

## Literaturverzeichnis

Abrams,E.S., Murdaugh,S.E., and Lerman,L.S. (1993). Comprehensive screening of the human KRAS2 gene for sequence variants. *Genes Chromosomes Cancer* 6, 73-85.

Adams,J.M. and Cory,S. (2002). Apoptosomes: engines for caspase activation. *Curr. Opin. Cell Biol.* 14, 715-720.

Almoguera,C., Shibata,D., Forrester,K., Martin,J., Arnheim,N., and Perucho,M. (1988). Most human carcinomas of the exocrine pancreas contain mutant c-K-ras genes. *Cell* 53, 549-554.

Alves,F., Borchers,U., Padge,B., Augustin,H., Nebendahl,K., Kloppel,G., and Tietze,L.F. (2001a). Inhibitory effect of a matrix metalloproteinase inhibitor on growth and spread of human pancreatic ductal adenocarcinoma evaluated in an orthotopic severe combined immunodeficient (SCID) mouse model. *Cancer Lett.* 165, 161-170.

Alves,F., Contag,S., Missbach,M., Kaspereit,J., Nebendahl,K., Borchers,U., Heidrich,B., Streich,R., and Hiddemann,W. (2001b). An orthotopic model of ductal adenocarcinoma of the pancreas in severe combined immunodeficient mice representing all steps of the metastatic cascade. *Pancreas* 23, 227-235.

Apolloni,A., Prior,I.A., Lindsay,M., Parton,R.G., and Hancock,J.F. (2000). H-ras but not K-ras traffics to the plasma membrane through the exocytic pathway. *Mol. Cell Biol.* 20, 2475-2487.

Baltimore,D. (1970). RNA-dependent DNA polymerase in virions of RNA tumour viruses. *Nature* 226, 1209-1211.

Banerji,S., Ni,J., Wang,S.X., Clasper,S., Su,J., Tammi,R., Jones,M., and Jackson,D.G. (1999). LYVE-1, a new homologue of the CD44 glycoprotein, is a lymph-specific receptor for hyaluronan. *J. Cell Biol.* 144, 789-801.

Bar-Sagi,D. (2001). A Ras by any other name. *Mol. Cell Biol.* 21, 1441-1443.

Barbacid,M. (1987). ras genes. *Annu. Rev. Biochem.* 56, 779-827.

Bardeesy,N. and DePinho,R.A. (2002). Pancreatic cancer biology and genetics. *Nat. Rev. Cancer* 2, 897-909.

Bardeesy,N., Sharpless,N.E., DePinho,R.A., and Merlino,G. (2001). The genetics of pancreatic adenocarcinoma: a roadmap for a mouse model. *Semin. Cancer Biol.* 11, 201-218.

Baumhueter,S., Dybdal,N., Kyle,C., and Lasky,L.A. (1994). Global vascular expression of murine CD34, a sialomucin-like endothelial ligand for L-selectin. *Blood* 84, 2554-2565.

Bergers,G. and Benjamin,L.E. (2003). Tumorigenesis and the angiogenic switch. *Nat. Rev. Cancer* 3, 401-410.

- Bissonnette, N. and Hunting, D.J. (1998). p21-induced cycle arrest in G1 protects cells from apoptosis induced by UV-irradiation or RNA polymerase II blockage. *Oncogene* 16, 3461-3469.
- Blagosklonny, M.V. and el Deiry, W.S. (1996). In vitro evaluation of a p53-expressing adenovirus as an anti-cancer drug. *Int. J. Cancer* 67, 386-392.
- Blandino, G., Levine, A.J., and Oren, M. (1999). Mutant p53 gain of function: differential effects of different p53 mutants on resistance of cultured cells to chemotherapy. *Oncogene* 18, 477-485.
- Bloomston, M., Zervos, E.E., and Rosemurgy, A.S. (2002). Matrix metalloproteinases and their role in pancreatic cancer: a review of preclinical studies and clinical trials. *Ann. Surg. Oncol.* 9, 668-674.
- Bordel, R., Laschke, M.W., Menger, M.D., and Vollmar, B. (2005). Inhibition of p53 during physiological angiogenesis in the hamster ovary does not affect extent of new vessel formation but delays vessel maturation. *Cell Tissue Res.* 320, 427-435.
- Bornstein, P., Agah, A., and Kyriakides, T.R. (2004). The role of thrombospondins 1 and 2 in the regulation of cell-matrix interactions, collagen fibril formation, and the response to injury. *Int. J. Biochem. Cell Biol.* 36, 1115-1125.
- Bos, J.L. (1989). ras oncogenes in human cancer: a review. *Cancer Res.* 49, 4682-4689.
- Bourne, H.R., Sanders, D.A., and McCormick, F. (1990). The GTPase superfamily: a conserved switch for diverse cell functions. *Nature* 348, 125-132.
- Brummelkamp, T.R., Bernards, R., and Agami, R. (2002). Stable suppression of tumorigenicity by virus-mediated RNA interference. *Cancer Cell* 2, 243-247.
- Bruns, C.J., Harbison, M.T., Kuniyasu, H., Eue, I., and Fidler, I.J. (1999). In vivo selection and characterization of metastatic variants from human pancreatic adenocarcinoma by using orthotopic implantation in nude mice. *Neoplasia*. 1, 50-62.
- Buckbinder, L., Talbott, R., Seizinger, B.R., and Kley, N. (1994). Gene regulation by temperature-sensitive p53 mutants: identification of p53 response genes. *Proc. Natl. Acad. Sci. U. S. A* 91, 10640-10644.
- Bujard, H. (1999). Controlling genes with tetracyclines. *J. Gene Med.* 1, 372-374.
- Bykov, V.J., Issaeva, N., Selivanova, G., and Wiman, K.G. (2002a). Mutant p53-dependent growth suppression distinguishes PRIMA-1 from known anticancer drugs: a statistical analysis of information in the National Cancer Institute database. *Carcinogenesis* 23, 2011-2018.
- Bykov, V.J., Issaeva, N., Shilov, A., Hultcrantz, M., Pugacheva, E., Chumakov, P., Bergman, J., Wiman, K.G., and Selivanova, G. (2002b). Restoration of the tumor suppressor function to mutant p53 by a low-molecular-weight compound. *Nat. Med.* 8, 282-288.
- Cadwell, C. and Zambetti, G.P. (2001). The effects of wild-type p53 tumor suppressor activity and mutant p53 gain-of-function on cell growth. *Gene* 277, 15-30.

