

**LITERATURVERZEICHNIS**

## References

1. **Du, P.L.**, The immune system of invertebrates and vertebrates. *Comp Biochem. Physiol B Biochem. Mol. Biol.* 2001. **129**: 1-15.
2. **Hoffmann, J.A., Kafatos, F.C., Janeway, C.A., and Ezekowitz, R.A.**, Phylogenetic perspectives in innate immunity. *Science* 1999. **284**: 1313-1318.
3. **Janeway, C.A., Jr. and Medzhitov, R.**, Innate immune recognition. *Annu. Rev. Immunol.* 2002. **20**: 197-216.
4. **Medzhitov, R. and Janeway, C.A., Jr.**, Innate immunity: impact on the adaptive immune response. *Curr. Opin. Immunol.* 1997. **9**: 4-9.
5. **Zinkernagel, R.M.**, On natural and artificial vaccinations. *Annu. Rev. Immunol.* 2003. **21**: 515-546.
6. **Zinkernagel, R.M.**, Grundlagen der Immunologie. In **Kayser, F.H., Bienz, K.A., Eckert, J., and Zinkernagel, R.M.** (Eds.) *Medizinische Mikrobiologie*. Thieme, Stuttgart 1998, pp 43-136.
7. **Bachmann, M.F. and Kopf, M.**, Balancing protective immunity and immunopathology. *Curr. Opin. Immunol.* 2002. **14**: 413-419.
8. **Ohashi, P.S. and DeFranco, A.L.**, Making and breaking tolerance. *Curr. Opin. Immunol.* 2002. **14**: 744-759.
9. **Guermontprez, P., Valladeau, J., Zitvogel, L., Thery, C., and Amigorena, S.**, Antigen presentation and T cell stimulation by dendritic cells. *Annu. Rev. Immunol.* 2002. **20**: 621-667.
10. **Moser, M. and Murphy, K.M.**, Dendritic cell regulation of TH1-TH2 development. *Nat. Immunol.* 2000. **1**: 199-205.
11. **Shi, F., Ljunggren, H.G., and Sarvetnick, N.**, Innate immunity and autoimmunity: from self-protection to self-destruction. *Trends Immunol.* 2001. **22**: 97-101.
12. **Kisielow, P., Teh, H.S., Bluthmann, H., and von Boehmer, H.**, Positive selection of antigen-specific T cells in thymus by restricting MHC molecules. *Nature* 1988. **335**: 730-733.
13. **Kappler, J.W., Roehm, N., and Marrack, P.**, T cell tolerance by clonal elimination in the thymus. *Cell* 1987. **49**: 273-280.
14. **Sprent, J., Lo, D., Gao, E.K., and Ron, Y.**, T cell selection in the thymus. *Immunol. Rev.* 1988. **101**: 173-190.
15. **Bluestone, J.A. and Abbas, A.K.**, Natural versus adaptive regulatory T cells. *Nat. Rev. Immunol.* 2003. **3**: 253-257.
16. **Goldschneider, I. and Cone, R.E.**, A central role for peripheral dendritic cells in the induction of acquired thymic tolerance. *Trends Immunol.* 2003. **24**: 77-81.
17. **Bradley, L.M., Watson, S.R., and Swain, S.L.**, Entry of naive CD4 T cells into peripheral lymph nodes requires L-selectin. *J. Exp. Med.* 1994. **180**: 2401-2406.
18. **Bradley, L.M. and Watson, S.R.**, Lymphocyte migration into tissue: the paradigm derived from CD4 subsets. *Curr. Opin. Immunol.* 1996. **8**: 312-320.
19. **Mackay, C.R., Andrew, D.P., Briskin, M., Ringler, D.J., and Butcher, E.C.**, Phenotype, and migration properties of three major subsets of tissue homing T cells in sheep. *Eur. J. Immunol.* 1996. **26**: 2433-2439.
20. **Reinhardt, R.L., Khoruts, A., Merica, R., Zell, T., and Jenkins, M.K.**, Visualizing the generation of memory CD4 T cells in the whole body. *Nature* 2001. **410**: 101-105.
21. **Picker, L.J. and Siegelman, M.H.**, Lymphoid tissues and organs. In **Paul, W.E.** (Ed.) *Fundamental Immunology*. Raven, New York 1993, pp 145-197.
22. **Steinman, R.M.**, The dendritic cell system and its role in immunogenicity. *Annu. Rev. Immunol.* 1991. **9**: 271-296.
23. **Levin, D., Constant, S., Pasqualini, T., Flavell, R., and Bottomly, K.**, Role of dendritic cells in the priming of CD4+ T lymphocytes to peptide antigen in vivo. *J. Immunol.* 1993. **151**: 6742-6750.
24. **Banchereau, J. and Steinman, R.M.**, Dendritic cells and the control of immunity. *Nature* 1998. **392**: 245-252.
25. **Jenkins, M.K., Khoruts, A., Ingulli, E., Mueller, D.L., McSorley, S.J., Reinhardt, R.L., Itano, A., and Pape, K.A.**, In vivo activation of antigen-specific CD4 T cells. *Annu. Rev. Immunol.* 2001. **19**: 23-45.
26. **Steinman, R.M., Pack, M., and Inaba, K.**, Dendritic cells in the T-cell areas of lymphoid organs. *Immunol. Rev.* 1997. **156**: 25-37.
27. **Dustin, M.L. and Cooper, J.A.**, The immunological synapse and the actin cytoskeleton: molecular hardware for T cell signaling. *Nat. Immunol.* 2000. **1**: 23-29.
28. **Chambers, C.A. and Allison, J.P.**, Costimulatory regulation of T cell function. *Curr. Opin. Cell Biol.* 1999. **11**: 203-210.

29. Allison, J.P. and Krummel, M.F., The Yin and Yang of T cell costimulation. *Science* 1995. **270**: 932-933.
30. Croft, M., Bradley, L.M., and Swain, S.L., Naive versus memory CD4 T cell response to antigen. Memory cells are less dependent on accessory cell costimulation and can respond to many antigen-presenting cell types including resting B cells. *J.Immunol.* 1994. **152**: 2675-2685.
31. Howland, K.C., Ausubel, L.J., London, C.A., and Abbas, A.K., The roles of CD28 and CD40 ligand in T cell activation and tolerance. *J.Immunol.* 2000. **164**: 4465-4470.
32. Schweitzer, A.N., Borriello, F., Wong, R.C., Abbas, A.K., and Sharpe, A.H., Role of costimulators in T cell differentiation: studies using antigen-presenting cells lacking expression of CD80 or CD86. *J.Immunol.* 1997. **158**: 2713-2722.
33. Lu, P., Wang, Y.L., and Linsley, P.S., Regulation of self-tolerance by CD80/CD86 interactions. *Curr.Opin.Immunol.* 1997. **9**: 858-862.
34. Salomon, B. and Bluestone, J.A., Complexities of CD28/B7: CTLA-4 costimulatory pathways in autoimmunity and transplantation. *Annu.Rev.Immunol.* 2001. **19**: 225-252.
35. Boise, L.H., Minn, A.J., Noel, P.J., June, C.H., Accavitti, M.A., Lindsten, T., and Thompson, C.B., CD28 costimulation can promote T cell survival by enhancing the expression of Bcl-XL. *Immunity.* 1995. **3**: 87-98.
36. Lucas, P.J., Negishi, I., Nakayama, K., Fields, L.E., and Loh, D.Y., Naive CD28-deficient T cells can initiate but not sustain an in vitro antigen-specific immune response. *J.Immunol.* 1995. **154**: 5757-5768.
37. Seder, R.A., Germain, R.N., Linsley, P.S., and Paul, W.E., CD28-mediated costimulation of interleukin 2 (IL-2) production plays a critical role in T cell priming for IL-4 and interferon gamma production. *J.Exp.Med.* 1994. **179**: 299-304.
38. Grewal, I.S. and Flavell, R.A., CD40 and CD154 in cell-mediated immunity. *Annu.Rev.Immunol.* 1998. **16**: 111-135.
39. Schoenberger, S.P., Toes, R.E., van der Voort, E.I., Offringa, R., and Melief, C.J., T-cell help for cytotoxic T lymphocytes is mediated by CD40-CD40L interactions. *Nature* 1998. **393**: 480-483.
40. Kweon, M.N., Fujihashi, K., Wakatsuki, Y., Koga, T., Yamamoto, M., McGhee, J.R., and Kiyono, H., Mucosally induced systemic T cell unresponsiveness to ovalbumin requires CD40 ligand-CD40 interactions. *J.Immunol.* 1999. **162**: 1904-1909.
41. Ridge, J.P., Fuchs, E.J., and Matzinger, P., Neonatal tolerance revisited: turning on newborn T cells with dendritic cells. *Science* 1996. **271** : 1723-1726.
42. Pulendran, B., Smith, J.L., Jenkins, M., Schoenborn, M., Maraskovsky, E., and Maliszewski, C.R., Prevention of peripheral tolerance by a dendritic cell growth factor: flt3 ligand as an adjuvant. *J.Exp.Med.* 1998. **188**: 2075-2082.
43. Mayordomo, J.I., Loftus, D.J., Sakamoto, H., De Cesare, C.M., Appasamy, P.M., Lotze, M.T., Storkus, W.J., Appella, E., and DeLeo, A.B., Therapy of murine tumors with p53 wild-type and mutant sequence peptide-based vaccines. *J.Exp.Med.* 1996. **183**: 1357-1365.
