpl Immunol* 3(3):245, 1995.
81. Johnsson C, Tufveson G: MC 1288a vitamin D analogue with immunosuppressive effects on heart and small bowel grafts. *Transpl Int* 7(6):392, 1994.
82. Jonuleit H, E. Schmitt, G. Schuler, J. Knop and A.H. Enk, Induction of interleukin 10-producing, nonproliferating CD4+ T cells with regulatory properties by repetitive stimulation with allogenic immature human dendritic cells, *J Exp Med* 192 pp. 1213–1222, 2000.
83. Jordan SC, Lemire JM, Sakai RS, Toyoda M, Adams JS: Exogenous interleukin-2 does not reverse the immunoinhibitory effects of 1,25-dihydroxyvitamin D<sub>3</sub> on human peripheral blood lymphocyte immunoglobulin production. *Mol Immunol* 27(1):95, 1990.

84. Kang S, Yi S, Griffiths CE, Fancher L, Hamilton TA, Choi JH: Calcipotriene-induced improvement in psoriasis is associated with reduced interleukin-8 and increased interleukin-10 levels within lesions. *Br J Dermatol* 138(1):77, 1998.
85. Kato K, E. Santana-Sahagun, L.Z. Rassenti, M.H. Weisman, N. Tamura and S. Kobayashi: The soluble CD40 ligand sCD154 in systemic lupus erythematosus, *J Clin Invest* 104 pp. 947–995, 1999.
86. Kiener P.A., P. Moran-Davis, B.M. Rankin, A.F. Wahl, A. Aruffo and D. Hollenbaugh, Stimulation of CD40 with purified soluble gp 39 induces proinflammatory responses in human monocytes, *J Immunol* 155 pp. 4917–4925, 1995.
87. Komori T, Nakano T, Ohsugi Y, Sugawara Y: The effect of 1 alpha-hydroxyvitamin D3 on primary antibody formation in mice. *Immunopharmacology* 9(3):141, 1985.
88. Koshy M, D. Berger and M.K. Crow, Increased expression of CD40 ligand on systemic lupus erythematosus lymphocytes, *J Clin Invest* 98 pp. 826–837, 1996.
89. Kreher CR, Dittrich MT, Guerkov R, Boehm BO, Tary-Lehmann M: CD4+ and CD8+ cells in cryopreserved human PBMC maintain full functionality in cytokine ELISPOT assays. *J Immunol Methods* 278(1-2):79, 2003.
90. Koizumi T, NakaoY, Matsui T, Nakagawa T, Matsuda S: Effects of corticosteroid and 1,24R-dihydroxy-vitamin D3 administration on lymphoproliferation and autoimmune disease in MRL/MPlpr/lpr mice. *Int. Arch. Allergy Appl. Immunol.* 77:396–404, 1985.
91. Lederer SR, N. Friedrich, R. Gruber, R. Landgraf, M. Toepfer and T. Sitter, Reduced CD40L expression on ex vivo activated CD4+ T lymphocytes from

patients with excellent renal allograft function measured with a rapid whole blood flow cytometry procedure, *Int Arch Allergy Immunol* 133 pp. 276–284, 2004.

92. Lemire J: 1,25-Dihydroxyvitamin D<sub>3</sub>--a hormone with immunomodulatory properties. *Z Rheumatol* 59 Suppl 1:24, 2000.
93. Lemire JM: Immunomodulatory role of 1,25-dihydroxyvitamin D<sub>3</sub>. *J Cell Biochem* 49(1):26, 1992.
94. Lemire JM: Immunomodulatory actions of 1,25-dihydroxyvitamin D<sub>3</sub>. *J Steroid Biochem Mol Biol* 53(1-6):599, 1995.
95. Lemire JM, Adams JS: 1,25-Dihydroxyvitamin D<sub>3</sub> inhibits the passive transfer of cellular immunity by a myelin basic protein-specific T cell clone. *J Bone Miner Res* 7(2):171, 1992.
96. Lemire JM, Adams JS, Kermani-Arab V, Bakke AC, Sakai R, Jordan SC: 1,25-Dihydroxyvitamin D<sub>3</sub> suppresses human T helper/inducer lymphocyte activity in vitro. *J Immunol* 134(5):3032, 1985.
97. Lemire JM, Adams JS, Sakai R, Jordan SC: 1 alpha,25-dihydroxyvitamin D<sub>3</sub> suppresses proliferation and immunoglobulin production by normal human peripheral blood mononuclear cells. *J Clin Invest* 74(2):657, 1984.
98. Lemire JM, Archer DC, Khulkarni A, Ince A, Uskokovic MR, Stepkowski S: Prolongation of the survival of murine cardiac allografts by the vitamin D<sub>3</sub> analogue 1,25-dihydroxy-delta 16-cholecalciferol. *Transplantation* 54(4):762, 1992.
99. Lemire JM, Ince A, Takashima M: 1,25-Dihydroxyvitamin D<sub>3</sub> attenuates the expression of experimental murine lupus of MRL/l mice. *Autoimmunity* 12(2):143, 1992.