Carmeliet,P. and Jain,R.K. (2000). Angiogenesis in cancer and other diseases. *Nature* 407, 249-257.

Cascallo,M., Mercade,E., Capella,G., Lluís,F., Fillat,C., Gomez-Foix,A.M., and Mazo,A. (1999). Genetic background determines the response to adenovirus-mediated wild-type p53 expression in pancreatic tumor cells. *Cancer Gene Ther.* 6, 428-436.

Cerny,W.L., Mangold,K.A., and Scarpelli,D.G. (1992). K-ras mutation is an early event in pancreatic duct carcinogenesis in the Syrian golden hamster. *Cancer Res.* 52, 4507-4513.

Chen,X., Ko,L.J., Jayaraman,L., and Prives,C. (1996). p53 levels, functional domains, and DNA damage determine the extent of the apoptotic response of tumor cells. *Genes Dev.* 10, 2438-2451.

Chi,T.Y., Chen,G.G., Ho,L.K., and Lai,P.B. (2005). Establishment of a doxycycline-regulated cell line with inducible, doubly-stable expression of the wild-type p53 gene from p53-deleted hepatocellular carcinoma cells. *Cancer Cell Int.* 5, 27.

Choy,E., Chiu,V.K., Silletti,J., Feoktistov,M., Morimoto,T., Michaelson,D., Ivanov,I.E., and Philips,M.R. (1999). Endomembrane trafficking of ras: the CAAX motif targets proteins to the ER and Golgi. *Cell* 98, 69-80.

Coqueret,O. (2003). New roles for p21 and p27 cell-cycle inhibitors: a function for each cell compartment? *Trends Cell Biol.* 13, 65-70.

Crespo,P. and Leon,J. (2000). Ras proteins in the control of the cell cycle and cell differentiation. *Cell Mol. Life Sci.* 57, 1613-1636.

Dameron,K.M., Volpert,O.V., Tainsky,M.A., and Bouck,N. (1994). The p53 tumor suppressor gene inhibits angiogenesis by stimulating the production of thrombospondin. *Cold Spring Harb. Symp. Quant. Biol.* 59, 483-489.

Delisser,H.M., Newman,P.J., and Albelda,S.M. (1993). Platelet endothelial cell adhesion molecule (CD31). *Curr. Top. Microbiol. Immunol.* 184, 37-45.

Dergham,S.T., Dugan,M.C., Sarkar,F.H., and Vaitkevicius,V.K. (1998). Molecular alterations associated with improved survival in pancreatic cancer patients treated with radiation or chemotherapy. *J. Hepatobiliary. Pancreat. Surg.* 5, 269-272.

Detjen,K.M., Farwig,K., Welzel,M., Wiedenmann,B., and Rosewicz,S. (2001). Interferon gamma inhibits growth of human pancreatic carcinoma cells via caspase-1 dependent induction of apoptosis. *Gut* 49, 251-262.

Digiuseppe,J.A., Hruban,R.H., Goodman,S.N., Polak,M., van den Berg,F.M., Allison,D.C., Cameron,J.L., and Offerhaus,G.J. (1994). Overexpression of p53 protein in adenocarcinoma of the pancreas. *Am. J. Clin. Pathol.* 101, 684-688.

Dittmer,D., Pati,S., Zambetti,G., Chu,S., Teresky,A.K., Moore,M., Finlay,C., and Levine,A.J. (1993). Gain of function mutations in p53. *Nat. Genet.* 4, 42-46.

DKFZ. [www.dkfz.de](http://www.dkfz.de). 2003.

Ref Type: Report

Do, T.N., Rosal, R.V., Drew, L., Raffo, A.J., Michl, J., Pincus, M.R., Friedman, F.K., Petrylak, D.P., Cassai, N., Szmulewicz, J., Sidhu, G., Fine, R.L., and Brandt-Rauf, P.W. (2003). Preferential induction of necrosis in human breast cancer cells by a p53 peptide derived from the MDM2 binding site. *Oncogene* 22, 1431-1444.

Donehower, L.A., Harvey, M., Slagle, B.L., McArthur, M.J., Montgomery, C.A., Jr., Butel, J.S., and Bradley, A. (1992). Mice deficient for p53 are developmentally normal but susceptible to spontaneous tumours. *Nature* 356, 215-221.

Downward, J. (2003). Targeting RAS signalling pathways in cancer therapy. *Nat. Rev. Cancer* 3, 11-22.

Ehrhardt, A., Ehrhardt, G.R., Guo, X., and Schrader, J.W. (2002). Ras and relatives--job sharing and networking keep an old family together. *Exp. Hematol.* 30, 1089-1106.

Einhauser, A. and Jungbauer, A. (2001). Affinity of the monoclonal antibody M1 directed against the FLAG peptide. *J. Chromatogr. A* 921, 25-30.

Elbashir, S.M., Harborth, J., Lendeckel, W., Yalcin, A., Weber, K., and Tuschl, T. (2001). Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. *Nature* 411, 494-498.

Endoline. [www.endoline.de](http://www.endoline.de). 2007.

Ref Type: Internet Communication

Ferrara, N. (2001). Role of vascular endothelial growth factor in regulation of physiological angiogenesis. *Am. J. Physiol Cell Physiol* 280, C1358-C1366.

Fidler, I.J. (1991). Orthotopic implantation of human colon carcinomas into nude mice provides a valuable model for the biology and therapy of metastasis. *Cancer Metastasis Rev.* 10, 229-243.

Fidler, I.J. (1995). Modulation of the organ microenvironment for treatment of cancer metastasis. *J. Natl. Cancer Inst.* 87, 1588-1592.