44. Ludewig, B., Odermatt, B., Landmann, S., Hengartner, H., and Zinkernagel, R.M., Dendritic cells induce autoimmune diabetes and maintain disease via de novo formation of local lymphoid tissue. *J.Exp.Med.* 1998. **188**: 1493-1501.
45. Steinman, R.M., Turley, S., Mellman, I., and Inaba, K., The induction of tolerance by dendritic cells that have captured apoptotic cells. *J.Exp.Med.* 2000. **191**: 411-416.
46. Roncarolo, M.G., Levings, M.K., and Traversari, C., Differentiation of T regulatory cells by immature dendritic cells. *J.Exp.Med.* 2001. **193**: F5-F9.
47. Jonuleit, H., Schmitt, E., Steinbrink, K., and Enk, A.H., Dendritic cells as a tool to induce anergic and regulatory T cells. *Trends Immunol.* 2001. **22**: 394-400.
48. Jonuleit, H., Schmitt, E., Schuler, G., Knop, J., and Enk, A.H., Induction of interleukin 10-producing, nonproliferating CD4(+) T cells with regulatory properties by repetitive stimulation with allogeneic immature human dendritic cells. *J.Exp.Med.* 2000. **192**: 1213-1222.
49. Maldonado-Lopez, R. and Moser, M., Dendritic cell subsets and the regulation of Th1/Th2 responses. *Semin.Immunol.* 2001. **13**: 275-282.
50. Mosmann, T.R., Cherwinski, H., Bond, M.W., Giedlin, M.A., and Coffman, R.L., Two types of murine helper T cell clone. I. Definition according to profiles of lymphokine activities and secreted proteins. *J.Immunol.* 1986. **136**: 2348-2357.
51. Rengarajan, J., Szabo, S.J., and Glimcher, L.H., Transcriptional regulation of Th1/Th2 polarization. *Immunol.Today* 2000. **21**: 479-483.
52. Liew, F.Y., T(H)1 and T(H)2 cells: a historical perspective. *Nat.Rev.Immunol.* 2002. **2**: 55-60.
53. Seder, R.A. and Paul, W.E., Acquisition of lymphokine-producing phenotype by CD4+ T cells. *Annu.Rev.Immunol.* 1994. **12**: 635-673.
54. Jankovic, D., Liu, Z., and Gause, W.C., Th1- and Th2-cell commitment during infectious disease: asymmetry in divergent pathways. *Trends Immunol.* 2001. **22**: 450-457.

55. **Swain,S.L., Weinberg,A.D., English,M., and Huston,G.,** IL-4 directs the development of Th2-like helper effectors. *J.Immunol.* 1990. **145:** 3796-3806.
56. **Le Gros,G., Ben Sasson,S.Z., Seder,R., Finkelman,F.D., and Paul,W.E.,** Generation of interleukin 4 (IL-4)-producing cells in vivo and in vitro: IL-2 and IL-4 are required for in vitro generation of IL-4-producing cells. *J.Exp.Med.* 1990. **172:** 921-929.
57. **Hsieh,C.S., Macatonia,S.E., Tripp,C.S., Wolf,S.F., O'Garra,A., and Murphy,K.M.,** Development of TH1 CD4+ T cells through IL-12 produced by Listeria-induced macrophages. *Science* 1993. **260:** 547-549.
58. **Seder,R.A., Gazzinelli,R., Sher,A., and Paul,W.E.,** Interleukin 12 acts directly on CD4+ T cells to enhance priming for interferon gamma production and diminishes interleukin 4 inhibition of such priming. *Proc.Natl.Acad.Sci.U.S.A* 1993. **90:** 10188-10192.
59. **Hsieh,C.S., Heimberger,A.B., Gold,J.S., O'Garra,A., and Murphy,K.M.,** Differential regulation of T helper phenotype development by interleukins 4 and 10 in an alpha beta T-cell-receptor transgenic system. *Proc.Natl.Acad.Sci.U.S.A* 1992. **89:** 6065-6069.
60. **Seder,R.A., Paul,W.E., Davis,M.M., and Fazekas de St,G.B.,** The presence of interleukin 4 during in vitro priming determines the lymphokine-producing potential of CD4+ T cells from T cell receptor transgenic mice. *J.Exp.Med.* 1992. **176:** 1091-1098.
61. **Murphy,K.M., Ouyang,W., Farrar,J.D., Yang,J., Ranganath,S., Asnagli,H., Afkarian,M., and Murphy,T.L.,** Signaling and transcription in T helper development. *Annu.Rev.Immunol.* 2000. **18:** 451-494.
62. **Diehl,S. and Rincon,M.,** The two faces of IL-6 on Th1/Th2 differentiation. *Mol.Immunol.* 2002. **39:** 531-536.
63. **Rincon,M., Anguita,J., Nakamura,T., Fikrig,E., and Flavell,R.A.,** Interleukin (IL)-6 directs the differentiation of IL-4-producing CD4+ T cells. *J.Exp.Med.* 1997. **185:** 461-469.
64. **Constant,S.L. and Bottomly,K.,** Induction of Th1 and Th2 CD4+ T cell responses: the alternative approaches. *Annu.Rev.Immunol.* 1997. **15:** 297-322.
65. **Firestein,G.S., Roeder,W.D., Laxer,J.A., Townsend,K.S., Weaver,C.T., Hom,J.T., Linton,J., Torbett,B.E., and Glasebrook,A.L.,** A new murine CD4+ T cell subset with an unrestricted cytokine profile. *J.Immunol.* 1989. **143:** 518-525.
66. **Kelso,A. and Gough,N.M.,** Coexpression of granulocyte-macrophage colony-stimulating factor, gamma interferon, and interleukins 3 and 4 is random in murine alloreactive T-lymphocyte clones. *Proc.Natl.Acad.Sci.U.S.A* 1988. **85:** 9189-9193.
67. **Street,N.E., Schumacher,J.H., Fong,T.A., Bass,H., Fiorentino,D.F., Leverah,J.A., and Mosmann,T.R.,** Heterogeneity of mouse helper T cells. Evidence from bulk cultures and limiting dilution cloning for precursors of Th1 and Th2 cells. *J.Immunol.* 1990. **144:** 1629-1639.
68. **Chen,Y., Kuchroo,V.K., Inobe,J., Hafler,D.A., and Weiner,H.L.,** Regulatory T cell clones induced by oral tolerance: suppression of autoimmune encephalomyelitis. *Science* 1994. **265:** 1237-1240.
69. **Groux,H., O'Garra,A., Bigler,M., Rouleau,M., Antonenko,S., de Vries,J.E., and Roncarolo,M.G.,** A CD4+ T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. *Nature* 1997. **389:** 737-742.
70. **Abbas,A.K., Murphy,K.M., and Sher,A.,** Functional diversity of helper T lymphocytes. *Nature* 1996. **383:** 787-793.
71. **Mosmann,T.R. and Coffman,R.L.,** TH1 and TH2 cells: different patterns of lymphokine secretion lead to different functional properties. *Annu.Rev.Immunol.* 1989. **7:** 145-173.
72. **Sadick,M.D., Locksley,R.M., Tubbs,C., and Raff,H.V.,** Murine cutaneous leishmaniasis: resistance correlates with the capacity to generate interferon-gamma in response to Leishmania antigens in vitro. *J.Immunol.* 1986. **136:** 655-661.
73. **Anggard,E.,** Nitric oxide: mediator, murderer, and medicine. *Lancet* 1994. **343:** 1199-1206.
74. **Heinzl,F.P., Sadick,M.D., Mutha,S.S., and Locksley,R.M.,** Production of interferon gamma, interleukin 2, interleukin 4, and interleukin 10 by CD4+ lymphocytes in vivo during healing and progressive murine leishmaniasis. *Proc.Natl.Acad.Sci.U.S.A* 1991. **88:** 7011-7015.
75. **Snapper,C.M. and Paul,W.E.,** Interferon-gamma and B cell stimulatory factor-1 reciprocally regulate Ig isotype production. *Science* 1987. **236:** 944-947.
76. **Stevens,T.L., Bossie,A., Sanders,V.M., Fernandez-Botran,R., Coffman,R.L., Mosmann,T.R., and Vitetta,E.S.,** Regulation of antibody isotype secretion by subsets of antigen-specific helper T cells. *Nature* 1988. **334:** 255-258.
77. **Coffman,R.L., Lebman,D.A., and Rothman,P.,** Mechanism and regulation of immunoglobulin isotype switching. *Adv.Immunol.* 1993. **54:** 229-270.
78. **Wardlaw,A.J., Moqbel,R., and Kay,A.B.,** Eosinophils: biology and role in disease. *Adv.Immunol.* 1995. **60:** 151-266.

79. **Collins,P.D., Marleau,S., Griffiths-Johnson,D.A., Jose,P.J., and Williams,T.J.,** Cooperation between interleukin-5 and the chemokine eotaxin to induce eosinophil accumulation in vivo. *J.Exp.Med.* 1995. **182:** 1169-1174.
80. **Wills-Karp,M.,** Immunologic basis of antigen-induced airway hyperresponsiveness. *Annu.Rev.Immunol.* 1999. **17:** 255-281.
81. **Paul,W.E.,** Interleukin-4: a prototypic immunoregulatory lymphokine. *Blood* 1991. **77:** 1859-1870.