100. Lemire JM, Archer DC, Reddy GS: 1,25-Dihydroxy-24-Oxo-16ene-vitamin D<sub>3</sub>, a renal metabolite of the vitamin D analog 1,25-dihydroxy-16ene-vitamin D<sub>3</sub>, exerts immunosuppressive activity equal to its parent without causing hypercalcemia in vivo. *Endocrinology* 135(6):2818, 1994.
101. Lemire JM, Archer DC, Beck L, Spiegelberg HL: Immunosuppressive actions of 1,25-dihydroxyvitamin D<sub>3</sub>: preferential inhibition of Th1 functions. *J Nutr* 125(6 Suppl):1704S, 1995.
102. Lewin E, Olgaard K: The in vivo effect of a new, in vitro, extremely potent vitamin D<sub>3</sub> analog KH1060 on the suppression of renal allograft rejection in the rat. *Calcif Tissue Int* 54(2):150, 1994.
103. Lillevang ST, Rosenkvist J, Andersen CB, Larsen S, Kemp E, Kristensen T: Single and combined effects of the vitamin D analogue KH1060 and cyclosporin A on mercuric-chloride-induced autoimmune disease in the BN rat. *Clin. Exp. Immunol.* 88:301–6, 1992.
104. Liossis SN and P.P. Sfikakis, Costimulation blockade in the treatment of rheumatic diseases, *BioDrugs* 18 pp. 95–102, 2004.
105. Liu MF, S.C. Chao, C.R. Wang and H.Y. Lei, Expression of CD40 and CD40 ligand among cell populations within rheumatoid synovial compartment, *Autoimmunity* 34 pp. 107–113, 2001.
106. Lu I, Gilleaudeau P, McLane JA, Heftler N, Kamber M, Gottlieb S, Krueger JG, Gottlieb AB: Modulation of epidermal differentiation, tissue inflammation, and T-lymphocyte infiltration in psoriatic plaques by topical calcitriol. *J Cutan Pathol* 23(5):419, 1996.
107. Luscinskas FW, Cybulsky MI, Kiely JM, Peckins CS, Davis VM, Gimbrone MA, Jr.: Cytokine-activated human endothelial monolayers support enhanced neutrophil transmigration via a mechanism involving both

- endothelial-leukocyte adhesion molecule-1 and intercellular adhesion molecule-1. *J Immunol* 146:1617, 1991.
108. Mahon BD, Gordon SA, Cruz J, Cosman F, Cantorna MT: Cytokine profile in patients with multiple sclerosis following vitamin D supplementation. *J Neuroimmunol* 134(1-2):128, 2003.
  109. Mahon BD, Wittke A, Weaver V, Cantorna MT: The targets of vitamin D depend on the differentiation and activation status of CD4 positive T cells. *J Cell Biochem* 89(5):922, 2003.
  110. Mahon BD, Gordon SA, Cruz J, Cosman F, Cantorna MT: Cytokine profile in patients with multiple sclerosis following vitamin D supplementation. *J Neurol* 134: 128-132, 2003.
  111. Manga DF, G. Welch and S. Walml, Lipopolysaccharide, tumor necrosis factor- $\alpha$ , and IL-1 prevent programmed cell death (apoptosis) in human peripheral blood monocytes, *J Immunol* 146 pp. 1541–1546, 1991.
  112. Mangan DF and S. Wahl, Differential regulation of human monocyte programmed cell death (apoptosis) by chemotactic factors and pro-inflammatory cytokines, *J Immunol* 147 pp. 3408–3412, 1991.
  113. Manolagas SC, Provvedini DM, Murray EJ, Tsoukas CD, Deftos LJ: The antiproliferative effect of calcitriol on human peripheral blood mononuclear cells. *J Clin Endocrinol Metab* 63(2):394, 1986.
  114. Manolagas SC, Provvedini DM, Tsoukas CD: Interactions of 1,25-dihydroxyvitamin D3 and the immune system. *Mol Cell Endocrinol* 43(2-3):113, 1985.
  115. Manolagas SC, Werntz DA, Tsoukas CD, Provvedini DM, Vaughan JH: 1,25- dihydroxyvitamin D3 receptors in lymphocytes from patients with rheumatoid arthritis . *J. Lab. Clin. Med.* 108:596–600, 1986.

