

## 9 Literaturverzeichnis

1. Abrahams VM, Kamsteeg M, Mor G. The Fas/Fas ligand system and cancer: immune privilege and apoptosis. *Mol Biotechnol.* 2003; 25(1):19-30.
2. Acton D, Domen J, Jacobs H, Vlaar M, Korsmeyer S, Berns A. Collaboration of pim-1 and bcl-2 in lymphomagenesis. *Curr Top Microbiol Immunol.* 1992, 182:293-298.
3. Adams JM, Cory S. Oncogene co-operation in leukaemogenesis. *Cancer Surv.* 1992, 15:119-141.
4. Alberts B. *Molecular Biology of the Cell*, 3<sup>rd</sup> Edition 1993
5. Albrecht-Buehler G. The simulation of microgravity conditions on the ground. *ASGSB Bull.* 1992, 5(2):3-10.
6. Alsanea O. Familial nonmedullary thyroid cancer. *Curr Treat Options Oncol.* 2000, 1(4):345-351.
7. Andrikoula M, Tsatsoulis A. The role of Fas-mediated apoptosis in thyroid disease. *Eur J Endocrinol.* 2001; 144(6):561-568.
8. Antonsson B, Montessuit S, Lauper S, Eskes R, Martinou JC. Bax oligomerization is required for channel-forming activity in liposomes and to trigger cytochrome c release from mitochondria. *Biochem J.* 2000, 15; 345:271-278.
9. Antonsson B, Montessuit S, Sanchez B, Martinou JC. Bax is present as a high molecular weight oligomer/complex in the mitochondrial membrane of apoptotic cells. *J Biol Chem.* 2001, 13; 276(15):11615-23.
10. Aoshiba K, Rennard SI, Spurzem JR. Cell-matrix and cell-cell interactions modulate apoptosis of bronchial epithelial cells. *Am J Physiol.* 1997; 272:28-37.
11. Arscott PL, Stokes T, Myc A, Giordano TJ, Thompson NW, Baker JR Jr. Fas (CD95) expression is up-regulated on papillary thyroid carcinoma. *J Clin Endocrinol Metab.* 1999; 84(11):4246-4252.

12. Avvisati G, Tallman MS. All-trans retinoic acid in acute promyelocytic leukaemia. *Best Pract Res Clin Haematol.* 2003; 16(3):419-432.
13. Ayed M, Pironneau O, Planel H, Gasset G, Richoille G. Theoretical and experimental investigations on the fast rotating clinostat. *Microgravity Sci Technol.* 1992; 5(2):98-102.
14. Basolo F, Fiore L, Baldanzi A, Giannini R, Dell'Omodarme M, Fontanini G, Pacini F, Danesi R, Miccoli P, Toniolo A. Suppression of Fas expression and down-regulation of Fas ligand in highly aggressive human thyroid carcinoma. *Lab Invest.* 2000; 80(9):1413-1419.
15. Battle T, Maguire T, Moulds H, Doyle A. Progressive maturation resistance to microcystin-LR cytotoxicity in two different hepatospheroidal models. *Cell Biol Toxicol.* 1999; 15(1):3-12.
16. Bauer J, Grimm D, Hofstaedter F, Wieland W. Techniques for studies on growth characteristics of human prostatic cancer cells. *Biotechnol Prog.* 1992; 8(6):494-500.
17. Bellgrau D, Gold D, Selawry H, Moore J, Franzusoff A, Duke RC. A role for CD95 ligand in preventing graft rejection. *Nature.* 1995, 377(6550):630-632.
18. Belichenko I, Morishima N, Separovic D. Caspase-resistant vimentin suppresses apoptosis after photodynamic treatment with a silicon phthalocyanine in Jurkat cells. *Arch Biochem Biophys.* 2001 Jun 1;390(1):57-63.
19. Birchmeier C, Birchmeier W, Gherardi E, Vande Woude GF. Met, metastasis, motility and more. *Nat Rev Mol Cell Biol.* 2003, 4(12):915-925.
20. Bischoff J. Cell adhesion and angiogenesis. *J Clin Invest.* 1997; 99(3):373-376.
21. Blobel CP. Remarkable roles of proteolysis on and beyond the cell surface. *Curr Opin Cell Biol.* 2000; 12(5):606-612.
22. Boland A, Ricard M, Opolon P, Bidart JM, Yeh P, Filetti S, Schlumberger M, Perricaudet M. Adenovirus-mediated transfer of the thyroid sodium/iodide symporter gene into tumors for a targeted radiotherapy. *Cancer Res.* 2000; 60(13):3484-3492.

23. Borges E, Jan Y, Ruoslahti E. () Platelet-derived growth factor receptor beta and vascular endothelial growth factor receptor 2 bind to the beta 3 integrin through its extracellular domain. *J Biol Chem.* 2000; 275(51):39867-39873.
24. Borner C. The Bcl-2 protein family: sensors and checkpoints for life-or-death decisions. *Mol Immunol.* 2003; 39(11):615-647.
25. Bos JL. ras oncogenes in human cancer: a review. *Cancer Res.* 1989; 49(17):4682-4689.
26. Bouchard VJ, Rouleau M, Poirier GG. PARP-1, a determinant of cell survival in response to DNA damage. *Exp Hematol.* 2003; 31(6):446-454.
27. Brandt-Mainz K, Görges R, Bockisch A. Diagnosis and Treatment of Thyroid Cancer. *Tumordiagn u Ther.* 2001;22:85-92.
28. Burlacu A. Regulation of apoptosis by Bcl-2 family proteins. *J Cell Mol Med.* 2003; 7(3):249-257.
29. Calderwood DA, Ginsberg MH. Talin forges the links between integrins and actin. *Nat Cell Biol.* 2003 Aug;5(8):694-7.
30. Cameron BR, Berean KW. Cytokeratin subtypes in thyroid tumours: immunohistochemical study with emphasis on the follicular variant of papillary carcinoma. *J Otolaryngol.* 2003; 32(5):319-322.
31. Carlsson SI, Bertilaccio MT, Ballabio E, Maier JA. Endothelial stress by gravitational unloading: effects on cell growth and cytoskeletal organization. *Biochim Biophys Acta.* 2003; 1642(3):173-179.
32. Cavolina JM, Evans GL, Harris SA, Zhang M, Westerlind KC, Turner RT. The effects of orbital spaceflight on bone histomorphometry and messenger ribonucleic acid levels for bone matrix proteins and skeletal signaling peptides in ovariectomized growing rats. *Endocrinology.* 1997; 138(4):1567-76.