82. **Romagnani,S.,** Lymphokine production by human T cells in disease states. *Annu.Rev.Immunol.* 1994. **12:** 227-257.
83. **Turk,J.L. and Bryceson,A.D.,** Immunological phenomena in leprosy and related diseases. *Adv.Immunol.* 1971. **13:** 209-266.
84. **Yamamura,M., Uyemura,K., Deans,R.J., Weinberg,K., Rea,T.H., Bloom,B.R., and Modlin,R.L.,** Defining protective responses to pathogens: cytokine profiles in leprosy lesions. *Science* 1991. **254:** 277-279.
85. **Howard,J.G., Hale,C., and Liew,F.Y.,** Immunological regulation of experimental cutaneous leishmaniasis. IV. Prophylactic effect of sublethal irradiation as a result of abrogation of suppressor T cell generation in mice genetically susceptible to *Leishmania tropica*. *J.Exp.Med.* 1981. **153:** 557-568.
86. **Heinzel,F.P., Sadick,M.D., Holaday,B.J., Coffman,R.L., and Locksley,R.M.,** Reciprocal expression of interferon gamma or interleukin 4 during the resolution or progression of murine leishmaniasis. Evidence for expansion of distinct helper T cell subsets. *J.Exp.Med.* 1989. **169:** 59-72.
87. **Rabinovitch,A.,** Immunoregulatory and cytokine imbalances in the pathogenesis of IDDM. Therapeutic intervention by immunostimulation? *Diabetes* 1994. **43:** 613-621.
88. **La Cava,A. and Sarvetnick,N.,** The role of cytokines in autoimmunity. *Curr.Dir.Autoimmun.* 1999. **1:** 56-71.
89. **O'Garra,A. and Murphy,K.,** T-cell subsets in autoimmunity. *Curr.Opin.Immunol.* 1993. **5:** 880-886.
90. **Powrie,F. and Coffman,R.L.,** Cytokine regulation of T-cell function: potential for therapeutic intervention. *Immunol.Today* 1993. **14:** 270-274.
91. **Scott,B., Liblau,R., Degermann,S., Marconi,L.A., Ogata,L., Caton,A.J., McDevitt,H.O., and Lo,D.,** A role for non-MHC genetic polymorphism in susceptibility to spontaneous autoimmunity. *Immunity.* 1994. **1:** 73-83.
92. **Liblau,R.S., Singer,S.M., and McDevitt,H.O.,** Th1 and Th2 CD4+ T cells in the pathogenesis of organ-specific autoimmune diseases. *Immunol.Today* 1995. **16:** 34-38.
93. **Kuchroo,V.K., Anderson,A.C., Waldner,H., Munder,M., Bettelli,E., and Nicholson,L.B.,** T cell response in experimental autoimmune encephalomyelitis (EAE): role of self and cross-reactive antigens in shaping, tuning, and regulating the autopathogenic T cell repertoire. *Annu.Rev.Immunol.* 2002. **20:** 101-123.
94. **Williams,K.C., Ulvestad,E., and Hickey,W.F.,** Immunology of multiple sclerosis. *Clin.Neurosci.* 1994. **2:** 229-245.
95. **Miller,S.D. and Karpus,W.J.,** The immunopathogenesis and regulation of T-cell-mediated demyelinating diseases. *Immunol.Today* 1994. **15:** 356-361.
96. **Mueller,R., Bradley,L.M., Krahl,T., and Sarvetnick,N.,** Mechanism underlying counterregulation of autoimmune diabetes by IL-4. *Immunity.* 1997. **7:** 411-418.
97. **Mueller,R., Krahl,T., and Sarvetnick,N.,** Pancreatic expression of interleukin-4 abrogates insulinitis and autoimmune diabetes in nonobese diabetic (NOD) mice. *J.Exp.Med.* 1996. **184:** 1093-1099.
98. **Savinov,A.Y., Wong,F.S., and Chervonsky,A.V.,** IFN-gamma affects homing of diabetogenic T cells. *J.Immunol.* 2001. **167:** 6637-6643.
99. **Myers,L.K., Tang,B., Stuart,J.M., and Kang,A.H.,** The role of IL-4 in regulation of murine collagen-induced arthritis. *Clin.Immunol.* 2002. **102:** 185-191.
100. **Mussener,A., Lorentzen,J.C., Kleinau,S., and Klareskog,L.,** Altered Th1/Th2 balance associated with non-major histocompatibility complex genes in collagen-induced arthritis in resistant and non-resistant rat strains. *Eur.J.Immunol.* 1997. **27:** 695-699.
101. **Mauri,C., Williams,R.O., Walmsley,M., and Feldmann,M.,** Relationship between Th1/Th2 cytokine patterns and the arthritogenic response in collagen-induced arthritis. *Eur.J.Immunol.* 1996. **26:** 1511-1518.
102. **Healey,D., Ozegbe,P., Arden,S., Chandler,P., Hutton,J., and Cooke,A.,** In vivo activity and in vitro specificity of CD4+ Th1 and Th2 cells derived from the spleens of diabetic NOD mice. *J.Clin.Invest* 1995. **95:** 2979-2985.
103. **Racke,M.K., Burnett,D., Pak,S.H., Albert,P.S., Cannella,B., Raine,C.S., McFarlin,D.E., and Scott,D.E.,** Retinoid treatment of experimental allergic encephalomyelitis. IL-4 production correlates with improved disease course. *J.Immunol.* 1995. **154:** 450-458.
104. **Racke,M.K., Bonomo,A., Scott,D.E., Cannella,B., Levine,A., Raine,C.S., Shevach,E.M., and Rocken,M.,** Cytokine-induced immune deviation as a therapy for inflammatory autoimmune disease. *J.Exp.Med.* 1994. **180:** 1961-1966.

105. **Falcone, M. and Bloom, B.R.**, A T helper cell 2 (Th2) immune response against non-self antigens modifies the cytokine profile of autoimmune T cells and protects against experimental allergic encephalomyelitis. *J.Exp.Med.* 1997. **185**: 901-907.
106. **Seddon, B. and Mason, D.**, Regulatory T cells in the control of autoimmunity: the essential role of transforming growth factor beta and interleukin 4 in the prevention of autoimmune thyroiditis in rats by peripheral CD4(+)CD. *J.Exp.Med.* 1999. **189**: 279-288.
107. **Hill, N. and Sarvetnick, N.**, Cytokines: promoters and dampeners of autoimmunity. *Curr.Opin.Immunol.* 2002. **14**: 791-797.
108. **Krakowski, M. and Owens, T.**, Interferon-gamma confers resistance to experimental allergic encephalomyelitis. *Eur.J.Immunol.* 1996. **26**: 1641-1646.
109. **Chu, C.Q., Wittmer, S., and Dalton, D.K.**, Failure to suppress the expansion of the activated CD4 T cell population in interferon gamma-deficient mice leads to exacerbation of experimental autoimmune encephalomyelitis. *J.Exp.Med.* 2000. **192**: 123-128.
110. **Furlan, R., Brambilla, E., Ruffini, F., Poliani, P.L., Bergami, A., Marconi, P.C., Franciotta, D.M., Penna, G., Comi, G., Adorini, L., and Martino, G.**, Intrathecal delivery of IFN-gamma protects C57BL/6 mice from chronic-progressive experimental autoimmune encephalomyelitis by increasing apoptosis of central nervous system-infiltrating lymphocytes. *J.Immunol.* 2001. **167**: 1821-1829.
111. **Serreze, D.V., Chapman, H.D., Post, C.M., Johnson, E.A., Suarez-Pinzon, W.L., and Rabinovitch, A.**, Th1 to Th2 cytokine shifts in nonobese diabetic mice: sometimes an outcome, rather than the cause, of diabetes resistance elicited by immunostimulation. *J.Immunol.* 2001. **166**: 1352-1359.
112. **Nagelkerken, L., Blauw, B., and Tielemans, M.**, IL-4 abrogates the inhibitory effect of IL-10 on the development of experimental allergic encephalomyelitis in SJL mice. *Int.Immunol.* 1997. **9**: 1243-1251.
113. **Nepom, G.T.**, Therapy of autoimmune diseases: clinical trials and new biologics. *Curr.Opin.Immunol.* 2002. **14**: 812-815.
114. **Rosen, O., Thiel, A., Massenkeil, G., Hiepe, F., Haupl, T., Radtke, H., Burmester, G.R., Gromnica-Ihle, E., Radbruch, A., and Arnold, R.**, Autologous stem-cell transplantation in refractory autoimmune diseases after in vivo immunoablation and ex vivo depletion of mononuclear cells. *Arthritis Res.* 2000. **2**: 327-336.
115. **ORTH, G., ATANASIU, P., BOIRON, M., REBI'ERE, J.P., and PAOLETTI, C.**, INFECTIOUS AND ONCOGENIC EFFECT OF DNA EXTRACTED FROM CELLS INFECTED WITH POLYOMA VIRUS. *Proc.Soc.Exp.Biol.Med.* 1964. **115**: 1090-1095.
116. **Israel, M.A., Chan, H.W., Hourihan, S.L., Rowe, W.P., and Martin, M.A.**, Biological activity of polyoma viral DNA in mice and hamsters. *J.Virol.* 1979. **29**: 990-996.
117. **Will, H., Cattaneo, R., Koch, H.G., Darai, G., Schaller, H., Schellekens, H., van Eerd, P.M., and Deinhardt, F.**, Cloned HBV DNA causes hepatitis in chimpanzees. *Nature* 1982. **299**: 740-742.