Fidler, I.J., Li, L.M., Ananthaswamy, H.N., Esumi, N., Radinsky, R., and Price, J.E. (1991). Correlation of growth capacity of cells in hard agarose with successful transfection by the activated c-Ha-ras oncogene and in vivo proliferative capacity at metastatic sites. *Anticancer Res.* 11, 17-24.

Flamme, I., von Reutern, M., Drexler, H.C., Syed-Ali, S., and Risau, W. (1995). Overexpression of vascular endothelial growth factor in the avian embryo induces hypervascularization and increased vascular permeability without alterations of embryonic pattern formation. *Dev. Biol.* 171, 399-414.

Forsythe, J.A., Jiang, B.H., Iyer, N.V., Agani, F., Leung, S.W., Koos, R.D., and Semenza, G.L. (1996). Activation of vascular endothelial growth factor gene transcription by hypoxia-inducible factor 1. *Mol. Cell Biol.* 16, 4604-4613.

Foster, B.A., Coffey, H.A., Morin, M.J., and Rastinejad, F. (1999). Pharmacological rescue of mutant p53 conformation and function. *Science* 286, 2507-2510.

- Fridman, J.S. and Lowe, S.W. (2003). Control of apoptosis by p53. *Oncogene* 22, 9030-9040.
- Friedman, P.N., Chen, X., Bargonetti, J., and Prives, C. (1993). The p53 protein is an unusually shaped tetramer that binds directly to DNA. *Proc. Natl. Acad. Sci. U. S. A* 90, 3319-3323.
- Friess, H., Berberat, P., Schilling, M., Kunz, J., Korc, M., and Buchler, M.W. (1996). Pancreatic cancer: the potential clinical relevance of alterations in growth factors and their receptors. *J. Mol. Med.* 74, 35-42.
- Ghaneh, P., Greenhalf, W., Humphreys, M., Wilson, D., Zumstein, L., Lemoine, N.R., and Neoptolemos, J.P. (2001). Adenovirus-mediated transfer of p53 and p16(INK4a) results in pancreatic cancer regression in vitro and in vivo. *Gene Ther.* 8, 199-208.
- Giaccia, A.J. and Kastan, M.B. (1998). The complexity of p53 modulation: emerging patterns from divergent signals. *Genes Dev.* 12, 2973-2983.
- Ginsberg, D., Mehta, F., Yaniv, M., and Oren, M. (1991). Wild-type p53 can down-modulate the activity of various promoters. *Proc. Natl. Acad. Sci. U. S. A* 88, 9979-9983.
- Giovanella, B.C., Yim, S.O., Stehlin, J.S., and Williams, L.J., Jr. (1972). Development of invasive tumors in the "nude" mouse after injection of cultured human melanoma cells. *J. Natl. Cancer Inst.* 48, 1531-1533.
- Gorunova, L., Hoglund, M., Andren-Sandberg, A., Dawiskiba, S., Jin, Y., Mitelman, F., and Johansson, B. (1998). Cytogenetic analysis of pancreatic carcinomas: intratumor heterogeneity and nonrandom pattern of chromosome aberrations. *Cancer* 23, 81-99.
- Gossen, M. and Bujard, H. (1992). Tight control of gene expression in mammalian cells by tetracycline-responsive promoters. *Proc. Natl. Acad. Sci. U. S. A* 89, 5547-5551.
- Gottlieb, T.M. and Oren, M. (1998). p53 and apoptosis. *Semin. Cancer Biol.* 8, 359-368.
- Hager, J.H. and Hanahan, D. (1999). Tumor cells utilize multiple pathways to down-modulate apoptosis. Lessons from a mouse model of islet cell carcinogenesis. *Ann. N. Y. Acad. Sci.* 887, 150-163.
- Hahn, S.A., Hoque, A.T., Moskaluk, C.A., da Costa, L.T., Schutte, M., Rozenblum, E., Seymour, A.B., Weinstein, C.L., Yeo, C.J., Hruban, R.H., and Kern, S.E. (1996). Homozygous deletion map at 18q21.1 in pancreatic cancer. *Cancer Res.* 56, 490-494.
- Hall, P.A., Meek, D., and Lane, D.P. (1996). p53--integrating the complexity. *J. Pathol.* 180, 1-5.
- Harper, J.W., Adami, G.R., Wei, N., Keyomarsi, K., and Elledge, S.J. (1993). The p21 Cdk-interacting protein Cip1 is a potent inhibitor of G1 cyclin-dependent kinases. *Cell* 75, 805-816.
- Harris, S.L. and Levine, A.J. (2005). The p53 pathway: positive and negative feedback loops. *Oncogene* 24, 2899-2908.

