

# Literatur

1. Uckun, F.M., et al., *Biology and treatment of childhood T-lineage acute lymphoblastic leukemia*. Blood, 1998. **91**(3): p. 735-46.
2. Reiter, A., et al., *Chemotherapy in 998 unselected childhood acute lymphoblastic leukemia patients. Results and conclusions of the multicenter trial ALL-BFM 86*. Blood, 1994. **84**(9): p. 3122-33.
3. Pieters, R., et al., *Relation between age, immunophenotype and in vitro drug resistance in 395 children with acute lymphoblastic leukemia--implications for treatment of infants*. Leukemia, 1998. **12**(9): p. 1344-8.
4. Kaspers, G.J., et al., *In vitro cellular drug resistance and prognosis in newly diagnosed childhood acute lymphoblastic leukemia*. Blood, 1997. **90**(7): p. 2723-9.
5. Bartram, C.R., *Molecular genetic aspects of myelodysplastic syndromes*. Hematol Oncol Clin North Am, 1992. **6**(3): p. 557-70.
6. Raskind, W.H., L. Steinmann, and V. Najfeld, *Clonal development of myeloproliferative disorders: clues to hematopoietic differentiation and multistep pathogenesis of cancer*. Leukemia, 1998. **12**(2): p. 108-16.
7. Fauser, A., ed. *Stammzellsystem. Hämatologie/Onkologie*. ed. Ostendorf. 1997, Urban+Schwarzenberg Verlag.
8. Pui, C.H., F.G. Behm, and W.M. Crist, *Clinical and biologic relevance of immunologic marker studies in childhood acute lymphoblastic leukemia*. Blood, 1993. **82**(2): p. 343-62.
9. Loken, M.R., et al., *Flow cytometric analysis of human bone marrow. II. Normal B lymphocyte development*. Blood, 1987. **70**(5): p. 1316-24.
10. Uckun, F.M., et al., *Biphenotypic leukemic lymphocyte precursors in CD2+CD19+ acute lymphoblastic leukemia and their putative normal counterparts in human fetal hematopoietic tissues*. Blood, 1989. **73**(4): p. 1000-15.
11. Greaves, M.F., *Differentiation-linked leukemogenesis in lymphocytes*. Science, 1986. **234**(4777): p. 697-704.
12. Smith, L.J., et al., *Lineage infidelity in acute leukemia*. Blood, 1983. **61**(6): p. 1138-45.
13. Ludwig, W.D. and E. Thiel, *[Diagnosis of acute leukemia with morphologic, immunologic and cytogenetic procedures]*. Internist Berl, 1993. **34**(6): p. 498-510.
14. Ludwig, W.-D., T. Haferlach, and C. Schoch, *Classification of Acute Leukemias*, in *Treatment of Acute Leukemias, New Directions for Clinical Research*, M. Ching-Hon Pui, Editor. Humana Press, USA 2003.
15. Bene, M.C., et al., *Proposals for the immunological classification of acute leukemias. European Group for the Immunological Characterization of Leukemias (EGIL)*. Leukemia, 1995. **9**(10): p. 1783-6.
16. Charles A. Janeway, P.T., Mark Walport, Mark Shlomchik, *Immunobiology: The Immune System in Health & Disease*. 2001: Garland Science Publishing.
17. Camitta, B.M., J. Pullen, and S. Murphy, *Biology and treatment of acute lymphocytic leukemia in children*. Semin Oncol, 1997. **24**(1): p. 83-91.
18. Schrappe, M., et al., *[Concept and interim result of the ALL-BFM 90 therapy study in treatment of acute lymphoblastic leukemia in children and adolescents: the significance of initial therapy response in blood and bone marrow]*. Klin Padiatr, 1994. **206**(4): p. 208-21.
19. Kerr, J.F., A.H. Wyllie, and A.R. Currie, *Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics*. Br J Cancer, 1972. **26**(4): p. 239-57.
20. Jacobson, M.D., M. Weil, and M.C. Raff, *Programmed cell death in animal development*. Cell, 1997. **88**(3): p. 347-54.
21. Bellamy, C.O., et al., *Cell death in health and disease: the biology and regulation of apoptosis*. Semin Cancer Biol, 1995. **6**(1): p. 3-16.
22. Majno, G. and I. Joris, *Apoptosis, oncosis, and necrosis. An overview of cell death*. Am J Pathol, 1995. **146**(1): p. 3-15.
23. Krammer, P.H., et al., *Regulation of apoptosis in the immune system*. Curr Opin Immunol, 1994. **6**(2): p. 279-89.
24. Krammer, P.H., in *Deutsches Ärzteblatt*. 2000.

25. Wyllie, A.H., *The genetic regulation of apoptosis*. *Curr Opin Genet Dev*, 1995. **5**(1): p. 97-104.
26. Nagata, S. and P. Golstein, *The Fas death factor*. *Science*, 1995. **267**(5203): p. 1449-56.
27. Trauth, B.C., et al., *Monoclonal antibody-mediated tumor regression by induction of apoptosis*. *Science*, 1989. **245**(4915): p. 301-5.
28. Zlotnik, A. and T.A. Moore, *Cytokine production and requirements during T-cell development*. *Curr Opin Immunol*, 1995. **7**(2): p. 206-13.
29. Akbar, A.N. and M. Salmon, *Cellular environments and apoptosis: tissue microenvironments control activated T-cell death*. *Immunol Today*, 1997. **18**(2): p. 72-6.
30. Karawajew, L., et al., *Differential CD95 expression and function in T and B lineage acute lymphoblastic leukemia cells*. *Leukemia*, 1997. **11**(8): p. 1245-52.
31. Manabe, A., et al., *Bone marrow-derived stromal cells prevent apoptotic cell death in B-lineage acute lymphoblastic leukemia*. *Blood*, 1992. **79**(9): p. 2370-7.
32. Kroemer, G., N. Zamzami, and S.A. Susin, *Mitochondrial control of apoptosis*. *Immunol Today*, 1997. **18**(1): p. 44-51.