33. Cesarone CF, Pippia P, Demori I, Scarabelli L, Fugassa E. Effect of simulated microgravity conditions on poly(ADP-ribose) polymerase activity in primary cultures of adult rat hepatocytes. *J Gravit Physiol.* 2001; 8(1):127-128.
34. Chappell DB, Zaks TZ, Rosenberg SA, Restifo NP. Human melanoma cells do not express Fas (Apo-1/CD95) ligand. *Cancer Res.* 1999; 59(1):59-62.
35. Chappell DB, Restifo NP. T cell-tumor cell: a fatal interaction? *Cancer Immunol Immunother.* 1998; 47(2):65-71.
36. Chen JH, Vercamer C, Li Z, Paulin D, Vandebunder B, Stehelin D. PEA3 transactivates vimentin promoter in mammary epithelial and tumor cells. *Oncogene.* 1996; 13(8):1667-1675.
37. Chomienne C, Fenaux P, Degos L. Retinoid differentiation therapy in promyelocytic leukemia. *FASEB J.* 1996; 10(9):1025-1030.
38. Chu PG, Weiss LM. Keratin expression in human tissues and neoplasms. *Histopathology.* 2002; 40(5):403-439.
39. Cogoli M. The fast rotating clinostat: a history of its use in gravitational biology and a comparison of ground-based and flight experiment results. *ASGSB Bull.* 1992; 5(2):59-67.
40. Cogoli-Greuter M, Meloni MA, Sciola L, Spano A, Pippia P, Monaco G, Cogoli A. Movements and interactions of leukocytes in microgravity. *J Biotechnol.* 1996, 47(2-3):279-287.
41. Coultas L, Strasser A. The role of the Bcl-2 protein family in cancer. *Semin Cancer Biol.* 2003; 13(2):115-123.
42. Coussens LM, Tinkle CL, Hanahan D, Werb Z. MMP-9 supplied by bone marrow-derived cells contributes to skin carcinogenesis. *Cell.* 2000; 103(3):481-490.
43. Critchley DR. Cytoskeletal proteins talin and vinculin in integrin-mediated adhesion. *Biochem Soc Trans.* 2004 Nov;32(Pt 5):831-6.

44. Crowe DL, Brown TN. Transcriptional inhibition of matrix metalloproteinase 9 (MMP-9) activity by a c-fos/estrogen receptor fusion protein is mediated by the proximal AP-1 site of the MMP-9 promoter and correlates with reduced tumor cell invasion. *Neoplasia*. 1999; 1(4):368-72.
45. Cubano LA, Lewis ML. Fas/APO-1 protein is increased in spaceflown lymphocytes (Jurkat). *Exp Gerontol*. 2000; 35(3):389-400.
46. Curcio F, Ambesi-Impiombato FS, Perrella G, Coon HG. Long-term culture and functional characterization of follicular cells from adult normal human thyroids. *Proc Natl Acad Sci U S A*. 1994; 91(19):9004-9008.
47. de Nigris F, Sica V, Herrmann J, Condorelli G, Chade AR, Tajana G, Lerman A, Lerman LO, Napoli C. c-Myc oncoprotein: cell cycle-related events and new therapeutic challenges in cancer and cardiovascular diseases. *Cell Cycle*. 2003; 2(4):325-328.
48. Degan P, Cesarone CF, Ottaggio L, Galleri G, Meloni MA, Zunino A, Viaggi S, Bonatti S, Abbondandolo A. Effects of simulated microgravity on metabolic activities related to DNA damage and repair in lymphoblastoid cells. *J Gravit Physiol*. 2001; 8(1):21-22.
49. DeGroot LJ, Zhang R. Clinical review 131: Gene therapy for thyroid cancer: where do we stand? *J Clin Endocrinol Metab*. 2001; 86(7):2923-2928.
50. Del Terra E, Francesconi A, Donnini D, Curcio F, Ambesi-Impiombato FS. Thyrotropin effects on ultraviolet radiation-dependent apoptosis in FRTL-5 cells. *Thyroid*. 2003; 13(8):747-753.
51. Dinsdale D, Lee JC, Dewson G, Cohen GM, Peter ME. Intermediate filaments control the intracellular distribution of caspases during apoptosis. *Am J Pathol*. 2004; 164(2):395-407.
52. Downing KH, Nogales E. Crystallographic structure of tubulin: implications for dynamics and drug binding. *Cell Struct Funct*. 1999; 24(5):269-275.
53. Eckes B, Dogic D, Colucci-Guyon E, Wang N, Maniotis A, Ingber D, Merckling A, Langa F, Aumailley M, Delouvee A, Koteliansky V, Babinet C, Krieg T. Impaired

- mechanical stability, migration and contractile capacity in vimentin-deficient fibroblasts. *J Cell Sci.* 1998; 111:1897-1907.
54. Eilers M, Schirm S, Bishop JM. The MYC protein activates transcription of the alpha-prothymosin gene. *EMBO J.* 1991; 10(1):133-141.
55. Elliott RL, Blobe GC. Role of transforming growth factor-beta in human cancer. *J Clin Oncol.* 2005; Mar 20;23(9):2078-93.
56. Erickson LA, Lloyd RV. Practical markers used in the diagnosis of endocrine tumors. *Adv Anat Pathol.* 2004; 11(4):175-189.
57. Fagin JA, Matsuo K, Karmakar A, Chen DL, Tang SH, Koeffler HP. High prevalence of mutations of the p53 gene in poorly differentiated human thyroid carcinomas. *J Clin Invest.* 1993; 91(1):179-184.
58. Fei R, Shaoyang L. Combination antigene therapy targeting c-myc and c-erbB(2) in the ovarian cancer COC(1) cell line. *Gynecol Oncol.* 2002; 85(1):40-44.
59. Frisch SM, Francis H. Disruption of epithelial cell-matrix interactions induces apoptosis. *J Cell Biol.* 1994; 124(4):619-626.
60. Fukai F, Mashimo M, Akiyama K, Goto T, Tanuma S, Katayama T. Modulation of apoptotic cell death by extracellular matrix proteins and a fibronectin-derived antiadhesive peptide. *Exp Cell Res.* 1998; 242(1):92-99.
61. Fusco A, Pinto A, Tramontano D, Tajana G, Vecchio G, Tsuchida N. Block in the expression of differentiation markers of rat thyroid epithelial cells by transformation with Kirsten murine sarcoma virus. *Cancer Res.* 1982; 42(2):618-626.
62. Germain M, Shore GC. Cellular distribution of Bcl-2 family proteins. *Sci STKE.* 2003; 2003(173):10.
63. Gmunder FK, Nordau CG, Tschopp A, Huber B, Cogoli A. Dynamic cell culture system: a new cell cultivation instrument for biological experiments in space. *J Biotechnol.* 1988;7:217-28.