- Hermanek,P. (1998). Pathology and biology of pancreatic ductal adenocarcinoma. *Langenbecks Arch. Surg.* 383, 116-120.
- Herzenberg,L.A., Parks,D., Sahaf,B., Perez,O., Roederer,M., and Herzenberg,L.A. (2002). The history and future of the fluorescence activated cell sorter and flow cytometry: a view from Stanford. *Clin. Chem.* 48, 1819-1827.
- Hezel,A.F., Kimmelman,A.C., Stanger,B.Z., Bardeesy,N., and DePinho,R.A. (2006). Genetics and biology of pancreatic ductal adenocarcinoma. *Genes Dev.* 20, 1218-1249.
- Higuchi,Y., Asaumi,J., Murakami,J., Matsuzaki,H., Wakasa,T., Inoue,T., Shigehara,H., Konouchi,H., Hisatomi,M., Kawasaki,S., Hiraki,Y., and Kishi,K. (2003). Effects of p53 gene therapy in radiotherapy or thermotherapy of human head and neck squamous cell carcinoma cell lines. *Oncol. Rep.* 10, 671-677.
- Hillen,W. and Berens,C. (1994). Mechanisms underlying expression of Tn10 encoded tetracycline resistance. *Annu. Rev. Microbiol.* 48, 345-369.
- Hollstein,M., Rice,K., Greenblatt,M.S., Soussi,T., Fuchs,R., Sorlie,T., Hovig,E., Smith-Sorensen,B., Montesano,R., and Harris,C.C. (1994). Database of p53 gene somatic mutations in human tumors and cell lines. *Nucleic Acids Res.* 22, 3551-3555.
- Hruban,R.H., Goggins,M., Parsons,J., and Kern,S.E. (2000). Progression model for pancreatic cancer. *Clin. Cancer Res.* 6, 2969-2972.
- Huh,J.J., Wolf,J.K., Fightmaster,D.L., Lotan,R., and Follen,M. (2003). Transduction of adenovirus-mediated wild-type p53 after radiotherapy in human cervical cancer cells. *Gynecol. Oncol.* 89, 243-250.
- Itoh,H., Komori,K., Okazaki,J., Mawatari,K., Kawasaki,K., Kuma,S., Eguchi,D., and Sugimachi,K. (1997). The effect of probucol on intimal thickening of autologous vein grafts in hyperlipidemic rabbit. *Cardiovasc. Surg.* 5, 497-503.
- Jacks,T. (1996). Lessons from the p53 mutant mouse. *J. Cancer Res. Clin. Oncol.* 122, 319-327.
- Jaenisch,R. (1988). Transgenic animals. *Science* 240, 1468-1474.
- Jemal,A., Murray,T., Ward,E., Samuels,A., Tiwari,R.C., Ghafoor,A., Feuer,E.J., and Thun,M.J. (2005). Cancer statistics, 2005. *CA Cancer J. Clin.* 55, 10-30.
- Jeong,J., Park,Y.N., Park,J.S., Yoon,D.S., Chi,H.S., and Kim,B.R. (2005). Clinical significance of p16 protein expression loss and aberrant p53 protein expression in pancreatic cancer. *Yonsei Med. J.* 46, 519-525.
- Joo,Y.E., Sohn,Y.H., Lee,W.S., Park,C.H., Choi,S.K., Rew,J.S., Park,C.S., and Kim,S.J. (2002). Expression of vascular endothelial growth factor and p53 in pancreatic carcinomas. *Korean J. Intern. Med.* 17, 153-159.
- Jura,N., Archer,H., and Bar-Sagi,D. (2005). Chronic pancreatitis, pancreatic adenocarcinoma and the black box in-between. *Cell Res.* 15, 72-77.

- Kameya, T., Shimosato, Y., Tumoraya, M., Ohsawa, N., and Nomura, T. (1976). Human gastric choriocarcinoma serially transplanted in nude mice. *J. Natl. Cancer Inst.* 56, 325-332.
- Karkkainen, M.J., Jussila, L., Ferrell, R.E., Finegold, D.N., and Alitalo, K. (2001). Molecular regulation of lymphangiogenesis and targets for tissue oedema. *Trends Mol. Med.* 7, 18-22.
- Keleg, S., Buchler, P., Ludwig, R., Buchler, M.W., and Friess, H. (2003). Invasion and metastasis in pancreatic cancer. *Mol. Cancer* 2, 14.
- Kim, A.L., Raffo, A.J., Brandt-Rauf, P.W., Pincus, M.R., Monaco, R., Abarzua, P., and Fine, R.L. (1999). Conformational and molecular basis for induction of apoptosis by a p53 C-terminal peptide in human cancer cells. *J. Biol. Chem.* 274, 34924-34931.
- Kirsten, W.H. and Mayer, L.A. (1969). Malignant lymphomas of extrathymic origin induced in rats by murine erythroblastosis virus. *J. Natl. Cancer Inst.* 43, 735-746.
- Korsmeyer, S.J. (1999). BCL-2 gene family and the regulation of programmed cell death. *Cancer Res.* 59, 1693s-1700s.
- Koshiba, T., Hosotani, R., Wada, M., Miyamoto, Y., Fujimoto, K., Lee, J.U., Doi, R., Aii, S., and Imamura, M. (1998). Involvement of matrix metalloproteinase-2 activity in invasion and metastasis of pancreatic carcinoma. *Cancer* 82, 642-650.
- Kranenburg, O., Gebbink, M.F., and Voest, E.E. (2004). Stimulation of angiogenesis by Ras proteins. *Biochim. Biophys. Acta* 1654, 23-37.
- Laemmli, U.K. (1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227, 680-685.
- Laheru, D. and Jaffee, E.M. (2005). Immunotherapy for pancreatic cancer - science driving clinical progress. *Nat. Rev. Cancer* 5, 459-467.
- Lane, D.P. and Beach, D. (1990). p53: oncogene or anti-oncogene? *Genes Dev.* 4, 1-8.
- Lang, D., Miknyoczki, S.J., Huang, L., and Ruggeri, B.A. (1998). Stable reintroduction of wild-type P53 (MTmp53ts) causes the induction of apoptosis and neuroendocrine-like differentiation in human ductal pancreatic carcinoma cells. *Oncogene* 16, 1593-1602.
- Leber, T.M. and Balkwill, F.R. (1997). Zymography: a single-step staining method for quantitation of proteolytic activity on substrate gels. *Anal. Biochem.* 249, 24-28.
- Leist, M. and Nicotera, P. (1997). The shape of cell death. *Biochem. Biophys. Res. Commun.* 236, 1-9.
- Leverro, M., de, L., V, Costanzo, A., Gong, J., Wang, J.Y., and Melino, G. (2000). The p53/p63/p73 family of transcription factors: overlapping and distinct functions. *J. Cell Sci.* 113 ( Pt 10), 1661-1670.
- Li, R., Sutphin, P.D., Schwartz, D., Matas, D., Almog, N., Wolkowicz, R., Goldfinger, N., Pei, H., Prokocimer, M., and Rotter, V. (1998). Mutant p53 protein expression interferes with p53-independent apoptotic pathways. *Oncogene* 16, 3269-3277.