33. Korsmeyer, S.J., *Regulators of cell death*. *Trends Genet*, 1995. **11**(3): p. 101-5.
34. Farrow, S.N. and R. Brown, *New members of the Bcl-2 family and their protein partners*. *Curr Opin Genet Dev*, 1996. **6**(1): p. 45-9.
35. Martin, S.J., et al., *Early redistribution of plasma membrane phosphatidylserine is a general feature of apoptosis regardless of the initiating stimulus: inhibition by overexpression of Bcl-2 and Abl*. *J Exp Med*, 1995. **182**(5): p. 1545-56.
36. Callahan, M.K., P. Williamson, and R.A. Schlegel, *Surface expression of phosphatidylserine on macrophages is required for phagocytosis of apoptotic thymocytes*. *Cell Death Differ*, 2000. **7**(7): p. 645-53.
37. Krahling, S., et al., *Exposure of phosphatidylserine is a general feature in the phagocytosis of apoptotic lymphocytes by macrophages*. *Cell Death Differ*, 1999. **6**(2): p. 183-9.
38. Martin, S.J. and D.R. Green, *Protease activation during apoptosis: death by a thousand cuts?* *Cell*, 1995. **82**(3): p. 349-52.
39. Yuan, J., et al., *The C. elegans cell death gene ced-3 encodes a protein similar to mammalian interleukin-1 beta-converting enzyme*. *Cell*, 1993. **75**(4): p. 641-52.
40. Thornberry, N.A., et al., *A novel heterodimeric cysteine protease is required for interleukin-1 beta processing in monocytes*. *Nature*, 1992. **356**(6372): p. 768-74.
41. Thornberry, N.A. and Y. Lazebnik, *Caspases: enemies within*. *Science*, 1998. **281**(5381): p. 1312-6.
42. Tsujimoto, Y. and C.M. Croce, *Analysis of the structure, transcripts, and protein products of bcl-2, the gene involved in human follicular lymphoma*. *Proc Natl Acad Sci U S A*, 1986. **83**(14): p. 5214-8.
43. Reed, J.C., *Regulation of apoptosis by bcl-2 family proteins and its role in cancer and chemoresistance*. *Curr Opin Oncol*, 1995. **7**(6): p. 541-6.
44. Reed, J.C., *Bcl-2 and the regulation of programmed cell death*. *J Cell Biol*, 1994. **124**(1-2): p. 1-6.
45. Boise, L.H., et al., *bcl-x, a bcl-2-related gene that functions as a dominant regulator of apoptotic cell death*. *Cell*, 1993. **74**(4): p. 597-608.
46. Adams, J.M. and S. Cory, *The Bcl-2 protein family: arbiters of cell survival*. *Science*, 1998. **281**(5381): p. 1322-6.
47. Schimmer, A.D., et al., *Receptor- and mitochondrial-mediated apoptosis in acute leukemia: a translational view*. *Blood*, 2001. **98**(13): p. 3541-53.
48. Adams, J.M. and S. Cory, *Life-or-death decisions by the Bcl-2 protein family*. *Trends Biochem Sci*, 2001. **26**(1): p. 61-6.
49. Reed, J.C., *Mechanisms of Bcl-2 family protein function and dysfunction in health and disease*. *Behring Inst Mitt*, 1996(97): p. 72-100.
50. Zha, H., et al., *Structure-function comparisons of the proapoptotic protein Bax in yeast and mammalian cells*. *Mol Cell Biol*, 1996. **16**(11): p. 6494-508.
51. Cory, S. and J.M. Adams, *The Bcl2 family: regulators of the cellular life-or-death switch*. *Nat Rev Cancer*, 2002. **2**(9): p. 647-56.

52. Green, D.R. and J.C. Reed, *Mitochondria and apoptosis*. Science, 1998. **281**(5381): p. 1309-12.
53. Hsu, Y.T., K.G. Wolter, and R.J. Youle, *Cytosol-to-membrane redistribution of Bax and Bcl-X(L) during apoptosis*. Proc Natl Acad Sci U S A, 1997. **94**(8): p. 3668-72.
54. Lithgow, T., et al., *The protein product of the oncogene bcl-2 is a component of the nuclear envelope, the endoplasmic reticulum, and the outer mitochondrial membrane*. Cell Growth Differ, 1994. **5**(4): p. 411-7.
55. Wolter, K.G., et al., *Movement of Bax from the cytosol to mitochondria during apoptosis*. J Cell Biol, 1997. **139**(5): p. 1281-92.
56. Akao, Y., et al., *Multiple subcellular localization of bcl-2: detection in nuclear outer membrane, endoplasmic reticulum membrane, and mitochondrial membranes*. Cancer Res, 1994. **54**(9): p. 2468-71.
57. Gross, A., J.M. McDonnell, and S.J. Korsmeyer, *BCL-2 family members and the mitochondria in apoptosis*. Genes Dev, 1999. **13**(15): p. 1899-911.
58. Kroemer, G., *The proto-oncogene Bcl-2 and its role in regulating apoptosis [published erratum appears in Nat Med 1997 Aug;3(8):934]*. Nat Med, 1997. **3**(6): p. 614-20.
59. Bellosillo, B., et al., *Complement-mediated cell death induced by rituximab in B-cell lymphoproliferative disorders is mediated in vitro by a caspase-independent mechanism involving the generation of reactive oxygen species*. Blood, 2001. **98**(9): p. 2771-7.
60. Shimizu, S., et al., *Bcl-2 prevents apoptotic mitochondrial dysfunction by regulating proton flux*. Proc Natl Acad Sci U S A, 1998. **95**(4): p. 1455-9.
61. Matsuyama, S., et al., *The Mitochondrial FOF1-ATPase proton pump is required for function of the proapoptotic protein Bax in yeast and mammalian cells*. Mol Cell, 1998. **1**(3): p. 327-36.