118. **Wolff, J.A., Malone, R.W., Williams, P., Chong, W., Acsadi, G., Jani, A., and Felgner, P.L.**, Direct gene transfer into mouse muscle in vivo. *Science* 1990. **247**: 1465-1468.
119. **Tang, D.C., DeVit, M., and Johnston, S.A.**, Genetic immunization is a simple method for eliciting an immune response. *Nature* 1992. **356**: 152-154.
120. **Ulmer, J.B., Donnelly, J.J., Parker, S.E., Rhodes, G.H., Felgner, P.L., Dwarki, V.J., Gromkowski, S.H., Deck, R.R., DeWitt, C.M., Friedman, A., and .**, Heterologous protection against influenza by injection of DNA encoding a viral protein. *Science* 1993. **259**: 1745-1749.
121. **Robinson, H.L., Hunt, L.A., and Webster, R.G.**, Protection against a lethal influenza virus challenge by immunization with a haemagglutinin-expressing plasmid DNA. *Vaccine* 1993. **11**: 957-960.
122. **Gurunathan, S., Wu, C.Y., Freidag, B.L., and Seder, R.A.**, DNA vaccines: a key for inducing long-term cellular immunity. *Curr.Opin.Immunol.* 2000. **12**: 442-447.
123. **Robinson, H.L. and Torres, C.A.**, DNA vaccines. *Semin.Immunol.* 1997. **9**: 271-283.
124. **Chattergoon, M., Boyer, J., and Weiner, D.B.**, Genetic immunization: a new era in vaccines and immune therapeutics. *FASEB J.* 1997. **11**: 753-763.
125. **Fensterle, J., Grode, L., Hess, J., and Kaufmann, S.H.**, Effective DNA vaccination against listeriosis by prime/boost inoculation with the gene gun. *J.Immunol.* 1999. **163**: 4510-4518.
126. **Svanholm, C., Bandholtz, L., Lobell, A., and Wigzell, H.**, Enhancement of antibody responses by DNA immunization using expression vectors mediating efficient antigen secretion. *J.Immunol.Methods* 1999. **228**: 121-130.
127. **Drew, D.R., Lightowers, M., and Strugnell, R.A.**, Humoral immune responses to DNA vaccines expressing secreted, membrane bound and non-secreted forms of the *Tania ovis* 45W antigen. *Vaccine* 2000. **18**: 2522-2532.
128. **Ramsay, A.J., Kent, S.J., Strugnell, R.A., Suhrbier, A., Thomson, S.A., and Ramshaw, I.A.**, Genetic vaccination strategies for enhanced cellular, humoral and mucosal immunity. *Immunol.Rev.* 1999. **171**: 27-44.
129. **Ulmer, J.B., Donnelly, J.J., and Liu, M.A.**, Toward the development of DNA vaccines. *Curr.Opin.Biotechnol.* 1996. **7**: 653-658.

130. **Raychaudhuri,S. and Rock,K.L.**, Fully mobilizing host defense: building better vaccines. *Nat.Biotechnol.* 1998. **16**: 1025-1031.
131. **Donnelly,J.J., Ulmer,J.B., Shiver,J.W., and Liu,M.A.**, DNA vaccines. *Annu.Rev.Immunol.* 1997. **15**: 617-648.
132. **Agadjanyan,M.G., Kim,J.J., Trivedi,N., Wilson,D.M., Monzavi-Karbassi,B., Morrison,L.D., Nottingham,L.K., Dentchev,T., Tsai,A., Dang,K., Chalian,A.A., Maldonado,M.A., Williams,W.V., and Weiner,D.B.**, CD86 (B7-2) can function to drive MHC-restricted antigen-specific CTL responses in vivo. *J.Immunol.* 1999. **162**: 3417-3427.
133. **Iwasaki,A., Stiernholm,B.J., Chan,A.K., Berinstein,N.L., and Barber,B.H.**, Enhanced CTL responses mediated by plasmid DNA immunogens encoding costimulatory molecules and cytokines. *J.Immunol.* 1997. **158**: 4591-4601.
134. **Torres,C.A., Iwasaki,A., Barber,B.H., and Robinson,H.L.**, Differential dependence on target site tissue for gene gun and intramuscular DNA immunizations. *J.Immunol.* 1997. **158**: 4529-4532.
135. **Corr,M., Lee,D.J., Carson,D.A., and Tighe,H.**, Gene vaccination with naked plasmid DNA: mechanism of CTL priming. *J.Exp.Med.* 1996. **184**: 1555-1560.
136. **Iwasaki,A., Torres,C.A., Ohashi,P.S., Robinson,H.L., and Barber,B.H.**, The dominant role of bone marrow-derived cells in CTL induction following plasmid DNA immunization at different sites. *J.Immunol.* 1997. **159**: 11-14.
137. **Doe,B., Selby,M., Barnett,S., Baenziger,J., and Walker,C.M.**, Induction of cytotoxic T lymphocytes by intramuscular immunization with plasmid DNA is facilitated by bone marrow-derived cells. *Proc.Natl.Acad.Sci.U.S.A* 1996. **93**: 8578-8583.
138. **Klinman,D.M., Sechler,J.M., Conover,J., Gu,M., and Rosenberg,A.S.**, Contribution of cells at the site of DNA vaccination to the generation of antigen-specific immunity and memory. *J.Immunol.* 1998. **160**: 2388-2392.
139. **Corr,M., von Damm,A., Lee,D.J., and Tighe,H.**, In vivo priming by DNA injection occurs predominantly by antigen transfer. *J.Immunol.* 1999. **163**: 4721-4727.
140. **Bouloc,A., Walker,P., Grivel,J.C., Vogel,J.C., and Katz,S.I.**, Immunization through dermal delivery of protein-encoding DNA: a role for migratory dendritic cells. *Eur.J.Immunol.* 1999. **29**: 446-454.
141. **Akbari,O., Panjwani,N., Garcia,S., Tascon,R., Lowrie,D., and Stockinger,B.**, DNA vaccination: transfection and activation of dendritic cells as key events for immunity. *J.Exp.Med.* 1999. **189**: 169-178.
142. **Bot,A., Stan,A.C., Inaba,K., Steinman,R., and Bona,C.**, Dendritic cells at a DNA vaccination site express the encoded influenza nucleoprotein and prime MHC class I-restricted cytolytic lymphocytes upon adoptive transfer. *Int.Immunol.* 2000. **12**: 825-832.
143. **Casares,S., Inaba,K., Brumeanu,T.D., Steinman,R.M., and Bona,C.A.**, Antigen presentation by dendritic cells after immunization with DNA encoding a major histocompatibility complex class II-restricted viral epitope. *J.Exp.Med.* 1997. **186**: 1481-1486.
144. **Porgador,A., Irvine,K.R., Iwasaki,A., Barber,B.H., Restifo,N.P., and Germain,R.N.**, Predominant role for directly transfected dendritic cells in antigen presentation to CD8+ T cells after gene gun immunization. *J.Exp.Med.* 1998. **188**: 1075-1082.
145. **Condon,C., Watkins,S.C., Celluzzi,C.M., Thompson,K., and Falo,L.D., Jr.**, DNA-based immunization by in vivo transfection of dendritic cells. *Nat.Med.* 1996. **2**: 1122-1128.
146. **Cho,J.H., Youn,J.W., and Sung,Y.C.**, Cross-priming as a predominant mechanism for inducing CD8(+) T cell responses in gene gun DNA immunization. *J.Immunol.* 2001. **167**: 5549-5557.
147. **Shimada,S., Yano,O., and Tokunaga,T.**, In vivo augmentation of natural killer cell activity with a deoxyribonucleic acid fraction of BCG. *Jpn.J.Cancer Res.* 1986. **77**: 808-816.
148. **Krieg,A.M., Yi,A.K., Matson,S., Waldschmidt,T.J., Bishop,G.A., Teasdale,R., Koretzky,G.A., and Klinman,D.M.**, CpG motifs in bacterial DNA trigger direct B-cell activation. *Nature* 1995. **374**: 546-549.
149. **Hemmi,H., Takeuchi,O., Kawai,T., Kaisho,T., Sato,S., Sanjo,H., Matsumoto,M., Hoshino,K., Wagner,H., Takeda,K., and Akira,S.**, A Toll-like receptor recognizes bacterial DNA. *Nature* 2000. **408**: 740-745.
150. **Krieg,A.M.**, CpG motifs in bacterial DNA and their immune effects. *Annu.Rev.Immunol.* 2002. **20**: 709-760.
151. **Sato,Y., Roman,M., Tighe,H., Lee,D., Corr,M., Nguyen,M.D., Silverman,G.J., Lotz,M., Carson,D.A., and Raz,E.**, Immunostimulatory DNA sequences necessary for effective intradermal gene immunization. *Science* 1996. **273**: 352-354.
152. **Klinman,D.M., Yamshchikov,G., and Ishigatsubo,Y.**, Contribution of CpG motifs to the immunogenicity of DNA vaccines. *J.Immunol.* 1997. **158**: 3635-3639.
153. **Leclerc,C., Deriaud,E., Rojas,M., and Whalen,R.G.**, The preferential induction of a Th1 immune response by DNA-based immunization is mediated by the immunostimulatory effect of plasmid DNA. *Cell Immunol.* 1997. **179**: 97-106.