64. Goodsell DS. The molecular perspective: cadherin. *Oncologist*. 2002;7(5):467-468.
65. Gottifredi V, McKinney K, Poyurovsky MV, Prives C. Decreased p21 levels are required for efficient restart of DNA synthesis after S phase block. *J Biol Chem*. 2004; 279(7):5802-5810.
66. Graham CH, Kobayashi H, Stankiewicz KS, Man S, Kapitan SJ, Kerbel RS. Rapid acquisition of multicellular drug resistance after a single exposure of mammary tumor cells to antitumor alkylating agents. *J Natl Cancer Inst*. 1994; 86(13):975-982.
67. Griffith TS, Brunner T, Fletcher SM, Green DR, Ferguson TA. Fas ligand-induced apoptosis as a mechanism of immune privilege. *Science*. 1995; 270(5239):1189-1192.
68. Grimm D, Bauer J, Hofstadter F, Riegger GA, Kromer EP. Characteristics of multicellular spheroids formed by primary cultures of human thyroid tumor cells. *Thyroid*. 1997; 7(6):859-865.
69. Grimm D, Bauer J, Kromer E, Steinbach P, Riegger G, Hofstadter F. Human follicular and papillary thyroid carcinoma cells interact differently with human venous endothelial cells. *Thyroid*. 1995; 5(3):155-164.
70. Grimm D, Hofstadter F, Bauer J, Spruss T, Steinbach P, Bernhardt G, Menze R. Establishment and characterization of a human papillary thyroid carcinoma cell line with oxyphilic differentiation (ONCO-DG 1). *Virchows Arch B Cell Pathol Incl Mol Pathol*. 1992; 62(2):97-104.
71. Grimm D, Bauer J, Kossmehl P, Shakibaei M, Schoberger J, Pickenhahn H, Schulze-Tanzil G, Vetter R, Eilles C, Paul M, Cogoli A. Simulated microgravity alters differentiation and increases apoptosis in human follicular thyroid carcinoma cells. *FASEB J*. 2002; 16(6):604-606.
72. Grimm D, Huber M, Jabusch HC, Shakibaei M, Fredersdorf S, Paul M, Riegger GA, Kromer EP. Extracellular matrix proteins in cardiac fibroblasts derived from rat hearts with chronic pressure overload: effects of beta-receptor blockade. *J Mol Cell Cardiol*. 2001; 33(3):487-501.

73. Grimm D, Kromer EP, Bocker W, Bruckschlegel G, Holmer SR, Riegger GA, Schunkert H. Regulation of extracellular matrix proteins in pressure-overload cardiac hypertrophy: effects of angiotensin converting enzyme inhibition. *J Hypertens.* 1998; 16(9):1345-1355.
74. Grunwald F, Menzel C, Bender H, Palmedo H, Otte R, Fimmers R, Risse J, Biersack HJ. Redifferentiation therapy-induced radioiodine uptake in thyroid cancer. *J Nucl Med.* 1998; 39(11):1903-1906.
75. Gualberto A, Aldape K, Kozakiewicz K, Tlsty TD. An oncogenic form of p53 confers a dominant, gain-of-function phenotype that disrupts spindle checkpoint control. *Proc Natl Acad Sci U S A.* 1998; 95(9):5166-5171.
76. Gunga HC. Effects of microgravity, thyroid-stimulating-hormone and plasma proteins in four astronauts. In Sahm PR, Keller MH, Schiewe B, eds. Scientific results of the German spacelab mission D-2. Aachen: WPF. 1994; 732-735.
77. Hahne M, Rimoldi D, Schroter M, Romero P, Schreier M, French LE, Schneider P, Bornand T, Fontana A, Lienard D, Cerottini J, Tschopp J. Melanoma cell expression of Fas(Apo-1/CD95) ligand: implications for tumor immune escape. *Science.* 1996; 274(5291):1363-1366.
78. Hammond TG, Benes E, O'Reilly KC, Wolf DA, Linnehan RM, Taher A, Kaysen JH, Allen PL, Goodwin TJ. Mechanical culture conditions effect gene expression: gravity-induced changes on the space shuttle. *Physiol Genomics.* 2000; 3(3):163-173.
79. Harandian F, Farookhi R. Contact-dependent cell interactions determine hormone responsiveness and desensitization in rat granulosa cells. *Endocrinology.* 1998; 139(4):1700-1707.
80. Havekes B, Schroder van der Elst JP, van der Pluijm G, Goslings BM, Romijn JA, Smit JW. Beneficial effects of retinoic acid on extracellular matrix degradation and attachment behaviour in follicular thyroid carcinoma cell lines. *J Endocrinol.* 2000; 167(2):229-238.
81. Hedlund TE, Duke RC, Miller GJ. Three-dimensional spheroid cultures of human prostate cancer cell lines. *Prostate.* 1999; 41(3):154-165.