62. Herr, I. and K.M. Debatin, *Cellular stress response and apoptosis in cancer therapy*. Blood, 2001. **98**(9): p. 2603-14.
63. Zimmermann, K.C., C. Bonzon, and D.R. Green, *The machinery of programmed cell death*. Pharmacol Ther, 2001. **92**(1): p. 57-70.
64. Liu, X., et al., *DFF, a heterodimeric protein that functions downstream of caspase-3 to trigger DNA fragmentation during apoptosis*. Cell, 1997. **89**(2): p. 175-84.
65. Marzo, I., et al., *Caspases disrupt mitochondrial membrane barrier function*. FEBS Lett, 1998. **427**(2): p. 198-202.
66. Smith, C.A., T. Farrar, and R.G. Goodwin, *The TNF receptor superfamily of cellular and viral proteins: activation, costimulation, and death*. Cell, 1994. **76**(6): p. 959-62.
67. Locksley, R.M., N. Killeen, and M.J. Lenardo, *The TNF and TNF receptor superfamilies: integrating mammalian biology*. Cell, 2001. **104**(4): p. 487-501.
68. Huang, B., et al., *NMR structure and mutagenesis of the Fas (APO-1/CD95) death domain*. Nature, 1996. **384**(6610): p. 638-41.
69. Chinnaiyan, A.M., et al., *FADD, a novel death domain-containing protein, interacts with the death domain of Fas and initiates apoptosis*. Cell, 1995. **81**(4): p. 505-12.
70. Boldin, M.P., et al., *Self-association of the "death domains" of the p55 tumor necrosis factor (TNF) receptor and Fas/APO1 prompts signaling for TNF and Fas/APO1 effects*. J Biol Chem, 1995. **270**(1): p. 387-91.
71. Ashkenazi, A. and V.M. Dixit, *Death receptors: signaling and modulation*. Science, 1998. **281**(5381): p. 1305-8.
72. Nagata, S., *Apoptosis by death factor*. Cell, 1997. **88**(3): p. 355-65.
73. Medema, J.P., et al., *FLICE is activated by association with the CD95 death-inducing signaling complex (DISC)*. Embo J, 1997. **16**(10): p. 2794-804.
74. Muggia, F.M. and M.D. Green, *New anthracycline antitumor antibiotics*. Crit Rev Oncol Hematol, 1991. **11**(1): p. 43-64.
75. Richardson, D.S. and S.A. Johnson, *Anthracyclines in haematology: preclinical studies, toxicity and delivery systems*. Blood Rev, 1997. **11**(4): p. 201-23.
76. Lowe, S.W., et al., *p53-dependent apoptosis modulates the cytotoxicity of anticancer agents*. Cell, 1993. **74**(6): p. 957-67.
77. Lowe, S.W., et al., *p53 is required for radiation-induced apoptosis in mouse thymocytes*. Nature, 1993. **362**(6423): p. 847-9.

78. Miyashita, T. and J.C. Reed, *Tumor suppressor p53 is a direct transcriptional activator of the human bax gene*. Cell, 1995. **80**(2): p. 293-9.
79. Kastan, M.B., et al., *Participation of p53 protein in the cellular response to DNA damage*. Cancer Res, 1991. **51**(23 Pt 1): p. 6304-11.
80. Kuerbitz, S.J., et al., *Wild-type p53 is a cell cycle checkpoint determinant following irradiation*. Proc Natl Acad Sci U S A, 1992. **89**(16): p. 7491-5.
81. Kastan, M.B., et al., *A mammalian cell cycle checkpoint pathway utilizing p53 and GADD45 is defective in ataxia-telangiectasia*. Cell, 1992. **71**(4): p. 587-97.
82. Livingstone, L.R., et al., *Altered cell cycle arrest and gene amplification potential accompany loss of wild-type p53*. Cell, 1992. **70**(6): p. 923-35.
83. Paulovich, A.G., D.P. Toczyski, and L.H. Hartwell, *When checkpoints fail*. Cell, 1997. **88**(3): p. 315-21.
84. Han, J., et al., *Expression of bbc3, a pro-apoptotic BH3-only gene, is regulated by diverse cell death and survival signals*. Proc Natl Acad Sci U S A, 2001. **98**(20): p. 11318-23.
85. Wu, X. and Y. Deng, *Bax and BH3-domain-only proteins in p53-mediated apoptosis*. Front Biosci, 2002. **7**: p. d151-6.
86. McCurrach, M.E., et al., *bax-deficiency promotes drug resistance and oncogenic transformation by attenuating p53-dependent apoptosis*. Proc Natl Acad Sci U S A, 1997. **94**(6): p. 2345-9.
87. Findley, H.W., et al., *Expression and regulation of Bcl-2, Bcl-xl, and Bax correlate with p53 status and sensitivity to apoptosis in childhood acute lymphoblastic leukemia*. Blood, 1997. **89**(8): p. 2986-93.
88. He, A.W. and J.G. Cory, *Effect of doxorubicin on wild-type and deoxyadenosine-resistant mouse leukemia L1210 cells*. Int J Oncol, 1999. **14**(5): p. 891-5.
89. Geley, S., et al., *p53-induced apoptosis in the human T-ALL cell line CCRF-CEM*. Oncogene, 1997. **15**(20): p. 2429-37.
90. Laurent, G. and J.P. Jaffrezou, *Signaling pathways activated by daunorubicin*. Blood, 2001. **98**(4): p. 913-24.
91. Decaudin, D., et al., *Bcl-2 and Bcl-XL antagonize the mitochondrial dysfunction preceding nuclear apoptosis induced by chemotherapeutic agents*. Cancer Res, 1997. **57**(1): p. 62-7.
92. Friesen, C., et al., *Involvement of the CD95 (APO-1/FAS) receptor/ligand system in drug-induced apoptosis in leukemia cells*. Nat Med, 1996. **2**(5): p. 574-7.