154. **Roman,M., Martin-Orozco,E., Goodman,J.S., Nguyen,M.D., Sato,Y., Ronaghy,A., Kornbluth,R.S., Richman,D.D., Carson,D.A., and Raz,E.,** Immunostimulatory DNA sequences function as T helper-1-promoting adjuvants. *Nat.Med.* 1997. **3**: 849-854.
155. **Carson,D.A. and Raz,E.,** Oligonucleotide adjuvants for T helper 1 (Th1)-specific vaccination. *J.Exp.Med.* 1997. **186**: 1621-1622.
156. **Chu,R.S., Targoni,O.S., Krieg,A.M., Lehmann,P.V., and Harding,C.V.,** CpG oligodeoxynucleotides act as adjuvants that switch on T helper 1 (Th1) immunity. *J.Exp.Med.* 1997. **186**: 1623-1631.
157. **Feltquate,D.M., Heaney,S., Webster,R.G., and Robinson,H.L.,** Different T helper cell types and antibody isotypes generated by saline and gene gun DNA immunization. *J.Immunol.* 1997. **158**: 2278-2284.
158. **Pertmer,T.M., Roberts,T.R., and Haynes,J.R.,** Influenza virus nucleoprotein-specific immunoglobulin G subclass and cytokine responses elicited by DNA vaccination are dependent on the route of vector DNA delivery. *J.Virol.* 1996. **70**: 6119-6125.
159. **Cardoso,A.I., Sixt,N., Vallier,A., Fayolle,J., Buckland,R., and Wild,T.F.,** Measles virus DNA vaccination: antibody isotype is determined by the method of immunization and by the nature of both the antigen and the coimmunized antigen. *J.Virol.* 1998. **72**: 2516-2518.
160. **Raz,E., Tighe,H., Sato,Y., Corr,M., Dudler,J.A., Roman,M., Swain,S.L., Spiegelberg,H.L., and Carson,D.A.,** Preferential induction of a Th1 immune response and inhibition of specific IgE antibody formation by plasmid DNA immunization. *Proc.Natl.Acad.Sci.U.S.A* 1996. **93**: 5141-5145.
161. **Barry,M.A. and Johnston,S.A.,** Biological features of genetic immunization. *Vaccine* 1997. **15**: 788-791.
162. **Ulmer,J.B., Deck,R.R., DeWitt,C.M., Donnhly,J.I., and Liu,M.A.,** Generation of MHC class I-restricted cytotoxic T lymphocytes by expression of a viral protein in muscle cells: antigen presentation by non-muscle cells. *Immunology* 1996. **89**: 59-67.
163. **Tarner,I.H. and Fathman,C.G.,** Gene therapy in autoimmune disease. *Curr.Opin.Immunol.* 2001. **13**: 676-682.
164. **Cohen,A.D., Boyer,J.D., and Weiner,D.B.,** Modulating the immune response to genetic immunization. *FASEB J.* 1998. **12**: 1611-1626.
165. **Kim,J.J., Trivedi,N.N., Nottingham,L.K., Morrison,L., Tsai,A., Hu,Y., Mahalingam,S., Dang,K., Ahn,L., Doyle,N.K., Wilson,D.M., Chattergoon,M.A., Chalian,A.A., Boyer,J.D., Agadjanyan,M.G., and Weiner,D.B.,** Modulation of amplitude and direction of in vivo immune responses by co-administration of cytokine gene expression cassettes with DNA immunogens. *Eur.J.Immunol.* 1998. **28**: 1089-1103.
166. **Chow,Y.H., Chiang,B.L., Lee,Y.L., Chi,W.K., Lin,W.C., Chen,Y.T., and Tao,M.H.,** Development of Th1 and Th2 populations and the nature of immune responses to hepatitis B virus DNA vaccines can be modulated by codelivery of various cytokine genes. *J.Immunol.* 1998. **160**: 1320-1329.
167. **Kim,J.J., Yang,J.S., Montaner,L., Lee,D.J., Chalian,A.A., and Weiner,D.B.,** Coimmunization with IFN-gamma or IL-2, but not IL-13 or IL-4 cDNA can enhance Th1-type DNA vaccine-induced immune responses in vivo. *J.Interferon Cytokine Res.* 2000. **20**: 311-319.
168. **Garren,H., Ruiz,P.J., Watkins,T.A., Fontoura,P., Nguyen,L.T., Estline,E.R., Hirschberg,D.L., and Steinman,L.,** Combination of gene delivery and DNA vaccination to protect from and reverse Th1 autoimmune disease via deviation to the Th2 pathway. *Immunity.* 2001. **15**: 15-22.
169. **Piccirillo,C.A., Chang,Y., and Prud'homme,G.J.,** TGF-beta1 somatic gene therapy prevents autoimmune disease in nonobese diabetic mice. *J.Immunol.* 1998. **161**: 3950-3956.
170. **Tisch,R., Wang,B., Weaver,D.J., Liu,B., Bui,T., Arthos,J., and Serreze,D.V.,** Antigen-specific mediated suppression of beta cell autoimmunity by plasmid DNA vaccination. *J.Immunol.* 2001. **166**: 2122-2132.
171. **Wolfe,T., Bot,A., Hughes,A., Mohrle,U., Rodrigo,E., Jaume,J.C., Baekkeskov,S., and von Herrath,M.,** Endogenous expression levels of autoantigens influence success or failure of DNA immunizations to prevent type 1 diabetes: addition of IL-4 increases safety. *Eur.J.Immunol.* 2002. **32**: 113-121.
172. **Daheshia,M., Kuklin,N., Kanangat,S., Manickan,E., and Rouse,B.T.,** Suppression of ongoing ocular inflammatory disease by topical administration of plasmid DNA encoding IL-10. *J.Immunol.* 1997. **159**: 1945-1952.
173. **Lobell,A., Weissert,R., Eltayeb,S., Svanholm,C., Olsson,T., and Wigzell,H.,** Presence of CpG DNA and the local cytokine milieu determine the efficacy of suppressive DNA vaccination in experimental autoimmune encephalomyelitis. *J.Immunol.* 1999. **163**: 4754-4762.
174. **Givan,A.L., Fisher,J.L., Waugh,M., Ernstoff,M.S., and Wallace,P.K.,** A flow cytometric method to estimate the precursor frequencies of cells proliferating in response to specific antigens. *J.Immunol.Methods* 1999. **230**: 99-112.

175. **Janeway,C.A., Jr., Travers,P., and Walport,M.**, Host Defense Against Infection. *Immunobiology: the immnesystem inhealth and disease*. Garland, New York 1999, p 407.
176. **Murphy,K.M., Heimberger,A.B., and Loh,D.Y.**, Induction by antigen of intrathymic apoptosis of CD4+CD8+TCR $\alpha$ 0 thymocytes in vivo. *Science* 1990. **250**: 1720-1723.
177. **Haskins,K., Kubo,R., White,J., Pigeon,M., Kappler,J., and Marrack,P.**, The major histocompatibility complex-restricted antigen receptor on T cells. I. Isolation with a monoclonal antibody. *J.Exp.Med.* 1983. **157**: 1149-1169.
178. **Hanahan,D.**, Studies on transformation of Escherichia coli with plasmids. *J.Mol.Biol.* 1983. **166**: 557-580.
179. **Andre,P., Kim,A., Khrapko,K., and Thilly,W.G.**, Fidelity and mutational spectrum of Pfu DNA polymerase on a human mitochondrial DNA sequence. *Genome Res.* 1997. **7**: 843-852.
180. **Cline,J., Braman,J.C., and Hogrefe,H.H.**, PCR fidelity of pfu DNA polymerase and other thermostable DNA polymerases. *Nucleic Acids Res.* 1996. **24**: 3546-3551.
181. **Lee,S.W., Youn,J.W., Seong,B.L., and Sung,Y.C.**, IL-6 induces long-term protective immunity against a lethal challenge of influenza virus. *Vaccine* 1999. **17**: 490-496.
182. **Watanabe,M., Fenton,R.G., Wigginton,J.M., McCormick,K.L., Volker,K.M., Fogler,W.E., Roessler,P.G., and Wiltrout,R.H.**, Intradermal delivery of IL-12 naked DNA induces systemic NK cell activation and Th1 response in vivo that is independent of endogenous IL-12 production. *J.Immunol.* 1999. **163**: 1943-1950.
183. **Fields,P.E., Finch,R.J., Gray,G.S., Zollner,R., Thomas,J.L., Sturmhoefel,K., Lee,K., Wolf,S., Gajewski,T.F., and Fitch,F.W.**, B7.1 is a quantitatively stronger costimulus than B7.2 in the activation of naive CD8+ TCR-transgenic T cells. *J.Immunol.* 1998. **161**: 5268-5275.
184. **Sarver,N., Gruss,P., Law,M.F., Khoury,G., and Howley,P.M.**, Bovine papilloma virus deoxyribonucleic acid: a novel eucaryotic cloning vector. *Mol.Cell Biol.* 1981. **1**: 486-496.
185. **Campo,M.S.**, In **Glover,D.M.** (Ed.) *DNA cloning: a practical approach*. IRL Press, London 1985, p 213.
186. *Flow Cytometry and Cell Sorting - a laboratory handbook*. Berlin 1992.
187. Löhning, M. Differenzierungsprogramme von T-Helfer-Lymphozyten. 2000. Mathematisch-Naturwissenschaftliche Fakultät der Universität zu Köln.  