- Loukopoulos,P., Kanetaka,K., Takamura,M., Shibata,T., Sakamoto,M., and Hirohashi,S. (2004). Orthotopic transplantation models of pancreatic adenocarcinoma derived from cell lines and primary tumors and displaying varying metastatic activity. *Pancreas* 29, 193-203.
- LOWRY,O.H., ROSEBROUGH,N.J., FARR,A.L., and RANDALL,R.J. (1951). Protein measurement with the Folin phenol reagent. *J. Biol. Chem.* 193, 265-275.
- Mack,D.H., Vartikar,J., Pipas,J.M., and Laimins,L.A. (1993). Specific repression of TATA-mediated but not initiator-mediated transcription by wild-type p53. *Nature* 363, 281-283.
- Malkin,D., Li,F.P., Strong,L.C., Fraumeni,J.F., Jr., Nelson,C.E., Kim,D.H., Kassel,J., Gryka,M.A., Bischoff,F.Z., Tainsky,M.A., and . (1990). Germ line p53 mutations in a familial syndrome of breast cancer, sarcomas, and other neoplasms. *Science* 250, 1233-1238.
- Malumbres,M. and Pellicer,A. (1998). RAS pathways to cell cycle control and cell transformation. *Front Biosci.* 3, d887-d912.
- Marin,M.C. and Kaelin,W.G., Jr. (2000). p63 and p73: old members of a new family. *Biochim. Biophys. Acta* 1470, M93-M100.
- Marme,D. (1999). [In Process Citation]. *Chirurg* 70, 30-35.
- Mathur,A., Hong,Y., Kemp,B.K., Barrientos,A.A., and Erusalimsky,J.D. (2000). Evaluation of fluorescent dyes for the detection of mitochondrial membrane potential changes in cultured cardiomyocytes. *Cardiovasc. Res.* 46, 126-138.
- Matsuda,T., Abe,T., Wu,J.L., Fujiki,M., and Kobayashi,H. (2005). Hypoxia-inducible factor-1alpha DNA induced angiogenesis in a rat cerebral ischemia model. *Neurol. Res.* 27, 503-508.
- McLure,K.G. and Lee,P.W. (1998). How p53 binds DNA as a tetramer. *EMBO J.* 17, 3342-3350.
- McLure,K.G. and Lee,P.W. (1999). p53 DNA binding can be modulated by factors that alter the conformational equilibrium. *EMBO J.* 18, 763-770.
- Mehlen,P. and Puisieux,A. (2006). Metastasis: a question of life or death. *Nat. Rev. Cancer* 6, 449-458.
- Michieli,P., Li,W., Lorenzi,M.V., Miki,T., Zakut,R., Givol,D., and Pierce,J.H. (1996). Inhibition of oncogene-mediated transformation by ectopic expression of p21Waf1 in NIH3T3 cells. *Oncogene* 12, 775-784.
- Mohammad,R.M., Al Katib,A., Pettit,G.R., Vaitkevicius,V.K., Joshi,U., Adsay,V., Majumdar,A.P., and Sarkar,F.H. (1998). An orthotopic model of human pancreatic cancer in severe combined immunodeficient mice: potential application for preclinical studies. *Clin. Cancer Res.* 4, 887-894.
- Momand,J. and Zambetti,G.P. (1997). Mdm-2: "big brother" of p53. *J. Cell Biochem.* 64, 343-352.



- Moon,W.S., Rhyu,K.H., Kang,M.J., Lee,D.G., Yu,H.C., Yeum,J.H., Koh,G.Y., and Tarnawski,A.S. (2003). Overexpression of VEGF and angiopoietin 2: a key to high vascularity of hepatocellular carcinoma? *Mod. Pathol.* 16, 552-557.
- Moore,P.S., Sipos,B., Orlandini,S., Sorio,C., Real,F.X., Lemoine,N.R., Gress,T., Bassi,C., Kloppel,G., Kalthoff,H., Ungefroren,H., Lohr,M., and Scarpa,A. (2001). Genetic profile of 22 pancreatic carcinoma cell lines. Analysis of K-ras, p53, p16 and DPC4/Smad4. *Virchows Arch.* 439, 798-802.
- Moretti,F., Farsetti,A., Soddu,S., Misiti,S., Crescenzi,M., Filetti,S., Andreoli,M., Sacchi,A., and Pontecorvi,A. (1997). p53 re-expression inhibits proliferation and restores differentiation of human thyroid anaplastic carcinoma cells. *Oncogene* 14, 729-740.
- Morgan,D.O. (1995). Principles of CDK regulation. *Nature* 374, 131-134.
- Mouta,C.C., Nasser,S.M., di Tomaso,E., Padera,T.P., Boucher,Y., Tomarev,S.I., and Jain,R.K. (2001). LYVE-1 is not restricted to the lymph vessels: expression in normal liver blood sinusoids and down-regulation in human liver cancer and cirrhosis. *Cancer Res.* 61, 8079-8084.
- Mukhopadhyay,D. and Datta,K. (2004). Multiple regulatory pathways of vascular permeability factor/vascular endothelial growth factor (VPF/VEGF) expression in tumors. *Semin. Cancer Biol.* 14, 123-130.
- Mullis,K.B. and Faloona,F.A. (1987). Specific synthesis of DNA in vitro via a polymerase-catalyzed chain reaction. *Methods Enzymol.* 155, 335-350.
- Munoz-Chapuli,R., Quesada,A.R., and Angel,M.M. (2004). Angiogenesis and signal transduction in endothelial cells. *Cell Mol. Life Sci.* 61, 2224-2243.
- Nakamori,S., Yashima,K., Murakami,Y., Ishikawa,O., Ohigashi,H., Imaoka,S., Yaegashi,S., Konishi,Y., and Sekiya,T. (1995). Association of p53 gene mutations with short survival in pancreatic adenocarcinoma. *Jpn. J. Cancer Res.* 86, 174-181.
- Nationales Krebsinstitut, Park City USA.  
<http://www.cancer.gov/cancertopics/factsheet/NCI/cancer-centers>. 1999.  
Ref Type: Conference Proceeding
- Neid,M., Datta,K., Stephan,S., Khanna,I., Pal,S., Shaw,L., White,M., and Mukhopadhyay,D. (2004). Role of insulin receptor substrates and protein kinase C-zeta in vascular permeability factor/vascular endothelial growth factor expression in pancreatic cancer cells. *J. Biol. Chem.* 279, 3941-3948.
- Niedergethmann,M., Hildenbrand,R., Wostbrock,B., Hartel,M., Sturm,J.W., Richter,A., and Post,S. (2002). High expression of vascular endothelial growth factor predicts early recurrence and poor prognosis after curative resection for ductal adenocarcinoma of the pancreas. *Pancreas* 25, 122-129.
- Novina,C.D., Murray,M.F., Dykxhoorn,D.M., Beresford,P.J., Riess,J., Lee,S.K., Collman,R.G., Lieberman,J., Shankar,P., and Sharp,P.A. (2002). siRNA-directed inhibition of HIV-1 infection. *Nat. Med.* 8, 681-686.