93. Posovszky, C., et al., *Chemotherapeutic drugs sensitize pre-B ALL cells for CD95- and cytotoxic T-lymphocyte-mediated apoptosis*. Leukemia, 1999. **13**(3): p. 400-9.
94. Micheau, O., et al., *Sensitization of cancer cells treated with cytotoxic drugs to fas-mediated cytotoxicity*. J Natl Cancer Inst, 1997. **89**(11): p. 783-9.
95. Friesen, C., S. Fulda, and K.M. Debatin, *Deficient activation of the CD95 (APO-1/Fas) system in drug-resistant cells*. Leukemia, 1997. **11**(11): p. 1833-41.
96. Landowski, T.H., M.C. Gleason Guzman, and W.S. Dalton, *Selection for drug resistance results in resistance to Fas-mediated apoptosis*. Blood, 1997. **89**(6): p. 1854-61.
97. McGahon, A.J., et al., *Chemotherapeutic drug-induced apoptosis in human leukaemic cells is independent of the Fas (APO-1/CD95) receptor/ligand system*. Br J Haematol, 1998. **101**(3): p. 539-47.
98. Gamen, S., et al., *Doxorubicin-induced apoptosis in human T-cell leukemia is mediated by caspase-3 activation in a Fas-independent way*. FEBS Lett, 1997. **417**(3): p. 360-4.
99. Eischen, C.M., et al., *Comparison of apoptosis in wild-type and Fas-resistant cells: chemotherapy-induced apoptosis is not dependent on Fas/Fas ligand interactions*. Blood, 1997. **90**(3): p. 935-43.
100. Villunger, A., et al., *Drug-induced apoptosis is associated with enhanced Fas (Apo-1/CD95) ligand expression but occurs independently of Fas (Apo-1/CD95) signaling in human T-acute lymphatic leukemia cells*. Cancer Res, 1997. **57**(16): p. 3331-4.
101. Wesselborg, S., et al., *Anticancer drugs induce caspase-8/FLICE activation and apoptosis in the absence of CD95 receptor/ligand interaction*. Blood, 1999. **93**(9): p. 3053-63.
102. Vacchio, M.S., L.B. King, and J.D. Ashwell, *Regulation of thymocyte development by glucocorticoids*. Behring Inst Mitt, 1996(97): p. 24-31.

103. Schimmer BP, B.K., in *Goodman and Gilman's: The pharmacological basis of therapeutics*, ed. L.L. Hardman JG. 1996. 1459-1485.
104. Gaynon, P.S. and R.H. Lustig, *The use of glucocorticoids in acute lymphoblastic leukemia of childhood. Molecular, cellular, and clinical considerations*. J Pediatr Hematol Oncol, 1995. **17**(1): p. 1-12.
105. Harmon, J.M., et al., *Dexamethasone induces irreversible G1 arrest and death of a human lymphoid cell line*. J Cell Physiol, 1979. **98**(2): p. 267-78.
106. Lanza, L., et al., *Prednisone increases apoptosis in in vitro activated human peripheral blood T lymphocytes*. Clin Exp Immunol, 1996. **103**(3): p. 482-90.
107. Rhee, K., et al., *c-Myc and cyclin D3 (CcnD3) genes are independent targets for glucocorticoid inhibition of lymphoid cell proliferation*. Cancer Res, 1995. **55**(18): p. 4188-95.
108. Paliogianni, F., et al., *Novel mechanism for inhibition of human T cells by glucocorticoids. Glucocorticoids inhibit signal transduction through IL-2 receptor*. J Immunol, 1993. **151**(8): p. 4081-9.
109. King, K.L. and J.A. Cidlowski, *Cell cycle regulation and apoptosis*. Annu Rev Physiol, 1998. **60**: p. 601-17.
110. Ausserlechner, M.J., et al., *The cell cycle inhibitor p16(INK4A) sensitizes lymphoblastic leukemia cells to apoptosis by physiologic glucocorticoid levels*. J Biol Chem, 2001. **276**(24): p. 10984-9.
111. Yoshida, N.L., et al., *Analysis of gene expression patterns during glucocorticoid-induced apoptosis using oligonucleotide arrays*. Biochem Biophys Res Commun, 2002. **293**(4): p. 1254-61.
112. Cohen, J.J. and R.C. Duke, *Glucocorticoid activation of a calcium-dependent endonuclease in thymocyte nuclei leads to cell death*. J Immunol, 1984. **132**(1): p. 38-42.
113. Ashwell, J.D., F.W. Lu, and M.S. Vacchio, *Glucocorticoids in T cell development and function\**. Annu Rev Immunol, 2000. **18**: p. 309-45.
114. Greenstein, S., et al., *Mechanisms of glucocorticoid-mediated apoptosis in hematological malignancies*. Clin Cancer Res, 2002. **8**(6): p. 1681-94.
115. Veis, D.J., et al., *Bcl-2-deficient mice demonstrate fulminant lymphoid apoptosis, polycystic kidneys, and hypopigmented hair*. Cell, 1993. **75**(2): p. 229-40.
116. Katsumata, M., et al., *Differential effects of Bcl-2 on T and B cells in transgenic mice*. Proc Natl Acad Sci U S A, 1992. **89**(23): p. 11376-80.
117. Smets, L.A., et al., *BCL-2 expression and mitochondrial activity in leukemic cells with different sensitivity to glucocorticoid-induced apoptosis*. Blood, 1994. **84**(5): p. 1613-9.
118. Tosi, P., et al., *Biological and clinical significance of in vitro prednisolone resistance in adult acute lymphoblastic leukaemia*. Eur J Haematol, 1996. **57**(2): p. 134-41.
119. McConkey, D.J., et al., *Apoptosis sensitivity in chronic lymphocytic leukemia is determined by endogenous endonuclease content and relative expression of BCL-2 and BAX*. J Immunol, 1996. **156**(7): p. 2624-30.
120. Salomons, G.S., et al., *The Bax alpha:Bcl-2 ratio modulates the response to dexamethasone in leukaemic cells and is highly variable in childhood acute leukaemia*. Int J Cancer, 1997. **71**(6): p. 959-65.