Ref Type: Thesis/Dissertation
188. **Fazekas de St.G.B., Smith,A.L., Koh,W.P., Girgis,L., Cook,M.C., and Bertolino,P.**, Carboxyfluorescein diacetate succinimidyl ester and the virgin lymphocyte: a marriage made in heaven. *Immunol.Cell Biol.* 1999. **77**: 530-538.
189. **Weston,S.A. and Parish,C.R.**, New fluorescent dyes for lymphocyte migration studies. Analysis by flow cytometry and fluorescence microscopy. *J.Immunol.Methods* 1990. **133**: 87-97.
190. **Lyons,A.B.**, Divided we stand: tracking cell proliferation with carboxyfluorescein diacetate succinimidyl ester. *Immunol.Cell Biol.* 1999. **77**: 509-515.
191. **Lapa e Silva JR, Possebon,d.S., Lefort,J., and Vargaftig,B.B.**, Endotoxins, asthma, and allergic immune responses. *Toxicology* 2000. **152**: 31-35.
192. **Herz,U., Lacy,P., Renz,H., and Erb,K.**, The influence of infections on the development and severity of allergic disorders. *Curr.Opin.Immunol.* 2000. **12**: 632-640.
193. **van Lent,P.L., van den Berg,W.B., Schalkwijk,J., van de Putte,L.B., and van den,B.L.**, The impact of protein size and charge on its retention in articular cartilage. *J.Rheumatol.* 1987. **14**: 798-805.
194. **Pape,K.A., Kearney,E.R., Khoruts,A., Mondino,A., Merica,R., Chen,Z.M., Ingulli,E., White,J., Johnson,J.G., and Jenkins,M.K.**, Use of adoptive transfer of T-cell-antigen-receptor-transgenic T cell for the study of T-cell activation in vivo. *Immunol.Rev.* 1997. **156**: 67-78.
195. **Rogers,W.O., Weaver,C.T., Kraus,L.A., Li,J., Li,L., and Bucy,R.P.**, Visualization of antigen-specific T cell activation and cytokine expression in vivo. *J.Immunol.* 1997. **158**: 649-657.
196. **Creusot,R.J., Thomsen,L.L., van Wely,C.A., Topley,P., Tite,J.P., and Chain,B.M.**, Early commitment of adoptively transferred CD4+ T cells following particle-mediated DNA vaccination: implications for the study of immunomodulation. *Vaccine* 2001. **19**: 1678-1687.
197. **Eisenbraun,M.D., Fuller,D.H., and Haynes,J.R.**, Examination of parameters affecting the elicitation of humoral immune responses by particle bombardment-mediated genetic immunization. *DNA Cell Biol.* 1993. **12**: 791-797.
198. Richter, A. Prägung des Zytokingedächtnisses in Th-Lymphozyten. 2000. Mathematisch-Naturwissenschaftliche Fakultät der Universität zu Köln.  
Ref Type: Thesis/Dissertation
199. **Dong,C., Juedes,A.E., Temann,U.A., Shresta,S., Allison,J.P., Ruddle,N.H., and Flavell,R.A.**, ICOS costimulatory receptor is essential for T-cell activation and function. *Nature* 2001. **409**: 97-101.
200. **Ogawa,S., Nagamatsu,G., Watanabe,M., Watanabe,S., Hayashi,T., Horita,S., Nitta,K., Nihei,H., Tezuka,K., and Abe,R.**, Opposing effects of anti-activation-inducible lymphocyte-immunomodulatory



- molecule/inducible costimulator antibody on the development of acute versus chronic graft-versus-host disease. *J.Immunol.* 2001. **167**: 5741-5748.
201. **Hoyne,G.F., Le,R., I, Corsin-Jimenez,M., Tan,K., Dunne,J., Forsyth,L.M., Dallman,M.J., Owen,M.J., Ish-Horowicz,D., and Lamb,J.R.,** Serratel-induced notch signalling regulates the decision between immunity and tolerance made by peripheral CD4(+) T cells. *Int.Immunol.* 2000. **12**: 177-185.
  202. **Moore,K.W., de Waal,M.R., Coffman,R.L., and O'Garra,A.,** Interleukin-10 and the interleukin-10 receptor. *Annu.Rev.Immunol.* 2001. **19**: 683-765.
  203. **Gorelik,L. and Flavell,R.A.,** Transforming growth factor-beta in T-cell biology. *Nat.Rev.Immunol.* 2002. **2**: 46-53.
  204. **Murphy,K.M. and Reiner,S.L.,** The lineage decisions of helper T cells. *Nat.Rev.Immunol.* 2002. **2**: 933-944.
  205. **Geissler,M., Gesien,A., Tokushige,K., and Wands,J.R.,** Enhancement of cellular and humoral immune responses to hepatitis C virus core protein using DNA-based vaccines augmented with cytokine-expressing plasmids. *J.Immunol.* 1997. **158**: 1231-1237.
  206. **Raz,E., Watanabe,A., Baird,S.M., Eisenberg,R.A., Parr,T.B., Lotz,M., Kipps,T.J., and Carson,D.A.,** Systemic immunological effects of cytokine genes injected into skeletal muscle. *Proc.Natl.Acad.Sci.U.S.A* 1993. **90**: 4523-4527.
  207. **Maecker,H.T., Umetsu,D.T., DeKruyff,R.H., and Levy,S.,** DNA vaccination with cytokine fusion constructs biases the immune response to ovalbumin. *Vaccine* 1997. **15**: 1687-1696.
  208. **Okada,E., Sasaki,S., Ishii,N., Aoki,I., Yasuda,T., Nishioka,K., Fukushima,J., Miyazaki,J., Wahren,B., and Okuda,K.,** Intranasal immunization of a DNA vaccine with IL-12- and granulocyte-macrophage colony-stimulating factor (GM-CSF)-expressing plasmids in liposomes induces strong mucosal and cell-mediated immune responses against HIV-1 antigens. *J.Immunol.* 1997. **159**: 3638-3647.
  209. **Song,K., Chang,Y., and Prud'homme,G.J.,** Regulation of T-helper-1 versus T-helper-2 activity and enhancement of tumor immunity by combined DNA-based vaccination and nonviral cytokine gene transfer. *Gene Ther.* 2000. **7**: 481-492.
  210. **Hochrein,H., O'Keefe,M., Luft,T., Vandenabeele,S., Grumont,R.J., Maraskovsky,E., and Shortman,K.,** Interleukin (IL)-4 is a major regulatory cytokine governing bioactive IL-12 production by mouse and human dendritic cells. *J.Exp.Med.* 2000. **192**: 823-833.
  211. **Shortman,K. and Liu,Y.J.,** Mouse and human dendritic cell subtypes. *Nat.Rev.Immunol.* 2002. **2**: 151-161.
  212. **Gudmundsdottir,H., Wells,A.D., and Turka,L.A.,** Dynamics and requirements of T cell clonal expansion in vivo at the single-cell level: effector function is linked to proliferative capacity. *J.Immunol.* 1999. **162**: 5212-5223.
  213. **Padovan,E., Casorati,G., Dellabona,P., Meyer,S., Brockhaus,M., and Lanzavecchia,A.,** Expression of two T cell receptor alpha chains: dual receptor T cells. *Science* 1993. **262**: 422-424.
  214. **Yoshida,A., Nagata,T., Uchijima,M., Higashi,T., and Koide,Y.,** Advantage of gene gun-mediated over intramuscular inoculation of plasmid DNA vaccine in reproducible induction of specific immune responses. *Vaccine* 2000. **18**: 1725-1729.
  215. **Wolff,J.A., Williams,P., Acsadi,G., Jiao,S., Jani,A., and Chong,W.,** Conditions affecting direct gene transfer into rodent muscle in vivo. *Biotechniques* 1991. **11**: 474-485.
  216. **Pertmer,T.M., Eisenbraun,M.D., McCabe,D., Prayaga,S.K., Fuller,D.H., and Haynes,J.R.,** Gene gun-based nucleic acid immunization: elicitation of humoral and cytotoxic T lymphocyte responses following epidermal delivery of nanogram quantities of DNA. *Vaccine* 1995. **13**: 1427-1430.
  217. **Danko,I., Fritz,J.D., Jiao,S., Hogan,K., Latendresse,J.S., and Wolff,J.A.,** Pharmacological enhancement of in vivo foreign gene expression in muscle. *Gene Ther.* 1994. **1**: 114-121.
  218. **Wells,D.J.,** Improved gene transfer by direct plasmid injection associated with regeneration in mouse skeletal muscle. *FEBS Lett.* 1993. **332**: 179-182.
  219. **Davis,H.L., Michel,M.L., and Whalen,R.G.,** DNA-based immunization induces continuous secretion of hepatitis B surface antigen and high levels of circulating antibody. *Hum.Mol.Genet.* 1993. **2**: 1847-1851.
  220. **Torres,C.A., Yang,K., Mustafa,F., and Robinson,H.L.,** DNA immunization: effect of secretion of DNA-expressed hemagglutinins on antibody responses. *Vaccine* 1999. **18**: 805-814.
  221. **Tuting,T., Gambotto,A., Robbins,P.D., Storkus,W.J., and DeLeo,A.B.,** Co-delivery of T helper 1-biasing cytokine genes enhances the efficacy of gene gun immunization of mice: studies with the model tumor antigen beta-galactosidase and the BALB/c Meth A p53 tumor-specific antigen. *Gene Ther.* 1999. **6**: 629-636.