Ohki,R., Nemoto,J., Murasawa,H., Oda,E., Inazawa,J., Tanaka,N., and Taniguchi,T. (2000). Reprimo, a new candidate mediator of the p53-mediated cell cycle arrest at the G2 phase. *J. Biol. Chem.* 275, 22627-22630.

Outzen,H.C. and Custer,R.P. (1975). Growth of human normal and neoplastic mammary tissues in the cleared mammary fat pad of the nude mouse. *J. Natl. Cancer Inst.* 55, 1461-1466.

Overholt,S.M., Liu,T.J., Taylor,D.L., Wang,M., El Naggar,A.K., Shillitoe,E., Adler-Storthz,K., John,L.S., Zhang,W.W., Roth,J.A., and Clayman,G.L. (1997). Head and neck squamous cell growth suppression using adenovirus-p53-FLAG: a potential marker for gene therapy trials. *Clin. Cancer Res.* 3, 185-191.

Owen-Schaub,L.B., Angelo,L.S., Radinsky,R., Ware,C.F., Gesner,T.G., and Bartos,D.P. (1995). Soluble Fas/APO-1 in tumor cells: a potential regulator of apoptosis? *Cancer Lett.* 94, 1-8.

p53\_database. [http://p53.free.fr/Database/p53\\_database.html](http://p53.free.fr/Database/p53_database.html). 2007.

Ref Type: Internet Communication

Papoutsi,M., Kurz,H., Schachtele,C., Marme,D., Christ,B., Prols,F., and Wilting,J. (2000). Induction of the blood-brain barrier marker neurothelin/HT7 in endothelial cells by a variety of tumors in chick embryos. *Histochem. Cell Biol.* 113, 105-113.

Partanen,T.A. and Paavonen,K. (2001). Lymphatic versus blood vascular endothelial growth factors and receptors in humans. *Microsc. Res. Tech.* 55, 108-121.

Pellegata,N.S., Sessa,F., Renault,B., Bonato,M., Leone,B.E., Solcia,E., and Ranzani,G.N. (1994). K-ras and p53 gene mutations in pancreatic cancer: ductal and nonductal tumors progress through different genetic lesions. *Cancer Res.* 54, 1556-1560.

Pennisi,E. (1999). Bracing p53 for the war on cancer. *Science* 286, 2431.

Pepper,M.S. (2001). Lymphangiogenesis and tumor metastasis: myth or reality? *Clin. Cancer Res.* 7, 462-468.

Pines,J. (1995). Cyclins and cyclin-dependent kinases: theme and variations. *Adv. Cancer Res.* 66, 181-212.

Pluquet,O. and Hainaut,P. (2001). Genotoxic and non-genotoxic pathways of p53 induction. *Cancer Lett.* 174, 1-15.

Prives,C. (1998). Signaling to p53: breaking the MDM2-p53 circuit. *Cell* 95, 5-8.

Prives,C. and Hall,P.A. (1999). The p53 pathway. *J. Pathol.* 187, 112-126.

Quaife,C.J., Pinkert,C.A., Ornitz,D.M., Palmiter,R.D., and Brinster,R.L. (1987). Pancreatic neoplasia induced by ras expression in acinar cells of transgenic mice. *Cell* 48, 1023-1034.

Rak,J., Mitsuhashi,Y., Sheehan,C., Tamir,A., Vilorio-Petit,A., Filmus,J., Mansour,S.J., Ahn,N.G., and Kerbel,R.S. (2000). Oncogenes and tumor angiogenesis: differential modes of

vascular endothelial growth factor up-regulation in ras-transformed epithelial cells and fibroblasts. *Cancer Res.* 60, 490-498.

Redston, M.S., Caldas, C., Seymour, A.B., Hruban, R.H., da Costa, L., Yeo, C.J., and Kern, S.E. (1994). p53 mutations in pancreatic carcinoma and evidence of common involvement of homocopolymer tracts in DNA microdeletions. *Cancer Res.* 54, 3025-3033.

Reuther, G.W. and Der, C.J. (2000). The Ras branch of small GTPases: Ras family members don't fall far from the tree. *Curr. Opin. Cell Biol.* 12, 157-165.

Risau, W. and Flamme, I. (1995). Vasculogenesis. *Annu. Rev. Cell Dev. Biol.* 11, 73-91.

Rosewicz, S. and Wiedenmann, B. (1997). Pancreatic carcinoma. *Lancet* 349, 485-489.

Rozenblum, E., Schutte, M., Goggins, M., Hahn, S.A., Panzer, S., Zahurak, M., Goodman, S.N., Sohn, T.A., Hruban, R.H., Yeo, C.J., and Kern, S.E. (1997). Tumor-suppressive pathways in pancreatic carcinoma. *Cancer Res.* 57, 1731-1734.

Ryding, A.D., Sharp, M.G., and Mullins, J.J. (2001). Conditional transgenic technologies. *J. Endocrinol.* 171, 1-14.

Sambrook J and Russel D.M. (2001). *Molecular Cloning - A Laboratory Manual*. (Cold Spring Harbor, NY, USA: Cold Spring Harbor Laboratory Press).

Scheffzek, K., Ahmadian, M.R., and Wittinghofer, A. (1998). GTPase-activating proteins: helping hands to complement an active site. *Trends Biochem. Sci.* 23, 257-262.

Schneider, G. and Schmid, R.M. (2003). Genetic alterations in pancreatic carcinoma. *Mol. Cancer* 2, 15.