82. Heldin NE, Westermark B. Epidermal growth factor, but not thyrotropin, stimulates the expression of c-fos and c-myc messenger ribonucleic acid in porcine thyroid follicle cells in primary culture. *Endocrinology*. 1988; 122(3):1042-1046.
83. Helmke BP, Thakker DB, Goldman RD, Davies PF. Spatiotemporal analysis of flow-induced intermediate filament displacement in living endothelial cells. *Biophys J*. 2001; 80(1):184-194.
84. Hoson T, Kamisaka S, Masuda Y, Yamashita M, Buchen B. Evaluation of the three-dimensional clinostat as a simulator of weightlessness. *Planta*. 1997; 203:187-197.
85. Houston A, O'Connell J. The Fas signalling pathway and its role in the pathogenesis of cancer. *Curr Opin Pharmacol*. 2004; 4(4):321-326.
86. Huang DC, Adams JM, Cory S. The conserved N-terminal BH4 domain of Bcl-2 homologues is essential for inhibition of apoptosis and interaction with CED-4. *EMBO J*. 1998; 17(4):1029-1039.
87. Huang Z, Bao SD. Roles of main pro- and anti-angiogenic factors in tumor angiogenesis. *World J Gastroenterol*. 2004; 10(4):463-470.
88. Hughes-Fulford M, Lewis ML. Effects of microgravity on osteoblast growth activation. *Exp Cell Res*. 1996; 224(1):103-109.
89. Ingber D. How cells (might) sense microgravity. *FASEB J*. 1999; 13:3-15.
90. Ingram M, Techy GB, Saroufeem R, Yazan O, Narayan KS, Goodwin TJ, Spaulding GF. Three-dimensional growth patterns of various human tumor cell lines in simulated microgravity of a NASA bioreactor. *In Vitro Cell Dev Biol Anim*. 1997; 33(6):459-466.
91. Islam MN, Iskander MN. Microtubulin binding sites as target for developing anticancer agents. *Mini Rev Med Chem*. 2004; 4(10):1077-1104.
92. Jianmin Z, Hongfang W, Meifu F. Resistance of multicellular aggregates to pharmorubicin observed in human hepatocarcinoma cells. *Braz J Med Biol Res*. 2002; 35(2):255-260.

93. Kakinuma H, Bergert ER, Spitzweg C, Cheville JC, Lieber MM, Morris JC. Probasin promoter (ARR(2)PB)-driven, prostate-specific expression of the human sodium iodide symporter (h-NIS) for targeted radioiodine therapy of prostate cancer. *Cancer Res.* 2003; 63(22):7840-7844.
94. Khaoustov VI, Darlington GJ, Soriano HE, Krishnan B, Risin D, Pellis NR, Yoffe B. Induction of three-dimensional assembly of human liver cells by simulated microgravity. *In Vitro Cell Dev Biol Anim.* 1999; 35(9):501-509.
95. Kiss JZ. Mechanisms of the early phases of plant gravitropism. *CRC Crit Rev Plant Sci.* 2000; 19(6):551-573.
96. Klaus DM. Clinostats and bioreactors. *Gravit Space Biol Bull.* 2001; 14(2):55-64.
97. Knudson CM, Johnson GM, Lin Y, Korsmeyer SJ. Bax accelerates tumorigenesis in p53-deficient mice. *Cancer Res.* 2001; 61(2):659-665.
98. Knuechel R, Siebert-Wellnhofer A, Traub O, Dermietzel R. Connexin expression and intercellular communication in two- and three-dimensional in vitro cultures of human bladder carcinoma. *Am J Pathol.* 1996; 149(4):1321-1332.
99. Kobayashi H, Man S, Graham CH, Kapitain SJ, Teicher BA, Kerbel RS. Acquired multicellular-mediated resistance to alkylating agents in cancer. *Proc Natl Acad Sci U S A.* 1993; 90(8):3294-3298.
100. Kossmehl P, Shakibaei M, Cogoli A, Infanger M, Curcio F, Schonberger J, Eilles C, Bauer J, Pickenhahn H, Schulze-Tanzil G, Paul M, Grimm D. Weightlessness induced apoptosis in normal thyroid cells and papillary thyroid carcinoma cells via extrinsic and intrinsic pathways. *Endocrinology.* 2003; 144(9):4172-4179.
101. Kumar A, Ta D, Henderson D, Mushinski JF, Reed JC, Kuus-Reichel K, Saedi MS. bcl2 and v-abl oncogenes cooperate to immortalize murine B cells that secrete antigen specific antibodies. *Immunol Lett.* 1999; 65(3):153-159.
102. Kunz-Schughart LA. Multicellular tumor spheroids: intermediates between monolayer culture and in vivo tumor. *Cell Biol Int.* 1999; 23(3):157-161.

103. Kunz-Schughart LA, Doetsch J, Mueller-Klieser W, Groebe K. Proliferative activity and tumorigenic conversion: impact on cellular metabolism in 3-D culture. *Am J Physiol Cell Physiol*. 2000; 278(4):765-780.
104. Kurebayashi J, Tanaka K, Otsuki T, Moriya T, Kunisue H, Uno M, Sonoo H. All-trans-retinoic acid modulates expression levels of thyroglobulin and cytokines in a new human poorly differentiated papillary thyroid carcinoma cell line, KTC-1. *J Clin Endocrinol Metab*. 2000; 85(8):2889-2896.
105. LaCasse EC, Baird S, Korneluk RG, MacKenzie AE. The inhibitors of apoptosis (IAPs) and their emerging role in cancer. *Oncogene*. 1998; 17(25):3247-3259.
106. Leach CS, Johnson PC, Driscoll TB. Prolonged weightlessness effect on postflight plasma thyroid hormones. *Aviat Space Environ Med*. 1977, 48(7):595-597.
107. Lebedeva IV, Su ZZ, Sarkar D, Fisher PB. Restoring apoptosis as a strategy for cancer gene therapy: focus on p53 and mda-7. *Semin Cancer Biol*. 2003; 13(2):169-178.
108. Lewis ML, Cubano LA, Zhao B, Dinh HK, Pabalan JG, Piepmeier EH, Bowman PD. cDNA microarray reveals altered cytoskeletal gene expression in space-flown leukemic T lymphocytes (Jurkat). *FASEB J*. 2001; 15(10):1783-1785.
109. Lewis ML, Reynolds JL, Cubano LA, Hatton JP, Lawless BD, Piepmeier EH. Spaceflight alters microtubules and increases apoptosis in human lymphocytes (Jurkat). *FASEB J*. 1998; 12(11):1007-18.
110. Lombard C, McKallip RJ, Hylemon PB, Nagarkatti PS, Nagarkatti M. Fas Ligand-dependent and -independent mechanisms of toxicity induced by T cell lymphomas in lymphoid organs and in the liver. *Clin Immunol*. 2003; 109(2):144-153.
111. Los M, Burek CJ, Stroh C, Benedyk K, Hug H, Mackiewicz A. Anticancer drugs of tomorrow: apoptotic pathways as targets for drug design. *Drug Discov Today*. 2003; 8(2):67-77.
112. Lowe SW, Lin AW. Apoptosis in cancer. *Carcinogenesis*. 2000; 21(3):485-495.