121. Stoetzer, O.J., et al., *Drug-induced apoptosis in chronic lymphocytic leukemia*. Leukemia, 1999. **13**(11): p. 1873-80.
122. Lotem, J. and L. Sachs, *Regulation of bcl-2, bcl-XL and bax in the control of apoptosis by hematopoietic cytokines and dexamethasone*. Cell Growth Differ, 1995. **6**(6): p. 647-53.
123. Osorio, L.M., et al., *CD6 ligation modulates the Bcl-2/Bax ratio and protects chronic lymphocytic leukemia B cells from apoptosis induced by anti-IgM*. Blood, 1997. **89**(8): p. 2833-41.
124. Casale, F., et al., *Determination of the in vivo effects of prednisone on Bcl-2 family protein expression in childhood acute lymphoblastic leukemia*. Int J Oncol, 2003. **22**(1): p. 123-8.
125. Kofler, R., *The molecular basis of glucocorticoid-induced apoptosis of lymphoblastic leukemia cells*. Histochem Cell Biol, 2000. **114**(1): p. 1-7.
126. Hirsch, T., et al., *The apoptosis-necrosis paradox. Apoptogenic proteases activated after mitochondrial permeability transition determine the mode of cell death*. Oncogene, 1997. **15**(13): p. 1573-81.

127. Schmidt, M., et al., *Role of the CD95/CD95 ligand system in glucocorticoid-induced monocyte apoptosis*. J Immunol, 2001. **166**(2): p. 1344-51.
128. Park, J.R., *Cytokine regulation of apoptosis in hematopoietic precursor cells*. Curr Opin Hematol, 1996. **3**(3): p. 191-6.
129. Williams, D.E., et al., *Cytokine regulation of hematopoietic stem cells*. Semin Immunol, 1991. **3**(6): p. 391-6.
130. Raff, M.C., *Social controls on cell survival and cell death*. Nature, 1992. **356**(6368): p. 397-400.
131. Manabe, A., et al., *Adhesion-dependent survival of normal and leukemic human B lymphoblasts on bone marrow stromal cells*. Blood, 1994. **83**(3): p. 758-66.
132. Duke, R.C. and J.J. Cohen, *IL-2 addiction: withdrawal of growth factor activates a suicide program in dependent T cells*. Lymphokine Res, 1986. **5**(4): p. 289-99.
133. Hernandez-Caselles, T., et al., *Interleukin-7 rescues human activated T lymphocytes from apoptosis induced by glucocorticosteroids and regulates bcl-2 and CD25 expression*. Hum Immunol, 1995. **43**(3): p. 181-9.
134. Di Santo, J.P., R. Kuhn, and W. Muller, *Common cytokine receptor gamma chain (gamma c)-dependent cytokines: understanding in vivo functions by gene targeting*. Immunol Rev, 1995. **148**: p. 19-34.
135. DiSanto, J.P., et al., *Lymphoid development in mice with a targeted deletion of the interleukin 2 receptor gamma chain*. Proc Natl Acad Sci U S A, 1995. **92**(2): p. 377-81.
136. Cao, X., et al., *Defective lymphoid development in mice lacking expression of the common cytokine receptor gamma chain*. Immunity, 1995. **2**(3): p. 223-38.
137. Di Santo, J.P. and H.R. Rodewald, *In vivo roles of receptor tyrosine kinases and cytokine receptors in early thymocyte development*. Curr Opin Immunol, 1998. **10**(2): p. 196-207.
138. Schorle, H., et al., *Development and function of T cells in mice rendered interleukin-2 deficient by gene targeting*. Nature, 1991. **352**(6336): p. 621-4.
139. Kuhn, R., K. Rajewsky, and W. Muller, *Generation and analysis of interleukin-4 deficient mice*. Science, 1991. **254**(5032): p. 707-10.
140. Hofmeister, R., et al., *Interleukin-7: physiological roles and mechanisms of action*. Cytokine Growth Factor Rev, 1999. **10**(1): p. 41-60.
141. Moore, T.A., et al., *Inhibition of gamma delta T cell development and early thymocyte maturation in IL-7 -/- mice*. J Immunol, 1996. **157**(6): p. 2366-73.
142. Oosterwegel, M.A., et al., *Induction of TCR gene rearrangements in uncommitted stem cells by a subset of IL-7 producing, MHC class-II-expressing thymic stromal cells*. Immunity, 1997. **6**(3): p. 351-60.
143. Funk, P.E., R.P. Stephan, and P.L. Witte, *Vascular cell adhesion molecule 1-positive reticular cells express interleukin-7 and stem cell factor in the bone marrow*. Blood, 1995. **86**(7): p. 2661-71.
144. Peschon, J.J., et al., *Early lymphocyte expansion is severely impaired in interleukin 7 receptor-deficient mice*. J Exp Med, 1994. **180**(5): p. 1955-60.
145. von Freeden-Jeffry, U., et al., *Lymphopenia in interleukin (IL)-7 gene-deleted mice identifies IL-7 as a nonredundant cytokine*. J Exp Med, 1995. **181**(4): p. 1519-26.
146. Plum, J., et al., *Interleukin-7 is a critical growth factor in early human T-cell development*. Blood, 1996. **88**(11): p. 4239-45.
147. Akashi, K., M. Kondo, and I.L. Weissman, *Two distinct pathways of positive selection for thymocytes*. Proc Natl Acad Sci U S A, 1998. **95**(5): p. 2486-91.
148. Kim, K., et al., *The trophic action of IL-7 on pro-T cells: inhibition of apoptosis of pro-T1, -T2, and -T3 cells correlates with Bcl-2 and Bax levels and is independent of Fas and p53 pathways*. J Immunol, 1998. **160**(12): p. 5735-41.
149. Akashi, K., et al., *Bcl-2 rescues T lymphopoiesis in interleukin-7 receptor-deficient mice*. Cell, 1997. **89**(7): p. 1033-41.