116. Martinez OM, Krams SM, Sterneck M, Villanueva JC, Falco DA, Ferrell LD, Lake J, Roberts JP, Ascher NL: Intragraft cytokine profile during human liver allograft rejection. *Transplantation* 53:449, 1992.
117. Mathieu C, Laureys J, Sobis H, Vandeputte M, Waer M, Bouillon R. 1,25-dihydroxyvitamin D3 prevents insulitis in NOD mice. *Diabetes* 41:1491–95, 1992.
118. Mathieu C, Van Etten E, Gysemans C, Decallonne B, Kato S: In vitro and in vivo analysis of the immune system of vitamin D receptor knockout mice. *J. Bone Mineral Res.* 16:2057–65, 2001.
119. Mattner F, Smiroldo S, Galbiati F, Muller M, Di Lucia P, Poliani PL, Martino G, Panina-Bordignon P, Adorini L: Inhibition of Th1 development and treatment of chronic-relapsing experimental allergic encephalomyelitis by a non-hypercalcemic analogue of 1,25-dihydroxyvitamin D(3). *Eur J Immunol* 30(2):498, 2000.
120. Mc Callum E.V. *J Biol Chem* 53: 293, 1922.
121. Meehan TF, DeLuca HF: CD8+ T cells are not necessary for 1<sup>®</sup>,25-dihydroxyvitamin D3 to suppress experimental autoimmune encephalomyelitis in mice. *Proc. Natl. Acad. Sci. USA* 99: 5557–60, 2002.
122. Meehan MA, Kerman RH, Lemire JM: 1,25-Dihydroxyvitamin D3 enhances the generation of nonspecific suppressor cells while inhibiting the induction of cytotoxic cells in a human MLR. *Cell Immunol* 140(2):400, 1992.
123. Mellman I, Steinman RM: Dendritic cells: specialized and regulated antigen processing machines. *Cell* 106:255–58, 2001.
124. Merino F, Alvarez-Mon M, de la Hera A, Ales JE, Bonilla F, Durantez A: Regulation of natural killer cytotoxicity by 1,25-dihydroxyvitamin D3. *Cell Immunol* 118(2):328, 1989.

125. Merlino LA, J. Curtis, T.R. Mikuls, J.R. Cerhan, L.A. Criswell and K.G. Saag, Iowa Women's Health Study. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study, *Arthritis Rheum* 50 pp. 72–77, 2004.
126. Mosmann TR, Sad S: The expanding universe of T-cell subsets: Th1, Th2 and more. *Immunol Today* 17:138, 1996.
127. Muller K, Gram J, Bollerslev J, Diamant M, Barington T, Hansen MB, Bendtzen K: Down-regulation of monocyte functions by treatment of healthy adults with 1 alpha,25 dihydroxyvitamin D3. *Int J Immunopharmacol* 13(5):525, 1991.
128. Müller K, P.M. Haahr, M. Diamant, K. Rieneck, A. Kharazmi and K. Bendtzen: 1,25-Dihydroxyvitamin D3 inhibits cytokine production by human blood monocytes at the post-transcriptional level, *Cytokine* 4, pp. 506–512, 1992.
129. Munger KL, S.M. Zhang, E. O'Reilly, M.A. Hernán, M.J. Olek and W.C. Willett: Vitamin D intake and incidence of multiple sclerosis, *Neurology* 62 pp. 60–65, 2004.
130. Nashold FE, Miller DJ, Hayes CE: 1,25-dihydroxyvitamin D3 treatment decreases macrophage accumulation in the CNS of mice with experimental autoimmune encephalomyelitis. *J Neuroimmunol* 103(2):171, 2000.
131. O'Herrin JK, Hullett DA, Heisey DM, Sollinger HW, Becker BN: A retrospective evaluation of 1,25-dihydroxyvitamin D(3) and its potential effects on renal allograft function. *Am J Nephrol* 22(5-6):515, 2002.
132. Overbergh L, Decallonne B, Valckx D, Verstuyf A, Depovere J: Identification and immune regulation of 25-hydroxyvitamin D-1-®-hydroxylase in murine macrophages. *Clin. Exp. Immunol.* 120:139–46, 2000.