113. Maccarrone M, Battista N, Meloni M, Bari M, Galleri G, Pippia P, Cogoli A, Finazzi-Agro A. Creating conditions similar to those that occur during exposure of cells to microgravity induces apoptosis in human lymphocytes by 5-lipoxygenase-mediated mitochondrial uncoupling and cytochrome c release. *J Leukoc Biol.* 2003;73:472-481.
114. Macho L, Kvetnansky R, Nemeth S, Fickova M, Popova I, Serova L, Grigoriev AI. Effects of space flight on endocrine system function in experimental animals. *Environ Med.* 1996; 40(2):95-111.
115. Makin G, Hickman JA. Apoptosis and cancer chemotherapy. *Cell Tissue Res.* 2000; 301(1):143-152.
116. Mandell RB, Mandell LZ, Link CJ Jr. Radioisotope concentrator gene therapy using the sodium/iodide symporter gene. *Cancer Res.* 1999; 59(3):661-668.
117. Marshall CJ. Ras effectors. *Curr Opin Cell Biol.* 1996; 8(2):197-204.
118. Martin A, Zhou A, Gordon RE, Henderson SC, Schwartz AE, Schwartz AE, Friedman EW, Davies TF. Thyroid organoid formation in simulated microgravity: influence of keratinocyte growth factor. *Thyroid.* 2000; 10(6):481-487.
119. Martin DA, Zheng L, Siegel RM, Huang B, Fisher GH, Wang J, Jackson CE, Puck JM, Dale J, Straus SE, Peter ME, Krammer PH, Fesik S, Lenardo MJ. Defective CD95/APO-1/Fas signal complex formation in the human autoimmune lymphoproliferative syndrome, type Ia. *Proc Natl Acad Sci U S A.* 1999 1; 96(8):4552-4557.
120. Martin SJ, Cotter TG. Disruption of microtubules induces an endogenous suicide pathway in human leukaemia HL-60 cells. *Cell Tissue Kinet.* 1990; 23(6):545-559.
121. McCurrach ME, Connor TM, Knudson CM, Korsmeyer SJ, Lowe SW. bax-deficiency promotes drug resistance and oncogenic transformation by attenuating p53-dependent apoptosis. *Proc Natl Acad Sci U S A.* 1997; 94(6):2345-2349.
122. Melcher A, Gough M, Todryk S, Vile R. Apoptosis or necrosis for tumor immunotherapy: what's in a name? *J Mol Med.* 1999; 77(12):824-833.

123. Meli A, Perrella G, Curcio F, Ambesi-Impiombato FS. Response to hypogravity of normal in vitro cultured follicular cells from thyroid. *Acta Astronaut.* 1998; 42(1-8):465-472.
124. Meli A, Perrella G, Curcio F, Ambesi-Impiombato FS. In vitro cultured cells as probes for space radiation effects on biological systems. *Mutat Res.* 1999; 430(2):229-234.
125. Mihailescu D, Shore-Freedman E, Mukani S, Lubin J, Ron E, Schneider AB. Multiple neoplasms in an irradiated cohort: pattern of occurrence and relationship to thyroid cancer outcome. *J Clin Endocrinol Metab.* 2002; 87(7):3236-3241.
126. Mitsiades N, Poulaki V, Mastorakos G, Tseleni-Balafouta ST, Kotoula V, Koutras DA, Tsokos M. Fas ligand expression in thyroid carcinomas: a potential mechanism of immune evasion. *J Clin Endocrinol Metab.* 1999; 84(8):2924-2932.
127. Mitsiades N, Poulaki V, Mitsiades CS, Koutras DA, Chrousos GP. Apoptosis induced by FasL and TRAIL/Apo2L in the pathogenesis of thyroid diseases. *Trends Endocrinol Metab.* 2001; 12(9):384-390.
128. Mizutani Y, Okada Y, Yoshida O, Fukumoto M, Bonavida B. Doxorubicin sensitizes human bladder carcinoma cells to Fas-mediated cytotoxicity. *Cancer.* 1997; 79(6):1180-1189.
129. Moretti F, Nanni S, Farsetti A, Narducci M, Crescenzi M, Giuliacci S, Sacchi A, Pontecorvi A. Effects of exogenous p53 transduction in thyroid tumor cells with different p53 status. *J Clin Endocrinol Metab.* 2000; 85(1):302-308.
130. Morrison DR. Cellular changes in microgravity and the design of space radiation experiments. *Adv Space Res.* 1994; 14(10):1005-1019.
131. Mueller-Klieser W. Tumor biology and experimental therapeutics. *Crit Rev Oncol Hematol.* 2000; 36(2-3):123-139.
132. Mueller-Klieser W. Microelectrode measurement of oxygen tension distributions in multicellular spheroids cultured in spinner flasks. *Recent Results Cancer Res.* 1984; 95:134-149.