150. Sudo, T., et al., *Expression and function of the interleukin 7 receptor in murine lymphocytes*. Proc Natl Acad Sci U S A, 1993. **90**(19): p. 9125-9.
151. Bennett, J.M., et al., *Proposals for the classification of the acute leukaemias. French-American-British (FAB) co-operative group*. Br J Haematol, 1976. **33**(4): p. 451-8.

152. Ludwig, W.D., et al., *Immunophenotypic and genotypic features, clinical characteristics, and treatment outcome of adult pro-B acute lymphoblastic leukemia: results of the German multicenter trials GMALL 03/87 and 04/89*. Blood, 1998. **92**(6): p. 1898-909.
153. Creutzig, U., et al., *Clinical significance of surface antigen expression in children with acute myeloid leukemia: results of study AML-BFM-87*. Blood, 1995. **86**(8): p. 3097-108.
154. Schrappe, M., et al., *Philadelphia chromosome-positive (Ph+) childhood acute lymphoblastic leukemia: good initial steroid response allows early prediction of a favorable treatment outcome*. Blood, 1998. **92**(8): p. 2730-41.
155. Steinherz, P.G., et al., *Cytoreduction and prognosis in acute lymphoblastic leukemia--the importance of early marrow response: report from the Childrens Cancer Group*. J Clin Oncol, 1996. **14**(2): p. 389-98.
156. Gaynon, P.S., et al., *Early response to therapy and outcome in childhood acute lymphoblastic leukemia: a review*. Cancer, 1997. **80**(9): p. 1717-26.
157. Schrappe, M., et al., *Improved outcome in childhood acute lymphoblastic leukemia despite reduced use of anthracyclines and cranial radiotherapy: results of trial ALL-BFM 90. German-Austrian-Swiss ALL-BFM Study Group*. Blood, 2000. **95**(11): p. 3310-22.
158. Dordelmann, M., et al., *Prednisone response is the strongest predictor of treatment outcome in infant acute lymphoblastic leukemia*. Blood, 1999. **94**(4): p. 1209-17.
159. Vella, A.T., et al., *Cytokine-induced survival of activated T cells in vitro and in vivo*. Proc Natl Acad Sci U S A, 1998. **95**(7): p. 3810-5.
160. Skjonsberg, C., et al., *Interleukin-7 differentiates a subgroup of acute lymphoblastic leukemias*. Blood, 1991. **77**(11): p. 2445-50.
161. Crissman, H.A., M.S. Oka, and J.A. Steinkamp, *Rapid staining methods for analysis of deoxyribonucleic acid and protein in mammalian cells*. J Histochem Cytochem, 1976. **24**(1): p. 64-71.
162. Crissman, H.A. and J.A. Steinkamp, *Rapid, one step staining procedures for analysis of cellular DNA and protein by single and dual laser flow cytometry*. Cytometry, 1982. **3**(2): p. 84-90.
163. Debatin, K.M. and P.H. Krammer, *Resistance to APO-1 (CD95) induced apoptosis in T-ALL is determined by a BCL-2 independent anti-apoptotic program*. Leukemia, 1995. **9**(5): p. 815-20.
164. Robertson, L.E., et al., *Bcl-2 expression in chronic lymphocytic leukemia and its correlation with the induction of apoptosis and clinical outcome*. Leukemia, 1996. **10**(3): p. 456-9.
165. Kitada, S., et al., *Expression of apoptosis-regulating proteins in chronic lymphocytic leukemia: correlations with In vitro and In vivo chemoresponses*. Blood, 1998. **91**(9): p. 3379-89.
166. Wuchter, C., et al., *Clinical significance of CD95, Bcl-2 and Bax expression and CD95 function in adult de novo acute myeloid leukemia in context of P-glycoprotein function, maturation stage, and cytogenetics*. Leukemia, 1999. **13**(12): p. 1943-53.
167. Haarman, E.G., et al., *BCL-2 expression in childhood leukemia versus spontaneous apoptosis, drug induced apoptosis, and in vitro drug resistance*. Adv Exp Med Biol, 1999. **457**: p. 325-33.
168. Ludwig, W.D., et al., *Incidence and prognostic significance of immunophenotypic subgroups in childhood acute lymphoblastic leukemia: experience of the BFM study 86*. Recent Results Cancer Res, 1993. **131**: p. 269-82.
169. Niehues, T., et al., *A classification based on T cell selection-related phenotypes identifies a subgroup of childhood T-ALL with favorable outcome in the COALL studies*. Leukemia, 1999. **13**(4): p. 614-7.
170. Pullen, J., et al., *Significance of commonly used prognostic factors differs for children with T cell acute lymphocytic leukemia (ALL), as compared to those with B-precursor ALL. A Pediatric Oncology Group (POG) study*. Leukemia, 1999. **13**(11): p. 1696-707.
171. Uckun, F.M., et al., *CD2 antigen expression on leukemic cells as a predictor of event-free survival after chemotherapy for T-lineage acute lymphoblastic leukemia: a Children's Cancer Group study*. Blood, 1996. **88**(11): p. 4288-95.

172. Dumont, C., et al., *Potent apoptotic signaling and subsequent unresponsiveness induced by a single CD2 mAb (BTI-322) in activated human peripheral T cells.* J Immunol, 1998. **160**(8): p. 3797-804.
173. Ida, H. and P. Anderson, *Activation-induced NK cell death triggered by CD2 stimulation.* Eur J Immunol, 1998. **28**(4): p. 1292-300.
174. Adriaansen, H.J., et al., *Acute myeloid leukemia M4 with bone marrow eosinophilia (M4Eo) and inv(16)(p13q22) exhibits a specific immunophenotype with CD2 expression.* Blood, 1993. **81**(11): p. 3043-51.