133. Overbergh L, Decallonne B, Waer M, Rutgeerts O, Valckx D: 1<sup>®</sup>,25-dihydroxyvitamin D3 induces an autoantigen-specific T-helper 1/T-helper 2 immune shift in NOD mice immunized with GAD65 (p524-542). *Diabetes* 49:1301–7, 2000.
134. Penna G, Adorini L: 1<sup>®</sup>,25-dihydroxyvitamin D3 inhibits differentiation, maturation, activation, and survival of dendritic cells leading to impaired alloreactive T cell activation. *J. Immunol.* 164:2405–11, 2000.
135. Penna G, S. Amuchastegui, N. Giarratana, K.C. Daniel, M. Vulcano and S. Sozzani: 1,25-Dihydroxyvitamin D3 selectively modulates tolerogenic properties in myeloid but not plasmacytoid dendritic cells, *J Immunol* 178 pp. 145–153, 2007.
136. Piemonti L, Monti P, Sironi M, Fraticelli P, Leono BE: Vitamin D3 affects differentiation, maturation, and function of human monocyte-derived dendritic cells. *J. Immunol.* 164:4443–51, 2000.
137. Platz KP, Mueller AR, Rossaint R, Steimuller T, Lemmens HP, Lobeck H, Neuhaus P: Cytokine pattern during rejection and infection after liver transplantation--improvements in postoperative monitoring? *Transplantation* 62:1441, 1996.
138. Provvedini DM, Tsoukas CD, Deftos LJ, Manolagas SC: 1,25-dihydroxyvitamin D3 receptors in human leukocytes. *Science* 221:1181–83, 1983.
139. Provvedini DM, Tsoukas CD, Deftos LJ, Manolagas SC: 1 alpha,25-Dihydroxyvitamin D3-binding macromolecules in human B lymphocytes: effects on immunoglobulin production. *J Immunol* 136(8):2734, 1986.

140. Provvedini DM, Manolagas SC: 1 $\alpha$ ,25-dihydroxyvitamin D3 receptor distribution effects subpopulations of normal human T lymphocytes. *J. Clin. Endocrinol. Metab.* 68:774–79, . 1989.
141. Redaelli CA, Wagner M, Gunter-Duwe D, Tian YH, Stahel PF, Mazzucchelli L, Schmid RA, Schilling MK: 1 $\alpha$ ,25-dihydroxyvitamin D3 shows strong and additive immunomodulatory effects with cyclosporine A in rat renal allotransplants. *Kidney Int* 61(1):288, 2002.
142. Redaelli CA, Wagner M, Tien YH, Mazzucchelli L, Stahel PF, Schilling MK, Dufour JF: 1  $\alpha$ ,25-Dihydroxycholecalciferol reduces rejection and improves survival in rat liver allografts. *Hepatology* 34(5):926, 2001.
143. Reinhardt TA, Horst RL, Littledike ET, Beitz DC: 1,25-dihydroxyvitamin D3 in bovine thymus gland. *Biochem. Biophys. Res. Comm.* 106:1012–18, 1982.
144. Reichel H, Koeffler HP, Tobler A, Norman AW: 1 $\alpha$ ,25-dihydroxyvitamin D3 inhibits  $\gamma$ -interferon synthesis by normal human peripheral blood lymphocytes. *Proc. Natl. Acad. Sci. USA* 84:3385–89, 1987.
145. Rigby WF: The immunobiology of vitamin D. *Immunol Today* 9(2):54, 1988.
146. Rigby WF, Denome S, Fanger MW: Regulation of lymphokine production and human T lymphocyte activation by 1,25-dihydroxyvitamin D3. Specific inhibition at the level of messenger RNA. *J Clin Invest* 79(6):1659, 1987.
147. Rigby WF, Hamilton BJ, Waugh MG: 1,25-Dihydroxyvitamin D3 modulates the effects of interleukin 2 independent of IL-2 receptor binding. *Cell Immunol* 125(2):396, 1990.