133. Mulligan LM, Kwok JB, Healey CS, Elsdon MJ, Eng C, Gardner E, Love DR, Mole SE, Moore JK, Papi L. Germ-line mutations of the RET proto-oncogene in multiple endocrine neoplasia type 2A. *Nature*. 1993; 363(6428):458-460.
134. Muschen M, Re D, Brauning A, Wolf J, Hansmann ML, Diehl V, Kuppers R, Rajewsky K. Somatic mutations of the CD95 gene in Hodgkin and Reed-Sternberg cells. *Cancer Res*. 2000; 60(20):5640-5643.
135. Musholt TJ, Musholt PB, Petrich T, Oetting G, Knapp WH, Klempnauer J. Familial papillary thyroid carcinoma: genetics, criteria for diagnosis, clinical features, and surgical treatment. *World J Surg*. 2000; 24(11):1409-1417.
136. Nadanaka S. Chondroitin Sulfate: Structure, Function, and Biosynthesis. *Trends in Glycoscience and Glycotechnology*. 1999; 11(60):233-238.
137. Nagata S. Apoptosis by death factor. *Cell*. 1997; 88(3):355-365.
138. Nagata S. Fas-mediated apoptosis. *Adv Exp Med Biol*. 1996; 406:119-124.
139. Nagayama Y, Yokoi H, Takeda K, Hasegawa M, Nishihara E, Namba H, Yamashita S, Niwa M. Adenovirus-mediated tumor suppressor p53 gene therapy for anaplastic thyroid carcinoma in vitro and in vivo. *J Clin Endocrinol Metab*. 2000; 85(11):4081-4086.
140. Nambu Y, Hughes SJ, Rehemtulla A, Hamstra D, Orringer MB, Beer DG. Lack of cell surface Fas/APO-1 expression in pulmonary adenocarcinomas. *J Clin Invest*. 1998; 101(5):1102-1110.
141. Nederman T, Norling B, Glimelius B, Carlsson J, Brunk U. Demonstration of an extracellular matrix in multicellular tumor spheroids. *Cancer Res*. 1984; 44(7):3090-3097.
142. Nicolai H, Steinbach P, Knuechel-Clarke R, **Grimm D**, Roessler W, Wieland WF, Hofstaedter F. Proliferation of tumor spheroids after shock-wave treatment. *J Cancer Res Clin Oncol*. 1994;120:438-441.

143. Nishihara E, Nagayama Y, Mawatari F, Tanaka K, Namba H, Niwa M, Yamashita S. Retrovirus-mediated herpes simplex virus thymidine kinase gene transduction renders human thyroid carcinoma cell lines sensitive to ganciclovir and radiation in vitro and in vivo. *Endocrinology*. 1997; 138(11):4577-4583.
144. Nomura J, Himeda J, Chen Z, Sugaya S, Takahashi S, Kita K, Ichinose M, Suzuki N. Establishment and characterization of GSA-1, a human cell line highly susceptible to apoptosis after free-fall. *J Radiat Res*. 2002; 43:251-255.
145. Ohnishi T, Takahashi A, Ohnishi K. Biological effects of space radiation. *Biol Sci Space*. 2001; 15:203-210.
146. Ohnishi T, Wang X, Fukuda S, Takahashi A, Ohnishi K, Nagaoka S. Accumulation of tumor suppressor p53 in rat muscle after a space flight. *Adv Space Res*. 2000; 25(10):2119-2122.
147. Orkinick JR, Elkon KB, Chao MV. Separate domains of the human fas ligand dictate self-association and receptor binding. *J Biol Chem*. 1997; 272(51):32221-32229.
148. Orkinick JR, Vaishnav A, Elkon KB, Chao MV. Requirement of cysteine-rich repeats of the Fas receptor for binding by the Fas ligand. *J Biol Chem*. 1997; 272(46):28889-28894.
149. Oshimi Y, Oda S, Honda Y, Nagata S, Miyazaki S. Involvement of Fas ligand and Fas-mediated pathway in the cytotoxicity of human natural killer cells. *J Immunol*. 1996; 157(7):2909-2915.
150. Pan G, O'Rourke K, Dixit VM. Caspase-9, Bcl-XL, and Apaf-1 form a ternary complex. *J Biol Chem*. 1998;273(10):5841-5845.
151. Pan J, Xu G, Yeung SC. Cytochrome c release is upstream to activation of caspase-9, caspase-8, and caspase-3 in the enhanced apoptosis of anaplastic thyroid cancer cells induced by manumycin and paclitaxel. *J Clin Endocrinol Metab*. 2001; 86(10):4731-4740.
152. Patterson AV, Saunders MP, Greco O. Prodrugs in genetic chemoradiotherapy. *Curr Pharm Des*. 2003; 9(26):2131-2154.

153. Paulus W, Huettner C, Tonn JC. Collagens, integrins and the mesenchymal drift in glioblastomas: a comparison of biopsy specimens, spheroid and early monolayer cultures. *Int J Cancer*. 1994; 58(6):841-6.
154. Pippia P, Sciola L, Cogoli-Greuter M, Meloni MA, Spano A, Cogoli A. Activation signals of T lymphocytes in microgravity. *J Biotechnol*. 1996; 47(2-3):215-222.
155. Redfield A, Nieman MT, Knudsen KA. Cadherins promote skeletal muscle differentiation in three-dimensional cultures. *J Cell Biol*. 1997; 138(6):1323-1331.
156. Risin D, Pellis NR. Modeled microgravity inhibits apoptosis in peripheral blood lymphocytes. *In Vitro Cell Dev Biol Anim*. 2001; 37(2):66-72.
157. Rozzo C, Chiesa V, Caridi G, Pagnan G, Ponzoni M. Induction of apoptosis in human neuroblastoma cells by abrogation of integrin-mediated cell adhesion. *Int J Cancer*. 1997; 70(6):688-698.
158. Rucci N, Migliaccio S, Zani BM, Taranta A, Teti A. Characterization of the osteoblast-like cell phenotype under microgravity conditions in the NASA-approved Rotating Wall Vessel bioreactor (RWV). *J Cell Biochem*. 2002; 85(1):167-179.
159. Saas P, Walker PR, Hahne M, Quiquerez AL, Schnuriger V, Perrin G, French L, Van Meir EG, de Tribolet N, Tschopp J, Dietrich PY. Fas ligand expression by astrocytoma in vivo: maintaining immune privilege in the brain? *J Clin Invest*. 1997; 99(6):1173-1178.
160. Sarkar D, Nagaya T, Koga K, Nomura Y, Gruener R, Seo H. Culture in vector-averaged gravity under clinostat rotation results in apoptosis of osteoblastic ROS 17/2.8 cells. *J Bone Miner Res*. 2000; 15(3):489-498.
161. Salvatore D, Celetti A, Fabien N, Paulin C, Martelli ML, Battaglia C, Califano D, Monaco C, Viglietto G, Santoro M, Fusco A. Low frequency of p53 mutations in human thyroid tumours; p53 and Ras mutation in two out of fifty-six thyroid tumours. *Eur J Endocrinol*. 1996; 134(2):177-183.