175. Wuchter, C., et al., *Constitutive expression levels of CD95 and Bcl-2 as well as CD95 function and spontaneous apoptosis in vitro do not predict the response to induction chemotherapy and relapse rate in childhood acute lymphoblastic leukaemia.* BRITISH JOURNAL OF HAEMATOLOGY, 2000. **110**(1): p. 154-160.
176. Uckun, F.M., et al., *Cellular expression of antiapoptotic BCL-2 oncoprotein in newly diagnosed childhood acute lymphoblastic leukemia: a Children's Cancer Group Study.* Blood, 1997. **89**(10): p. 3769-77.
177. Coustan Smith, E., et al., *Clinical relevance of BCL-2 overexpression in childhood acute lymphoblastic leukemia.* Blood, 1996. **87**(3): p. 1140-6.
178. Bellosillo, B., et al., *Spontaneous and drug-induced apoptosis is mediated by conformational changes of Bax and Bak in B-cell chronic lymphocytic leukemia.* Blood, 2002. **100**(5): p. 1810-6.
179. Migliorati, G., et al., *Interleukin-2 induces apoptosis in mouse thymocytes.* Cell Immunol, 1993. **146**(1): p. 52-61.
180. Erb, K.J., et al., *Impaired survival of T cell receptor V gamma 3+ cells in interleukin-4 transgenic mice.* Eur J Immunol, 1995. **25**(5): p. 1442-5.
181. Genestier, L., et al., *T cell sensitivity to HLA class I-mediated apoptosis is dependent on interleukin-2 and interleukin-4.* Eur J Immunol, 1997. **27**(2): p. 495-9.
182. Manabe, A., et al., *Interleukin-4 induces programmed cell death (apoptosis) in cases of high-risk acute lymphoblastic leukemia.* Blood, 1994. **83**(7): p. 1731-7.
183. Smiers, F.J., et al., *Heterogeneity of proliferative responses of human B cell precursor acute lymphoblastic leukemia (BCP-ALL) cells to interleukin 7 (IL-7): no correlation with immunoglobulin gene status and expression of IL-7 receptor or IL-2/IL-4/IL-7 receptor common gamma chain genes.* Leukemia, 1995. **9**(6): p. 1039-45.
184. Duyn, A.E., et al., *Effects of interleukin 3, interleukin 7, and B-cell growth factor on proliferation and drug resistance in vitro in childhood acute lymphoblastic leukemia.* Ann Hematol, 1999. **78**(4): p. 163-71.
185. Wuchter, C., et al., *In vitro susceptibility to dexamethasone- and doxorubicin-induced apoptotic cell death in context of maturation stage, responsiveness to interleukin 7, and early cyto-reduction in vivo in childhood T-cell acute lymphoblastic leukemia.* Blood, 2002. **99**(11): p. 4109-15.
186. Suda, T. and A. Zlotnik, *IL-7 maintains the T cell precursor potential of CD3-CD4-CD8-thymocytes.* J Immunol, 1991. **146**(9): p. 3068-73.
187. Fischer, M., et al., *Cytokine production by mature and immature thymocytes.* J Immunol, 1991. **146**(10): p. 3452-6.
188. McCulloch, E.A., *Stem cell renewal and determination during clonal expansion in normal and leukaemic haemopoiesis.* Cell Prolif, 1993. **26**(5): p. 399-425.
189. Greaves, M.F., et al., *Lineage promiscuity in hemopoietic differentiation and leukemia.* Blood, 1986. **67**(1): p. 1-11.
190. Greaves, M.F., *Stem cell origins of leukaemia and curability.* Br J Cancer, 1993. **67**(3): p. 413-23.
191. Dibirdik, I., et al., *Engagement of interleukin-7 receptor stimulates tyrosine phosphorylation, phosphoinositide turnover, and clonal proliferation of human T-lineage acute lymphoblastic leukemia cells.* Blood, 1991. **78**(3): p. 564-70.
192. Uckun, F.M., et al., *Interleukin 7 receptor engagement stimulates tyrosine phosphorylation, inositol phospholipid turnover, proliferation, and selective differentiation to the CD4 lineage by human fetal thymocytes.* Proc Natl Acad Sci U S A, 1991. **88**(14): p. 6323-7.



193. Pallard, C., et al., *Distinct roles of the phosphatidylinositol 3-kinase and STAT5 pathways in IL-7-mediated development of human thymocyte precursors*. *Immunity*, 1999. **10**(5): p. 525-35.
194. Cerezo, A., et al., *IL-2 deprivation triggers apoptosis which is mediated by c-Jun N-terminal kinase 1 activation and prevented by Bcl-2*. *Cell Death Differ*, 1999. **6**(1): p. 87-94.
195. Hockenbery, D., et al., *Bcl-2 is an inner mitochondrial membrane protein that blocks programmed cell death*. *Nature*, 1990. **348**(6299): p. 334-6.
196. Oltvai, Z.N., C.L. Milliman, and S.J. Korsmeyer, *Bcl-2 heterodimerizes in vivo with a conserved homolog, Bax, that accelerates programmed cell death*. *Cell*, 1993. **74**(4): p. 609-19.
197. Lisovsky, M., et al., *Flt3 ligand stimulates proliferation and inhibits apoptosis of acute myeloid leukemia cells: regulation of Bcl-2 and Bax*. *Blood*, 1996. **88**(10): p. 3987-97.
198. Tangye, S.G. and R.L. Raison, *Human cytokines suppress apoptosis of leukaemic CD5+ B cells and preserve expression of bcl-2*. *Immunol Cell Biol*, 1997. **75**(2): p. 127-35.
199. Akbar, A.N., et al., *Interleukin-2 receptor common gamma-chain signaling cytokines regulate activated T cell apoptosis in response to growth factor withdrawal: selective induction of anti-apoptotic (bcl-2, bcl-xL) but not pro-apoptotic (bax, bcl-xS) gene expression*. *Eur J Immunol*, 1996. **26**(2): p. 294-9.