148. Rigby WF, Noelle RJ, Krause K, Fanger MW: The effects of 1,25-dihydroxyvitamin D<sub>3</sub> on human T lymphocyte activation and proliferation: a cell cycle analysis. *J Immunol* 135(4):2279, 1985.
149. Rigby WF, Shen L, Ball ED, Guyre PM, Fanger MW: Differentiation of a human monocytic cell line by 1,25-dihydroxyvitamin D<sub>3</sub> (calcitriol): a morphologic, phenotypic, and functional analysis. *Blood* 64(5):1110, 1984.
150. Rigby WF, Stacy T, Fanger MW: Inhibition of T lymphocyte mitogenesis by 1,25-dihydroxyvitamin D<sub>3</sub> (calcitriol). *J Clin Invest* 74(4):1451, 1984.
151. Rigby WF, Waugh M, Graziano RF: Regulation of human monocyte HLA-DR and CD4 antigen expression, and antigen presentation by 1,25-dihydroxyvitamin D<sub>3</sub>. *Blood* 76(1):189, 1990.
152. Rigby WF, Waugh MG: Decreased accessory cell function and costimulatory activity by 1,25-dihydroxyvitamin D<sub>3</sub>-treated monocytes. *Arthritis Rheum* 35(1):110, 1992.
153. Rigby WF, Yirinec B, Oldershaw RL, Fanger MW: Comparison of the effects of 1,25-dihydroxyvitamin D<sub>3</sub> on T lymphocyte subpopulations. *Eur J Immunol* 17(4):563, 1987.
154. Saggese G, Federico G, Balestri M, Toniolo A: Calcitriol inhibits the PHA-induced production of IL-2 and IFN-gamma and the proliferation of human peripheral blood leukocytes while enhancing the surface expression of HLA class II molecules. *J Endocrinol Invest* 12(5):329, 1989.
155. Schirren CA, Jung M, Worzfeld T, Mamin M, Baretton GB, Gruener NH, Gerlach JT, Diepolder HM, Zachoval R, Pape GR: Cytokine profile of liver- and blood-derived nonspecific T cells after liver transplantation: T helper cells type 1/0 lymphokines dominate in recurrent hepatitis C virus infection and rejection. *Liver Transpl* 6:222, 2000.

156. Schleithoff S, Zittermann A, Tenderich G, Berthold H, Stehle P, Koerfer R: Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double blind, randomized, placebo-controlled trial. *Am J Clin Nutr* 83: 754-759, 2006.
157. Simmons JD, Mullighan C, Welsh KI, Jewell DP: Vitamin D receptor gene polymorphism: association with Crohn's disease susceptibility. *Gut* 47:211–14, . 2000.
158. Staeva-Vieira TP, Freedman LP: 1,25-dihydroxyvitamin D<sub>3</sub> inhibits IFN-gamma and IL-4 levels during in vitro polarization of primary murine CD4+ T cells. *J Immunol* 168(3):1181, 2002.
159. Stein M, A. Keshav, N. Harris and S. Gordon, Interleukin 4 potently enhances murine macrophage mannose receptor activity: a marker of alternative immunologic macrophage activation, *J Exp Med* 176 pp. 287–292, 1992.
160. Stio M, Treves C, Celli A, Tarantino O, d'Albasio G, Bonanomi AG: Synergistic inhibitory effect of cyclosporin A and vitamin D derivatives on T-lymphocyte proliferation in active ulcerative colitis. *Am J Gastroenterol* 97(3):679, 2002.
161. Takeuchi A, Reddy GS, Kobayashi T, Okano T, Park J, Sharma S: Nuclear factor of activated T cells (NFAT) as a molecular target for 1alpha,25-dihydroxyvitamin D<sub>3</sub>-mediated effects. *J Immunol* 160(1):209, 1998.
162. Tamura N, S. Kobayashi, K. Kato, H. Bando, K. Haruta and M. Oyanagi: Soluble CD154 in rheumatoid arthritis: elevated plasma levels in cases with vasculitis, *J Rheumatol* 228 pp. 2583–2590, 2001.
163. Thomasset M: [Vitamin D and the immune system]. *Pathol Biol (Paris)* 42:163, 1994.