Schuler, M., Herrmann, R., De Greve, J.L., Stewart, A.K., Gatzemeier, U., Stewart, D.J., Laufman, L., Gralla, R., Kuball, J., Buhl, R., Heussel, C.P., Kommos, F., Perruchoud, A.P., Shepherd, F.A., Fritz, M.A., Horowitz, J.A., Huber, C., and Rochlitz, C. (2001). Adenovirus-mediated wild-type p53 gene transfer in patients receiving chemotherapy for advanced non-small-cell lung cancer: results of a multicenter phase II study. *J. Clin. Oncol.* 19, 1750-1758.

Schutte, M., Hruban, R.H., Geradts, J., Maynard, R., Hilgers, W., Rabindran, S.K., Moskaluk, C.A., Hahn, S.A., Schwarte-Waldhoff, I., Schmiegel, W., Baylin, S.B., Kern, S.E., and Herman, J.G. (1997). Abrogation of the Rb/p16 tumor-suppressive pathway in virtually all pancreatic carcinomas. *Cancer Res.* 57, 3126-3130.

Sedivy, R., Beck-Mannagetta, J., Haverkamp, C., Battistutti, W., and Honigschnabl, S. (2003). Expression of vascular endothelial growth factor-C correlates with the lymphatic microvessel density and the nodal status in oral squamous cell cancer. *J. Oral Pathol. Med.* 32, 455-460.

Selivanova, G., Iotsova, V., Okan, I., Fritsche, M., Strom, M., Groner, B., Grafstrom, R.C., and Wiman, K.G. (1997). Restoration of the growth suppression function of mutant p53 by a synthetic peptide derived from the p53 C-terminal domain. *Nat. Med.* 3, 632-638.

Selivanova, G., Ryabchenko, L., Jansson, E., Iotsova, V., and Wiman, K.G. (1999). Reactivation of mutant p53 through interaction of a C-terminal peptide with the core domain. *Mol. Cell Biol.* 19, 3395-3402.

- Semenza, G.L. (2001). HIF-1 and mechanisms of hypoxia sensing. *Curr. Opin. Cell Biol.* *13*, 167-171.
- Serrano, M., Gomez-Lahoz, E., DePinho, R.A., Beach, D., and Bar-Sagi, D. (1995). Inhibition of ras-induced proliferation and cellular transformation by p16INK4. *Science* *267*, 249-252.
- Sharkey, F.E. and Fogh, J. (1984). Considerations in the use of nude mice for cancer research. *Cancer Metastasis Rev.* *3*, 341-360.
- Sherr, C.J. and Roberts, J.M. (1995). Inhibitors of mammalian G1 cyclin-dependent kinases. *Genes Dev.* *9*, 1149-1163.
- Shi, Q. and Xie, K. (2000). Experimental animal models of pancreatic cancer (review). *Int. J. Oncol.* *17*, 217-225.
- Shields, J.M., Pruitt, K., McFall, A., Shaub, A., and Der, C.J. (2000). Understanding Ras: 'it ain't over 'til it's over'. *Trends Cell Biol.* *10*, 147-154.
- Shimosato, Y., Kameya, T., Nagai, K., Hirohashi, S., Koide, T., Hayashi, H., and Nomura, T. (1976). Transplantation of human tumors in nude mice. *J. Natl. Cancer Inst.* *56*, 1251-1260.
- Sipos, B., Moser, S., Kalthoff, H., Torok, V., Lohr, M., and Kloppel, G. (2003). A comprehensive characterization of pancreatic ductal carcinoma cell lines: towards the establishment of an in vitro research platform. *Virchows Arch.* *442*, 444-452.
- Sirivatanauskorn, V., Sirivatanauskorn, Y., and Lemoine, N.R. (1998). Molecular pattern of ductal pancreatic cancer. *Langenbecks Arch. Surg.* *383*, 105-115.
- Smith, M.L. and Fornace, A.J., Jr. (2002). Chemotherapeutic targeting of p53. *Cancer Biol. Ther.* *1*, 56-57.
- Soussi, T. and Beroud, C. (2001). Assessing TP53 status in human tumours to evaluate clinical outcome. *Nat. Rev. Cancer* *1*, 233-240.
- Soussi, T. and Beroud, C. (2003). Significance of TP53 mutations in human cancer: a critical analysis of mutations at CpG dinucleotides. *Hum. Mutat.* *21*, 192-200.
- Soussi, T. and Lozano, G. (2005). p53 mutation heterogeneity in cancer. *Biochem. Biophys. Res. Commun.* *331*, 834-842.
- Spandidos, D.A., Sourvinos, G., Tsatsanis, C., and Zafiropoulos, A. (2002). Normal ras genes: their onco-suppressor and pro-apoptotic functions (review). *Int. J. Oncol.* *21*, 237-241.
- Stanbridge, E.J. and Perkins, F.T. (1976). Tumourigenicity testing in immunosuppressed mice: advantages and disadvantages. *Dev. Biol. Stand.* *37*, 211-217.
- Standop, J., Schneider, M.B., Ulrich, A., and Pour, P.M. (2001). Experimental animal models in pancreatic carcinogenesis: lessons for human pancreatic cancer. *Dig. Dis.* *19*, 24-31.
- Stetler-Stevenson, W.G. (1999). Matrix metalloproteinases in angiogenesis: a moving target for therapeutic intervention. *J. Clin. Invest* *103*, 1237-1241.