162. Santini MT, Rainaldi G, Indovina PL. Apoptosis, cell adhesion and the extracellular matrix in the three-dimensional growth of multicellular tumor spheroids. *Crit Rev Oncol Hematol.* 2000; 36(2-3):75-87.
163. Santoro M, Carlomagno F, Hay ID, Herrmann MA, Grieco M, Melillo R, Pierotti MA, Bongarzone I, Della Porta G, Berger N. Ret oncogene activation in human thyroid neoplasms is restricted to the papillary cancer subtype. *J Clin Invest.* 1992; 89(5):1517-1522.
164. Saunders WH, Wakely J. Atlas of Head and Neck Pathology. 1993
165. Scaffidi C, Schmitz I, Krammer PH, Peter ME. The role of c-FLIP in modulation of CD95-induced apoptosis. *J Biol Chem.* 1999; 274(3):1541-1548.
166. Schatten H, Lewis ML, Chakrabarti A. Spaceflight and clinorotation cause cytoskeleton and mitochondria changes and increases in apoptosis in cultured cells. *Acta Astronaut.* 2001; 49(3-10):399-418.
167. Schlumberger MJ. Papillary and follicular thyroid carcinoma. *N Engl J Med.* 1998; 338(5):297-306.
168. Schmutzler C, Koehrlle J. Innovative strategies for the treatment of thyroid cancer. *Eur J Endocrinol.* 2000; 143(1):15-24.
169. Schmutzler C, Kohrle J. Retinoic acid redifferentiation therapy for thyroid cancer. *Thyroid.* 2000; 10(5):393-406.
170. Schnee JM, Hsueh WA. Angiotensin II, adhesion, and cardiac fibrosis. *Cardiovasc Res.* 2000; 46(2):264-268.
171. Schonberger J, Bauer J, Spruss T, Weber G, Chahoud I, Eilles C, Grimm D. Establishment and characterization of the follicular thyroid carcinoma cell line ML-1. *J Mol Med.* 2000; 78(2):102-110.
172. Schwartz MA, Assoian RK. Integrins and cell proliferation: regulation of cyclin-dependent kinases via cytoplasmic signaling pathways. *J Cell Sci.* 2001; 114:2553-2560.

173. Schwarzenberg M, Pippia P, Meloni MA, Cossu G, Cogoli-Greuter M, Cogoli A. Signal transduction in T lymphocytes, a comparison of the data from space, the free fall machine and the random positioning machine. *Adv Space Res.* 1999; 24(6):793-800.
174. Sciola L, Cogoli-Greuter M, Cogoli A, Spano A, Pippia P. Influence of microgravity on mitogen binding and cytoskeleton in Jurkat cells. *Adv Space Res.* 1999; 24(6):801-805.
175. Scott G, Cassidy L, Busacco A. Fibronectin suppresses apoptosis in normal human melanocytes through an integrin-dependent mechanism. *J Invest Dermatol.* 1997; 108(2):147-153.
176. Sedlak TW, Oltvai ZN, Yang E, Wang K, Boise LH, Thompson CB, Korsmeyer SJ. Multiple Bcl-2 family members demonstrate selective dimerizations with Bax. *Proc Natl Acad Sci U S A.* 1995; 92(17):7834-7838.
177. Sharma K, Wang RX, Zhang LY, Yin DL, Luo XY, Solomon JC, Jiang RF, Markos K, Davidson W, Scott DW, Shi YF. Death the Fas way: regulation and pathophysiology of CD95 and its ligand. *Pharmacol Ther.* 2000; 88(3):333-347.
178. Sherman SI. Thyroid carcinoma. *Lancet.* 2003; 361(9356):501-511.
179. Shibata MA, Liu ML, Knudson MC, Shibata E, Yoshidome K, Bandey T, Korsmeyer SJ, Green JE. Haploid loss of bax leads to accelerated mammary tumor development in C3(1)/SV40-TAg transgenic mice: reduction in protective apoptotic response at the preneoplastic stage. *EMBO J.* 1999; 18(10):2692-2701.
180. Shimura H, Haraguchi K, Miyazaki A, Endo T, Onaya T. Iodide uptake and experimental 131I therapy in transplanted undifferentiated thyroid cancer cells expressing the Na<sup>+</sup>/I<sup>-</sup> symporter gene. *Endocrinology.* 1997; 138(10):4493-4496.
181. Sievers A. Gravity sensing mechanisms in plant cells. *ASGSB Bull.* 1991; 4(2):43-50.
182. Simon D, Koehrlé J, Reiners C, Boerner AR, Schmutzler C, Mainz K, Goretzki PE, Roeher HD. Redifferentiation therapy with retinoids: therapeutic option for advanced follicular and papillary thyroid carcinoma. *World J Surg.* 1998; 22(6):569-574.

183. Singer GG, Carrera AC, Marshak-Rothstein A, Martinez C, Abbas AK. Apoptosis, Fas and systemic autoimmunity: the MRL-lpr/lpr model. *Curr Opin Immunol.* 1994; 6(6):913-920.
184. Spitzweg C, O'Connor MK, Bergert ER, Tindall DJ, Young CY, Morris JC. Treatment of prostate cancer by radioiodine therapy after tissue-specific expression of the sodium iodide symporter. *Cancer Res.* 2000; 60(22):6526-6530.
185. Stein GS, van Wijnen AJ, Stein JL, Lian JB, Pockwinse SH, McNeil S. Implications for interrelationships between nuclear architecture and control of gene expression under microgravity conditions. *FASEB J.* 1999; 13:157-66.
186. Stein TP, Schluter MD, Moldawer LL. Endocrine relationships during human spaceflight. *Am J Physiol.* 1999; 276:155-162.
187. Stout SC, Porterfield DM, Briarty LG, Kuang A, Musgrave ME. Evidence of root zone hypoxia in *Brassica rapa* L. grown in microgravity. *Int J Plant Sci.* 2001; 162(2):249-255.
188. Strand S, Hofmann WJ, Hug H, Muller M, Otto G, Strand D, Mariani SM, Stremmel W, Krammer PH, Galle PR. Lymphocyte apoptosis induced by CD95 (APO-1/Fas) ligand-expressing tumor cells--a mechanism of immune evasion? *Nat Med.* 1996; 2(12):1361-1366.
189. Strasser A, Harris AW, Cory S. E mu-bcl-2 transgene facilitates spontaneous transformation of early pre-B and immunoglobulin-secreting cells but not T cells. *Oncogene.* 1993; 8(1):1-9.
190. Straus SE, Sneller M, Lenardo MJ, Puck JM, Strober W. An inherited disorder of lymphocyte apoptosis: the autoimmune lymphoproliferative syndrome. *Ann Intern Med.* 1999; 130(7):591-601.
191. Strollo F. Hormonal changes in humans during spaceflight. *Adv Space Biol Med.* 1999; 7:99-129.