  222. **McCluskie,M.J., Brazolot Millan,C.L., Gramzinski,R.A., Robinson,H.L., Santoro,J.C., Fuller,J.T., Widera,G., Haynes,J.R., Purcell,R.H., and Davis,H.L.,** Route and method of delivery of

- DNA vaccine influence immune responses in mice and non-human primates. *Mol.Med.* 1999. **5**: 287-300.
223. **Leitner,W.W., Seguin,M.C., Ballou,W.R., Seitz,J.P., Schultz,A.M., Sheehy,M.J., and Lyon,J.A.,** Immune responses induced by intramuscular or gene gun injection of protective deoxyribonucleic acid vaccines that express the circumsporozoite protein from *Plasmodium berghei* malaria parasites. *J.Immunol.* 1997. **159**: 6112-6119.
224. **Boyle,J.S., Koniaras,C., and Lew,A.M.,** Influence of cellular location of expressed antigen on the efficacy of DNA vaccination: cytotoxic T lymphocyte and antibody responses are suboptimal when antigen is cytoplasmic after intramuscular DNA immunization. *Int.Immunol.* 1997. **9**: 1897-1906.
225. **Jankovic,D., Sher,A., and Yap,G.,** Th1/Th2 effector choice in parasitic infection: decision making by committee. *Curr.Opin.Immunol.* 2001. **13**: 403-409.
226. **Trinchieri,G.,** Interleukin-12 and the regulation of innate resistance and adaptive immunity. *Nat.Rev.Immunol.* 2003. **3**: 133-146.
227. **Li-Weber,M. and Krammer,P.H.,** Regulation of IL4 gene expression by T cells and therapeutic perspectives. *Nat.Rev.Immunol.* 2003. **3**: 534-543.
228. **Manetti,R., Parronchi,P., Giudizi,M.G., Piccinni,M.P., Maggi,E., Trinchieri,G., and Romagnani,S.,** Natural killer cell stimulatory factor (interleukin 12 [IL-12]) induces T helper type 1 (Th1)-specific immune responses and inhibits the development of IL-4-producing Th cells. *J.Exp.Med.* 1993. **177**: 1199-1204.
229. **Wu,C.Y., Demeure,C., Kiniwa,M., Gately,M., and Delespesse,G.,** IL-12 induces the production of IFN-gamma by neonatal human CD4 T cells. *J.Immunol.* 1993. **151**: 1938-1949.
230. **Magram,J., Connaughton,S.E., Warriar,R.R., Carvajal,D.M., Wu,C.Y., Ferrante,J., Stewart,C., Sarmiento,U., Faherty,D.A., and Gately,M.K.,** IL-12-deficient mice are defective in IFN gamma production and type 1 cytokine responses. *Immunity.* 1996. **4**: 471-481.
231. **Mattner,F., Magram,J., Ferrante,J., Launois,P., Di Padova,K., Behin,R., Gately,M.K., Louis,J.A., and Alber,G.,** Genetically resistant mice lacking interleukin-12 are susceptible to infection with *Leishmania major* and mount a polarized Th2 cell response. *Eur.J.Immunol.* 1996. **26**: 1553-1559.
232. **Sypek,J.P., Chung,C.L., Mayor,S.E., Subramanyam,J.M., Goldman,S.J., Sieburth,D.S., Wolf,S.F., and Schaub,R.G.,** Resolution of cutaneous leishmaniasis: interleukin 12 initiates a protective T helper type 1 immune response. *J.Exp.Med.* 1993. **177**: 1797-1802.
233. **Morris,S.C., Madden,K.B., Adamovicz,J.J., Gause,W.C., Hubbard,B.R., Gately,M.K., and Finkelman,F.D.,** Effects of IL-12 on in vivo cytokine gene expression and Ig isotype selection. *J.Immunol.* 1994. **152**: 1047-1056.
234. **Elser,B., Lohoff,M., Kock,S., Giaisi,M., Kirchhoff,S., Krammer,P.H., and Li-Weber,M.,** IFN-gamma represses IL-4 expression via IRF-1 and IRF-2. *Immunity.* 2002. **17**: 703-712.
235. **Okubo,T., Hagiwara,E., Ohno,S., Tsuji,T., Ihata,A., Ueda,A., Shirai,A., Aoki,I., Okuda,K., Miyazaki,J., and Ishigatsubo,Y.,** Administration of an IL-12-encoding DNA plasmid prevents the development of chronic graft-versus-host disease (GVHD). *J.Immunol.* 1999. **162**: 4013-4017.
236. **Oshikawa,K., Shi,F., Rakhmilevich,A.L., Sondel,P.M., Mahvi,D.M., and Yang,N.S.,** Synergistic inhibition of tumor growth in a murine mammary adenocarcinoma model by combinational gene therapy using IL-12, pro-IL-18, and IL-1beta converting enzyme cDNA. *Proc.Natl.Acad.Sci.U.S.A* 1999. **96**: 13351-13356.
237. **Sin,J.I., Kim,J.J., Arnold,R.L., Shroff,K.E., McCallus,D., Pachuk,C., McElhiney,S.P., Wolf,M.W., Pompa-de Bruin,S.J., Higgins,T.J., Ciccarelli,R.B., and Weiner,D.B.,** IL-12 gene as a DNA vaccine adjuvant in a herpes mouse model: IL-12 enhances Th1-type CD4+ T cell-mediated protective immunity against herpes simplex virus-2 challenge. *J.Immunol.* 1999. **162**: 2912-2921.
238. **Fallon,P.G., Jolin,H.E., Smith,P., Emson,C.L., Townsend,M.J., Fallon,R., Smith,P., and McKenzie,A.N.,** IL-4 induces characteristic Th2 responses even in the combined absence of IL-5, IL-9, and IL-13. *Immunity.* 2002. **17** : 7-17.
239. **Chatelain,R., Varkila,K., and Coffman,R.L.,** IL-4 induces a Th2 response in *Leishmania major*-infected mice. *J.Immunol.* 1992. **148**: 1182-1187.
240. **Vercelli,D., Jabara,H.H., Lauener,R.P., and Geha,R.S.,** IL-4 inhibits the synthesis of IFN-gamma and induces the synthesis of IgE in human mixed lymphocyte cultures. *J.Immunol.* 1990. **144**: 570-573.
241. **Nelms,K., Keegan,A.D., Zamorano,J., Ryan,J.J., and Paul,W.E.,** The IL-4 receptor: signaling mechanisms and biologic functions. *Annu.Rev.Immunol.* 1999. **17**: 701-738.
242. **dcbuch,** sfgregerg. 2003.
243. **Garside,P., Ingulli,E., Merica,R.R., Johnson,J.G., Noelle,R.J., and Jenkins,M.K.,** Visualization of specific B and T lymphocyte interactions in the lymph node. *Science* 1998. **281**: 96-99.
244. **Luther,S.A., Gulbranson-Judge,A., Acha-Orbea,H., and MacLennan,I.C.,** Viral superantigen drives extrafollicular and follicular B cell differentiation leading to virus-specific antibody production. *J.Exp.Med.* 1997. **185**: 551-562.

245. **Biedermann,T., Zimmermann,S., Himmelrich,H., Gumy,A., Egeter,O., Sakrauski,A.K., Seegmuller,I., Voigt,H., Launois,P., Levine,A.D., Wagner,H., Heeg,K., Louis,J.A., and Rocken,M.,** IL-4 instructs TH1 responses and resistance to Leishmania major in susceptible BALB/c mice. *Nat.Immunol.* 2001. **2:** 1054-1060.
246. **Kobayashi,M., Fitz,L., Ryan,M., Hewick,R.M., Clark,S.C., Chan,S., Loudon,R., Sherman,F., Perussia,B., and Trinchieri,G.,** Identification and purification of natural killer cell stimulatory factor (NKSF), a cytokine with multiple biologic effects on human lymphocytes. *J.Exp.Med.* 1989. **170:** 827-845.
247. **Wolf,S.F., Temple,P.A., Kobayashi,M., Young,D., Dicig,M., Lowe,L., Dzialo,R., Fitz,L., Ferenz,C., Hewick,R.M., and .,** Cloning of cDNA for natural killer cell stimulatory factor, a heterodimeric cytokine with multiple biologic effects on T and natural killer cells. *J.Immunol.* 1991. **146:** 3074-3081.
248. **Gubler,U., Chua,A.O., Schoenhaut,D.S., Dwyer,C.M., McComas,W., Motyka,R., Nabavi,N., Wolitzky,A.G., Quinn,P.M., Familletti,P.C., and .,** Coexpression of two distinct genes is required to generate secreted bioactive cytotoxic lymphocyte maturation factor. *Proc.Natl.Acad.Sci.U.S.A* 1991. **88:** 4143-4147.
249. **D'Andrea,A., Rengaraju,M., Valiante,N.M., Chehimi,J., Kubin,M., Aste,M., Chan,S.H., Kobayashi,M., Young,D., Nickbarg,E., and .,** Production of natural killer cell stimulatory factor (interleukin 12) by peripheral blood mononuclear cells. *J.Exp.Med.* 1992. **176:** 1387-1398.
250. **Heinzel,F.P., Hujer,A.M., Ahmed,F.N., and Rerko,R.M.,** In vivo production and function of IL-12 p40 homodimers. *J.Immunol.* 1997. **158:** 4381-4388.