- Sullivan,A., Syed,N., Gasco,M., Bergamaschi,D., Trigiante,G., Attard,M., Hiller,L., Farrell,P.J., Smith,P., Lu,X., and Crook,T. (2004). Polymorphism in wild-type p53 modulates response to chemotherapy in vitro and in vivo. *Oncogene* 23, 3328-3337.
- Takimoto,R., Wang,W., Dicker,D.T., Rastinejad,F., Lyssikatos,J., and el Deiry,W.S. (2002). The mutant p53-conformation modifying drug, CP-31398, can induce apoptosis of human cancer cells and can stabilize wild-type p53 protein. *Cancer Biol. Ther.* 1, 47-55.
- Tan,M.H. and Chu,T.M. (1985). Characterization of the tumorigenic and metastatic properties of a human pancreatic tumor cell line (AsPC-1) implanted orthotopically into nude mice. *Tumour. Biol.* 6, 89-98.
- Tang,R.F., Itakura,J., Aikawa,T., Matsuda,K., Fujii,H., Korc,M., and Matsumoto,Y. (2001). Overexpression of lymphangiogenic growth factor VEGF-C in human pancreatic cancer. *Pancreas* 22, 285-292.
- Tao,W. and Levine,A.J. (1999). Nucleocytoplasmic shuttling of oncoprotein Hdm2 is required for Hdm2-mediated degradation of p53. *Proc. Natl. Acad. Sci. U. S. A* 96, 3077-3080.
- Temin,H.M. and Mizutani,S. (1970). RNA-dependent DNA polymerase in virions of Rous sarcoma virus. *Nature* 226, 1211-1213.
- Tilleray,V., Constantinou,C., and Clemens,M.J. (2006). Regulation of protein synthesis by inducible wild-type p53 in human lung carcinoma cells. *FEBS Lett.* 580, 1766-1770.
- Trahey,M. and McCormick,F. (1987). A cytoplasmic protein stimulates normal N-ras p21 GTPase, but does not affect oncogenic mutants. *Science* 238, 542-545.
- Uchima,Y., Sawada,T., Nishihara,T., Maeda,K., Ohira,M., and Hirakawa,K. (2004). Inhibition and mechanism of action of a protease inhibitor in human pancreatic cancer cells. *Pancreas* 29, 123-131.
- van de,W.M., Oving,I., Muncan,V., Pon Fong,M.T., Brantjes,H., van Leenen,D., Holstege,F.C., Brummelkamp,T.R., Agami,R., and Clevers,H. (2003). Specific inhibition of gene expression using a stably integrated, inducible small-interfering-RNA vector. *EMBO Rep.* 4, 609-615.
- van Oijen,M.G. and Slootweg,P.J. (2000). Gain-of-function mutations in the tumor suppressor gene p53. *Clin. Cancer Res.* 6, 2138-2145.
- Von Marschall,Z., Scholz,A., Stacker,S.A., Achen,M.G., Jackson,D.G., Alves,F., Schirner,M., Haberey,M., Thierauch,K.H., Wiedenmann,B., and Rosewicz,S. (2005). Vascular endothelial growth factor-D induces lymphangiogenesis and lymphatic metastasis in models of ductal pancreatic cancer. *Int. J. Oncol.* 27, 669-679.
- Wadler,S., Makower,D., Yu,B., Tan,J.Y., Rozenblit,A., Kaufman,H., Edelman,M., Lane,M.E., and Zwiebel,J. (2002). Clinical applications of p53-directed gene therapy. *Suppl Tumori* 1, S21.
- Wagner,M., Greten,F.R., Weber,C.K., Koschnick,S., Mattfeldt,T., Deppert,W., Kern,H., Adler,G., and Schmid,R.M. (2001). A murine tumor progression model for pancreatic cancer recapitulating the genetic alterations of the human disease. *Genes Dev.* 15, 286-293.

- Wang,W., Rastinejad,F., and el Deiry,W.S. (2003). Restoring p53-dependent tumor suppression. *Cancer Biol. Ther.* 2, S55-S63.
- Wang,W., Wang,C.Y., Dong,J.H., Chen,X., Zhang,M., and Zhao,G. (2005). Identification of effective siRNA against K-ras in human pancreatic cancer cell line MiaPaCa-2 by siRNA expression cassette. *World J. Gastroenterol.* 11, 2026-2031.
- Wang,Y., You,M., and Wang,Y. (2001). Alternative splicing of the K-ras gene in mouse tissues and cell lines. *Exp. Lung Res.* 27, 255-267.
- Watzinger,F., Mayr,B., Haring,E., and Lion,T. (1998). High sequence similarity within ras exons 1 and 2 in different mammalian species and phylogenetic divergence of the ras gene family. *Mamm. Genome* 9, 214-219.
- Weidner,N., Semple,J.P., Welch,W.R., and Folkman,J. (1991). Tumor angiogenesis and metastasis--correlation in invasive breast carcinoma. *N. Engl. J. Med.* 324, 1-8.
- Weisz,B., Giehl,K., Gana-Weisz,M., Egozi,Y., Ben Baruch,G., Marciano,D., Gierschik,P., and Kloog,Y. (1999). A new functional Ras antagonist inhibits human pancreatic tumor growth in nude mice. *Oncogene* 18, 2579-2588.
- Wen,S.F., Mahavni,V., Quijano,E., Shinoda,J., Grace,M., Musco-Hobkinson,M.L., Yang,T.Y., Chen,Y., Runnenbaum,I., Horowitz,J., Maneval,D., Hutchins,B., and Buller,R. (2003). Assessment of p53 gene transfer and biological activities in a clinical study of adenovirus-p53 gene therapy for recurrent ovarian cancer. *Cancer Gene Ther.* 10, 224-238.
- Wu,G.S., Burns,T.F., McDonald,E.R., III, Jiang,W., Meng,R., Krantz,I.D., Kao,G., Gan,D.D., Zhou,J.Y., Muschel,R., Hamilton,S.R., Spinner,N.B., Markowitz,S., Wu,G., and el Deiry,W.S. (1997). KILLER/DR5 is a DNA damage-inducible p53-regulated death receptor gene. *Nat. Genet.* 17, 141-143.
- Xirodimas,D.P., Stephen,C.W., and Lane,D.P. (2001). Cocompartmentalization of p53 and Mdm2 is a major determinant for Mdm2-mediated degradation of p53. *Exp. Cell Res.* 270, 66-77.
- Yokoyama,M., Yamanaka,Y., Friess,H., Buchler,M., and Korc,M. (1994). p53 expression in human pancreatic cancer correlates with enhanced biological aggressiveness. *Anticancer Res.* 14, 2477-2483.
- Yu,J. and Zhang,L. (2005). The transcriptional targets of p53 in apoptosis control. *Biochem. Biophys. Res. Commun.* 331, 851-858.
- Zhang,Y., Fujita,N., and Tsuruo,T. (1999). Caspase-mediated cleavage of p21Waf1/Cip1 converts cancer cells from growth arrest to undergoing apoptosis. *Oncogene* 18, 1131-1138.