192. Stromblad S, Becker JC, Yebra M, Brooks PC, Cheresh DA. Suppression of p53 activity and p21WAF1/CIP1 expression by vascular cell integrin  $\alpha$ V $\beta$ 3 during angiogenesis. *J Clin Invest.* 1996; 98(2):426-433.
193. Suda T, Okazaki T, Naito Y, Yokota T, Arai N, Ozaki S, Nakao K, Nagata S. Expression of the Fas ligand in cells of T cell lineage. *J Immunol.* 1995; 154(8):3806-3813.
194. Sutherland RM, JA McCredie, Inch WR. Growth of multicell spheroids in tissue culture as a model of nodular carcinomas. *J Natl Cancer Inst.* 1971;46:113–120.
195. Sutherland RM. Cell and environment interactions in tumor microregions: the multicell spheroid model. *Science.* 1988; 240(4849):177-184.
196. Sutherland RM, Sordat B, Bamat J, Gabbert H, Bourrat B, Mueller-Klieser W. Oxygenation and differentiation in multicellular spheroids of human colon carcinoma. *Cancer Res.* 1986; 46(10):5320-5329.
197. Tabony J, Pochon N, Papaseit C. Microtubule self-organisation depends upon gravity. *Adv Space Res.* 2001; 28(4):529-535.
198. Taipale J, Saharinen J, Keski-Oja J. Extracellular matrix-associated transforming growth factor- $\beta$ : role in cancer cell growth and invasion. *Adv Cancer Res.* 1998; 75:87-134.
199. Tanimoto C, Hirakawa S, Kawasaki H, Hayakawa N, Ota Z. Apoptosis in thyroid diseases: a histochemical study. *Endocr J.* 1995; 42(2):193-201.
200. Tentori L, Portarena I, Graziani G. Potential clinical applications of poly(ADP-ribose) polymerase (PARP) inhibitors. *Pharmacol Res.* 2002; 45(2):73-85.
201. Thornberry NA, Lazebnik Y. Caspases: enemies within. *Science.* 1998; 281(5381):1312-1316.
202. Todd P. Gravity-dependent phenomena at the scale of the single cell. *ASGSB Bull.* 1989; 2:95-113.

203. Tsatsoulis A. The role of apoptosis in thyroid disease. *Minerva Med.* 2002; 93(3):169-180.
204. Tsujimoto Y, Cossman J, Jaffe E, Croce CM. Involvement of the bcl-2 gene in human follicular lymphoma. *Science.* 1985;228(4706):1440-1443.
205. Tunggal JK, Cowan DS, Shaikh H, Tannock IF. Penetration of anticancer drugs through solid tissue: a factor that limits the effectiveness of chemotherapy for solid tumors. *Clin Cancer Res.* 1999; 5(6):1583-1586.
206. Tuttle RM, Becker DV. The Chernobyl accident and its consequences: update at the millennium. *Semin Nucl Med.* 2000; 30(2):133-140.
207. Unsworth BR, Lelkes PI. Growing tissues in microgravity. *Nat Med.* 1998; 4(8):901-907.
208. Uva BM, Masini MA, Sturla M, Prato P, Passalacqua M, Giuliani M, Tagliafierro G, Strollo F. Clinorotation-induced weightlessness influences the cytoskeleton of glial cells in culture. *Brain Res.* 2002; 934(2):132-139.
209. Vassy J, Portet S, Beil M, Millot G, Fauvel-Lafeve F, Karniguian A, Gasset G, Irinopoulou T, Calvo F, Rigaut JP, Schoevaert D. The effect of weightlessness on cytoskeleton architecture and proliferation of human breast cancer cell line MCF-7. *FASEB J.* 2001; 15(6):1104-1106.
210. Vaux DL, Strasser A The molecular biology of apoptosis *Proc Natl Acad Sci USA.* 1996; 93(6):2239-2244
211. Verrills NM, Kavallaris M. Improving the targeting of tubulin-binding agents: lessons from drug resistance studies. *Curr Pharm Des.* 2005; 11(13):1719-1733.
212. Vogelstein B, Kinzler KW. The multistep nature of cancer. *Trends Genet.* 1993; 9(4):138-141.
213. White RJ, Averner M. Humans in space. *Nature.* 2001; 409(6823):1115-1118.

214. Wolter KG, Hsu YT, Smith CL, Nechushtan A, Xi XG, Youle RJ. Movement of Bax from the cytosol to mitochondria during apoptosis. *J Cell Biol.* 1997; 139(5):1281-1292.
215. Wright PA, Lemoine NR, Mayall ES, Wyllie FS, Hughes D, Williams ED, Wynford-Thomas D. Papillary and follicular thyroid carcinomas show a different pattern of ras oncogene mutation. *Br J Cancer.* 1989; 60(4):576-577.
216. Yoffe B, Darlington GJ, Soriano HE, Krishnan B, Risin D, Pellis NR, Khaoustov VI. Cultures of human liver cells in simulated microgravity environment. *Adv Space Res.* 1999; 24(6):829-836.
217. Yuhas JM, Li AP, Martinez AO, Ladman AJ. A simplified method for production and growth of multicellular tumor spheroids. *Cancer Res.* 1977; 37(10):3639-3643.
218. Zha J, Harada H, Osipov K, Jockel J, Waksman G, Korsmeyer SJ. BH3 domain of BAD is required for heterodimerization with BCL-XL and pro-apoptotic activity. *J Biol Chem.* 1997; 272(39):24101-24104.
219. Zhang R, Baunoch D, DeGroot LJ. Genetic immunotherapy for medullary thyroid carcinoma: destruction of tumors in mice by in vivo delivery of adenoviral vector transducing the murine interleukin-2 gene. *Thyroid.* 1998; 8(12):1137-1146.
220. Zuzarte-Luis V, Hurle JM. Programmed cell death in the developing limb. *Int J Dev Biol.* 2002; 46(7):871-876.