251. **Gillessen,S., Carvajal,D., Ling,P., Podlaski,F.J., Stremlo,D.L., Familletti,P.C., Gubler,U., Presky,D.H., Stern,A.S., and Gately,M.K.,** Mouse interleukin-12 (IL-12) p40 homodimer: a potent IL-12 antagonist. *Eur.J.Immunol.* 1995. **25:** 200-206.
252. **Ling,P., Gately,M.K., Gubler,U., Stern,A.S., Lin,P., Hollfelder,K., Su,C., Pan,Y.C., and Hakimi,J.,** Human IL-12 p40 homodimer binds to the IL-12 receptor but does not mediate biologic activity. *J.Immunol.* 1995. **154:** 116-127.
253. **Brombacher,F., Kastelein,R.A., and Alber,G.,** Novel IL-12 family members shed light on the orchestration of Th1 responses. *Trends Immunol.* 2003. **24:** 207-212.
254. **Larregina,A.T. and Falot,L.D., Jr.,** Dendritic cells in the context of skin immunity. *Dendritic Cells: Biology and Clinical Application.* Academic Press, 2001, pp 301-314.
255. **Kalinski,P., Schuitemaker,J.H., Hilkens,C.M., Wierenga,E.A., and Kapsenberg,M.L.,** Final maturation of dendritic cells is associated with impaired responsiveness to IFN-gamma and to bacterial IL-12 inducers: decreased ability of mature dendritic cells to produce IL-12 during the interaction with Th cells. *J.Immunol.* 1999. **162:** 3231-3236.
256. **Cumberbatch,M., Dearman,R.J., and Kimber,I.,** Constitutive and inducible expression of interleukin-6 by Langerhans cells and lymph node dendritic cells. *Immunology* 1996. **87:** 513-518.
257. **Sallusto,F. and 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:** 1109-1118.
258. **Ruedl,C., Koebel,P., Bachmann,M., Hess,M., and Karjalainen,K.,** Anatomical Origin of Dendritic Cells Determines Their Life Span in Peripheral Lymph Nodes. *J Immunol* 2000. **165:** 4910-4916.
259. **Schweitzer,A.N. and Sharpe,A.H.,** Studies using antigen-presenting cells lacking expression of both B7-1 (CD80) and B7-2 (CD86) show distinct requirements for B7 molecules during priming versus restimulation of Th2 but not Th1 cytokine production. *J.Immunol.* 1998. **161:** 2762-2771.
260. **Rulifson,I.C., Sperling,A.I., Fields,P.E., Fitch,F.W., and Bluestone,J.A.,** CD28 costimulation promotes the production of Th2 cytokines. *J.Immunol.* 1997. **158:** 658-665.
261. **Salomon,B. and Bluestone,J.A.,** LFA-1 interaction with ICAM-1 and ICAM-2 regulates Th2 cytokine production. *J.Immunol.* 1998. **161:** 5138-5142.
262. **de Waal,M.R., Haanen,J., Spits,H., Roncarolo,M.G., te,V.A., Figdor,C., Johnson,K., Kastelein,R., Yssel,H., and de Vries,J.E.,** Interleukin 10 (IL-10) and viral IL-10 strongly reduce antigen-specific human T cell proliferation by diminishing the antigen-presenting capacity of monocytes via downregulation of class II major histocompatibility complex expression. *J.Exp.Med.* 1991. **174:** 915-924.
263. **Fiorentino,D.F., Zlotnik,A., Vieira,P., Mosmann,T.R., Howard,M., Moore,K.W., and O'Garra,A.,** IL-10 acts on the antigen-presenting cell to inhibit cytokine production by Th1 cells. *J.Immunol.* 1991. **146:** 3444-3451.
264. **Kehrl,J.H., Wakefield,L.M., Roberts,A.B., Jakowlew,S., Alvarez-Mon,M., Derynck,R., Sporn,M.B., and Fauci,A.S.,** Production of transforming growth factor beta by human T lymphocytes and its potential role in the regulation of T cell growth. *J.Exp.Med.* 1986. **163:** 1037-1050.
265. **Kuklin,N.A., Daheshia,M., Chun,S., and Rouse,B.T.,** Immunomodulation by mucosal gene transfer using TGF-beta DNA. *J.Clin.Invest* 1998. **102:** 438-444.

266. **Song,X.Y., Gu,M., Jin,W.W., Klinman,D.M., and Wahl,S.M.,** Plasmid DNA encoding transforming growth factor-beta1 suppresses chronic disease in a streptococcal cell wall-induced arthritis model. *J.Clin.Invest* 1998. **101**: 2615-2621.
267. **Rogy,M.A., Auffenberg,T., Espat,N.J., Philip,R., Remick,D., Wollenberg,G.K., Copeland,E.M., III, and Moldawer,L.L.,** Human tumor necrosis factor receptor (p55) and interleukin 10 gene transfer in the mouse reduces mortality to lethal endotoxemia and also attenuates local inflammatory responses. *J.Exp.Med.* 1995. **181**: 2289-2293.
268. **MacNeil,I.A., Suda,T., Moore,K.W., Mosmann,T.R., and Zlotnik,A.,** IL-10, a novel growth cofactor for mature and immature T cells. *J.Immunol.* 1990. **145**: 4167-4173.
269. **Go,N.F., Castle,B.E., Barrett,R., Kastelein,R., Dang,W., Mosmann,T.R., Moore,K.W., and Howard,M.,** Interleukin 10, a novel B cell stimulatory factor: unresponsiveness of X chromosome-linked immunodeficiency B cells. *J.Exp.Med.* 1990. **172**: 1625-1631.
270. **Diehl,S., Chow,C.W., Weiss,L., Palmethofer,A., Twardzik,T., Rounds,L., Serfling,E., Davis,R.J., Anguita,J., and Rincon,M.,** Induction of NFATc2 expression by interleukin 6 promotes T helper type 2 differentiation. *J.Exp.Med.* 2002. **196**: 39-49.
271. **O'Garra,A.,** Cytokines induce the development of functionally heterogeneous T helper cell subsets. *Immunity.* 1998. **8**: 275-283.
272. **Reiner,S.L.,** Helper T cell differentiation, inside and out. *Curr.Opin.Immunol.* 2001. **13**: 351-355.
273. **Grabstein,K.H., Eisenman,J., Shanebeck,K., Rauch,C., Srinivasan,S., Fung,V., Beers,C., Richardson,J., Schoenborn,M.A., Ahdieh,M., and .,** Cloning of a T cell growth factor that interacts with the beta chain of the interleukin-2 receptor. *Science* 1994. **264**: 965-968.
274. **Burton,J.D., Bamford,R.N., Peters,C., Grant,A.J., Kurys,G., Goldman,C.K., Brennan,J., Roessler,E., and Waldmann,T.A.,** A lymphokine, provisionally designated interleukin T and produced by a human adult T-cell leukemia line, stimulates T-cell proliferation and the induction of lymphokine-activated killer cells. *Proc.Natl.Acad.Sci.U.S.A* 1994. **91**: 4935-4939.
275. **Korholz,D., Banning,U., Bonig,H., Grewe,M., Schneider,M., Mauz-Korholz,C., Klein-Vehne,A., Krutmann,J., and Burdach,S.,** The role of interleukin-10 (IL-10) in IL-15-mediated T-cell responses. *Blood* 1997. **90**: 4513-4521.
276. **Waldmann,T.,** The contrasting roles of IL-2 and IL-15 in the life and death of lymphocytes: implications for the immunotherapy of rheumatological diseases. *Arthritis Res.* 2002. **4 Suppl 3**: S161-S167.
277. **Minami,Y., Kono,T., Miyazaki,T., and Taniguchi,T.,** The IL-2 receptor complex: its structure, function, and target genes. *Annu.Rev.Immunol.* 1993. **11**: 245-268.
278. **Waldmann,T.A.,** The IL-2/IL-15 receptor systems: targets for immunotherapy. *J.Clin.Immunol.* 2002. **22**: 51-56.
279. **O'Shea,J.J., Ma,A., and Lipsky,P.,** Cytokines and autoimmunity. *Nat.Rev.Immunol.* 2002. **2**: 37-45.
280. **Lauzurica,P., Sancho,D., Torres,M., Albella,B., Marazuela,M., Merino,T., Bueren,J.A., Martinez,A., and Sanchez-Madrid,F.,** Phenotypic and functional characteristics of hematopoietic cell lineages in CD69-deficient mice. *Blood* 2000. **95**: 2312-2320.
281. **Murata,K., Inami,M., Hasegawa,A., Kubo,S., Kimura,M., Yamashita,M., Hosokawa,H., Nagao,T., Suzuki,K., Hashimoto,K., Shinkai,H., Koseki,H., Taniguchi,M., Ziegler,S.F., and Nakayama,T.,** CD69-null mice protected from arthritis induced with anti-type II collagen antibodies. *Int.Immunol.* 2003. **15**: 987-992.
282. **Esplugues,E., Sancho,D., Vega-Ramos,J., Martinez,C., Syrbe,U., Hamann,A., Engel,P., Sanchez-Madrid,F., and Lauzurica,P.,** Enhanced antitumor immunity in mice deficient in CD69. *J.Exp.Med.* 2003. **197**: 1093-1106.
283. **Feng,C., Woodside,K.J., Vance,B.A., El Khoury,D., Canelles,M., Lee,J., Gress,R., Fowlkes,B.J., Shores,E.W., and Love,P.E.,** A potential role for CD69 in thymocyte emigration. *Int.Immunol.* 2002. **14**: 535-544.