200. Kinoshita, T., et al., *Suppression of apoptotic death in hematopoietic cells by signalling through the IL-3/GM-CSF receptors*. *Embo J*, 1995. **14**(2): p. 266-75.
201. Lee, S.H., et al., *Interleukin-7 inhibits apoptosis of mouse malignant T-lymphoma cells by both suppressing the CPP32-like protease activation and inducing the Bcl-2 expression*. *Oncogene*, 1996. **13**(10): p. 2131-9.
202. Pepper, C., T. Hoy, and D.P. Bentley, *Bcl-2/Bax ratios in chronic lymphocytic leukaemia and their correlation with in vitro apoptosis and clinical resistance*. *Br J Cancer*, 1997. **76**(7): p. 935-8.
203. Thomas, A., et al., *Drug-induced apoptosis in B-cell chronic lymphocytic leukemia: relationship between p53 gene mutation and bcl-2/bax proteins in drug resistance*. *Oncogene*, 1996. **12**(5): p. 1055-62.
204. Stoetzer, O.J., et al., *Association of bcl-2, bax, bcl-xL and interleukin-1 beta-converting enzyme expression with initial response to chemotherapy in acute myeloid leukemia*. *Leukemia*, 1996. **10 Suppl 3**: p. S18-S22.
205. Nakayama, K., et al., *Disappearance of the lymphoid system in Bcl-2 homozygous mutant chimeric mice*. *Science*, 1993. **261**(5128): p. 1584-8.
206. von Freeden-Jeffry, U., et al., *The earliest T lineage-committed cells depend on IL-7 for Bcl-2 expression and normal cell cycle progression*. *Immunity*, 1997. **7**(1): p. 147-54.
207. Amos, C.L., et al., *The role of caspase 3 and BclxL in the action of interleukin 7 (IL-7): a survival factor in activated human T cells*. *Cytokine*, 1998. **10**(9): p. 662-8.
208. Kordes, U., et al., *Transcription factor NF-kappaB is constitutively activated in acute lymphoblastic leukemia cells*. *Leukemia*, 2000. **14**(3): p. 399-402.
209. Wuchter, C., et al., *In vitro susceptibility to TRAIL-induced apoptosis of acute leukemia cells in the context of TRAIL receptor gene expression and constitutive NF-kappa B activity*. *Leukemia*, 2001. **15**(6): p. 921-8.
210. Nissen, R.M. and K.R. Yamamoto, *The glucocorticoid receptor inhibits NFkappaB by interfering with serine-2 phosphorylation of the RNA polymerase II carboxy-terminal domain*. *Genes Dev*, 2000. **14**(18): p. 2314-29.
211. Heck, S., et al., *I kappaB alpha-independent downregulation of NF-kappaB activity by glucocorticoid receptor*. *Embo J*, 1997. **16**(15): p. 4698-707.
212. Wissink, S., et al., *Distinct domains of the RelA NF-kappaB subunit are required for negative cross-talk and direct interaction with the glucocorticoid receptor*. *J Biol Chem*, 1997. **272**(35): p. 22278-84.
213. Banerjee, A. and P. Rothman, *IL-7 reconstitutes multiple aspects of v-Abl-mediated signaling*. *J Immunol*, 1998. **161**(9): p. 4611-7.
214. Chene, L., et al., *Thymocyte-thymic epithelial cell interaction leads to high-level replication of human immunodeficiency virus exclusively in mature CD4(+) CD8(-) CD3(+) thymocytes: a critical role for tumor necrosis factor and interleukin-7*. *J Virol*, 1999. **73**(9): p. 7533-42.

215. Chene, L., et al., *High-level replication of human immunodeficiency virus in thymocytes requires NF-kappaB activation through interaction with thymic epithelial cells.* J Virol, 1999. **73**(3): p. 2064-73.
216. Cella, N., B. Groner, and N.E. Hynes, *Characterization of Stat5a and Stat5b homodimers and heterodimers and their association with the glucocorticoid receptor in mammary cells.* Mol Cell Biol, 1998. **18**(4): p. 1783-92.
217. Stocklin, E., et al., *Functional interactions between Stat5 and the glucocorticoid receptor.* Nature, 1996. **383**(6602): p. 726-8.
218. Ward, A.C., I. Touw, and A. Yoshimura, *The Jak-Stat pathway in normal and perturbed hematopoiesis.* Blood, 2000. **95**(1): p. 19-29.
219. Ihle, J.N., *STATs: signal transducers and activators of transcription.* Cell, 1996. **84**(3): p. 331-4.
220. Kaspers, G.J., et al., *Prednisolone resistance in childhood acute lymphoblastic leukemia: vitro-vivo correlations and cross-resistance to other drugs.* Blood, 1998. **92**(1): p. 259-66.
221. Pieters, R., et al., *Relation of cellular drug resistance to long-term clinical outcome in childhood acute lymphoblastic leukaemia.* Lancet, 1991. **338**(8764): p. 399-403.
222. Kaspers, G.J., et al., *Clinical and cell biological features related to cellular drug resistance of childhood acute lymphoblastic leukemia cells.* Leuk Lymphoma, 1995. **19**(5-6): p. 407-16.
223. Pieters, R., et al., *Cellular drug sensitivity of immunophenotypic subgroups of childhood acute lymphoblastic leukemia.* Recent Results Cancer Res, 1993. **131**: p. 249-56.
224. Smith, B.D., et al., *Inhibited apoptosis and drug resistance in acute myeloid leukaemia.* Br J Haematol, 1998. **102**(4): p. 1042-9.
225. Barnes, P.J., *Anti-inflammatory mechanisms of glucocorticoids.* Biochem Soc Trans, 1995. **23**(4): p. 940-5.
226. Chresta, C.M., E.L. Arriola, and J.A. Hickman, *Apoptosis and cancer chemotherapy.* Behring Inst Mitt, 1996(97): p. 232-40.
227. Hannun, Y.A., *Apoptosis and the dilemma of cancer chemotherapy.* Blood, 1997. **89**(6): p. 1845-53.