164. Toss G, Symreng T: Delayed hypersensitivity response and vitamin D deficiency. *Int. J. Vitam. Nutr. Res.* 53:27–31, 1983.
165. Tsoukas CD, Provvedini DM, Manolagas SC: 1,25-dihydroxyvitamin D<sub>3</sub>: a novel immunoregulatory hormone. *Science* 224(4656):1438, 1984.
166. Tsoukas CD, D. Watry, S.S. Escobar, D.M. Provvedini, C.A. Dinarello and F.G. Hustmyer: Inhibition of interleukin-1 production by 1,25-dihydroxyvitamin D<sub>3</sub>, *J Clin Endocrinol Metab* 69, pp. 127–133, 1989.
167. Vanham G, Ceuppens JL, Bouillon R: T lymphocytes and their CD4 subset are direct targets for the inhibitory effect of calcitriol. *Cell Immunol* 124:320, 1989.
168. Van Etten E, Branisteanu DD, Verstuyf A, Waer M, Bouillon R, Mathieu C: Analogs of 1,25-dihydroxyvitamin D<sub>3</sub> as dose-reducing agents for classical immunosuppressants. *Transplantation* 69(9):1932, 2000.
169. Van Halteren AG, van Etten E, de Jong EC, Bouillon R, Roep BO, Mathieu C: Redirection of human autoreactive T-cells upon interaction with dendritic cells modulated by TX527, an analog of 1,25 dihydroxyvitamin D<sub>3</sub>. *Diabetes* 51:2119–25, 2002.
170. Veldman CM, Cantorna MT, DeLuca HF: Expression of 1,25-dihydroxyvitamin D(3) receptor in the immune system. *Arch Biochem Biophys* 374(2):334, 2000.
171. Veyron P, Pamphile R, Binderup L, Touraine JL: Two novel vitamin D analogues, KH 1060 and CB 966, prolong skin allograft survival in mice. *Transpl Immunol* 1(1):72, 1993.
172. Walunas TL, C.Y. Bakker and J.A. Bluestone, CTLA-4 ligation blocks CD28-dependent T cell activation, *J Exp Med* 183 pp. 2541–2550, 1996.

173. Wittke A, Weaver V, Mahon BD, August A, Cantorna MT: Vitamin D receptor-deficient mice fail to develop experimental allergic asthma. *J Immunol* 173(5):3432, 2004.
174. Xu H, A. Soruri, R.K.H. Gieseler and J.H. Peters, 1,25-Dihydroxyvitamin D<sub>3</sub> exerts opposing effects to IL-4 on MHC-class II antigen expression, accessory activity and phagocytosis of human monocytes, *Scand J Immunol* 38 pp. 535–540, 1993.
175. Yang S, Smith C, Prahl JM, Luo X, DeLuca HF: Vitamin D deficiency suppresses cell-mediated immunity in vivo. *Arch. Biochem. Biophys.* 303:98–106, 993.
176. Yang S, Smith C, DeLuca HF: 1®,25-dihydroxyvitamin D<sub>3</sub> and 19-nordihydroxyvitamin D<sub>2</sub> suppress immunoglobulin production and thymic lymphocyte proliferation in vivo. *Biochem. Biophys. Acta* 1158:279–86, 1993.
177. Yu X-P, Bellido T, Manolagas SC: Down-regulation of NF-·B protein levels in activated human lymphocytes by 1,25-dihydroxyvitamin D<sub>3</sub>. *Proc. Natl. Acad. Sci. USA* 92:10990–94, 1995.
178. Zarrabeitia MT, Riancho JA, de Francisco AL, Gonzalez-Macias J: Effect of physiological concentrations of calcitriol on lymphocyte proliferation in normal subjects and in patients with renal failure. *Nephron* 55(2):110, 1990.
179. Zhu K, Gläser R, Mrowietz U: Vitamin D<sub>3</sub> and analogues modulate the expression of CSF-1 and its receptor in human dendritic cells. *Biochem. Biophys. Res. Comm.* 297:1211–17, 2002.
180. Zhu Y, Mahon BD, Froicu M, Cantorna MT: Calcium and 1 alpha,25-dihydroxyvitamin D<sub>3</sub> target the TNF-alpha pathway to suppress experimental inflammatory bowel disease. *Eur J Immunol* 35(1):217, 2005.