

---

**7 LITERATURVERZEICHNIS**

**Acharya MR**, Sparreboom A, Venitz J und Figg WD (2005). Rational development of histone deacetylase inhibitors as anticancer agents: a review. *Mol Pharmacol* 68: 917-932.

**Adams J** (2003). The proteasome: structure, function, and role in the cell. *Cancer Treat Rev* 29(Suppl. 1) : 3-9.

**Adams J und Kauffman M** (2004). Development of the proteasome inhibitor Velcade (Bortezomib). *Cancer Invest* 22: 304-311.

**Aden DP**, Fogel A, Plotkin S, Damjanov I und Knowles BB (1979). Controlled synthesis of HBsAg in a differentiated human liver carcinoma-derived cell line. *Nature* 282: 615-616

**Ahmad T**, Farnie G, Bundred NJ und Anderson NG (2004). The mitogenic action of insulin-like growth factor I in normal human mammary epithelial cells requires the epidermal growth factor receptor tyrosine kinase. *J Biol Chem* 279: 1713-1719.

**Armeanu S**, Pathil A, Venturelli S, Mascagni P, Weiss TS, Göttlicher M, Gregor M, Lauer UM und Bitzer M (2005). Apoptosis on hepatoma cells but not on primary hepatocytes by histone deacetylase inhibitors valproate and ITF2357. *J Hepatol* 42: 210-217.

**Archer SY und Hodin RA** (1999). Histone acetylation and cancer. *Curr Opin Genet Dev* 9 :171-174.

**Arnold C** (2007). Neuroendocrine tumors of the gastrointestinal tract. *Schweiz Rundsch Med Prax* 96: 19-28.

**Ashkenazi A** (2002). Targeting death and decoy receptors of the tumor-necrosis factor superfamily. *Nat Rev Cancer* 2: 420-430

**Banker DE**, Mayer SJ, Li HY, Willman CL, Appelbaum FR und Zager RA (2004). Cholesterol synthesis and import contribute to protective cholesterol increments in acute myeloid leukemia cells. *Blood* 104: 1816-1824.

**Baroni MG**, Cavallo MG, Mark M, Monetini L, Stoehrer B und Pozzilli P (1999). Beta-cell gene expression and functional characterisation of the human insulinoma cell line CM. *J Endocrinol* 161: 59-68.

**Baserga R** (1994). Oncogenes and the strategy of growth factors. *Cell* 79: 927-930.

**Baserga R**, Hongo A, Rubini M, Prisco M und Valentinis B (1997). The IGF-I receptor in cell growth, transformation and apoptosis. *Biochim Biophys Acta* 1332: 105-126

**Baserga R** (2000). The contradictions of the insulin-like growth factor 1 receptor. *Oncogene* 19: 5574-5581.

- Baserga R**, Peruzzi F und Reiss K (2003). The IGF-1 receptor in cancer biology. *Int J Cancer* 107:873-877.
- Baxter RC** (2000). Insulin-like growth factor (IGF)-binding proteins: interactions with IGFs and intrinsic bioactivities. *Am J Physiol Endocrinol Metab* 278: 967-976.
- Beeram M**, Patnaik A und Rowinsky EK (2005). Raf: a strategic target for therapeutic development against cancer. *J Clin Oncol* 23: 6771-6790.
- Bhalla K und List A** (2004). Histone deacetylase inhibitors in myelodysplastic syndrome. *Best Pract Res Clin Haematol* 17: 595-611.
- Bianco R**, Gelardi T, Damiano V, Ciardiello F und Tortora G (2007). Rational bases for the development of EGFR inhibitors for cancer treatment. *Int J Biochem Cell Biol* 39: 1416-1431.
- Boffa LC**, Vidali G, Manns RS und Allfrey VG (1978). Suppression of histone deacetylation in vivo and in vitro by sodium butyrate. *J Biol Chem* 253: 3364-3366.
- Brattain MG**, Fine WD, Khaled FM, Thompson J und Brattain DE (1981). Heterogeneity of malignant cells from a human colonic carcinoma. *Cancer Res.* 41: 1751-1756.
- Burtrum D**, Zhu Z, Lu D, Anderson DM, Prewett M, Pereira DS, Bassi R, Abdullah R, Hooper AT, Koo H, Jimenez X, Johnson D, Apblett R, Kussie P, Bohlen P, Witte L, Hicklin DJ und Ludwig DL (2003). A fully human monoclonal antibody to the insulin-like growth factor I receptor blocks ligand-dependent signaling and inhibits human tumor growth in vivo. *Cancer Res* 63: 8912-8921.
- Butler LM**, Zhou X, Xu WS, Scher HI, Rifkind RA, Marks PA und Richon VM (2002). The histone deacetylase inhibitor SAHA arrests cancer cell growth, up-regulated thioredoxin-binding protein-2, and down-regulate thioredoxin. *Proc Natl Acad Sci U S A* 99: 11700-11705.
- Campos L**, Rouault JP, Sabido O, Oriol P, Roubi N, Vasselon C, Archimbaud E, Magaud JP und Guyotat D (1993). High expression of bcl-2 protein in acute myeloid leucemia cells is associated with poor response to chemotherapy. *Blood* 81: 3091-3096.
- Chakravarti A**, Loeffler JS und Dyson NJ (2002). Insulin-like growth factor receptor I mediates resistance to anti-epidermal growth factor receptor therapy in primary human glioblastoma cells through continued activation of phosphoinositide 3-kinase signaling. *Cancer Res* 62:200-207
- Chan-Hui PY und Weaver R** (1998). Human mitogen-activated protein kinase kinase mediates the stress-induced activation of mitogen-activated protein kinase cascades. *Biochem J* 336: 599-609.
- Chen JS und Faller DV** (2005). Histone deacetylase inhibition-mediated post-translational elevation of p27KIP1 protein levels is required for G1 arrest in fibroblasts. *J Cell Physiol* 202: 87-99.

**Cheng M**, Sexl V, Sherr CJ und Roussel MF (1998). Assembly of cyclin D-dependent kinase and titration of p27Kip1 regulated by mitogenactivated protein kinase kinase (MEK1). *Proc Natl Acad Sci USA* 95: 1091-1096.

**Coustan-Smith E**, Kitanaka A, Pui CH, McNinch L, Evans WE, Raimondi SC, Behm FG, Arico M und Campana D (1996). Clinical relevance of BCL-2 overexpression in childhood acute lymphoblastic leukemia. *Blood* 87: 1140-1146.

**Cory S und Adams JM** (2002). The Bcl2 family: regulators of the cellular life-or-death switch. *Nat Rev Cancer* 2: 647-656.

**Cross TG**, Scheel-Toellner D, Henriquez NV, Deacon E, Salmon M und Lord JM (2000). Serine/threonine protein kinases and apoptosis. *Exp Cell Res* 256: 34-41.

**Della Ragione F**, Criniti V, Della Pietra V, Borriello A, Oliva A, Indaco S, Yamamoto T und Zappia V (2001). Genes modulated by histone acetylation as new effectors of butyrate activity. *FEBS Lett* 499: 199-204

**Denlinger CE**, Keller MD, Mayo MW, Broad RM und Jones DR (2004). Combined histone deacetylation and proteasome inhibition enhances apoptosis in non-small cell lung cancer. *J Thorac Cardiovas Surg* 127: 1078-1086.

**Dai Y**, Rahmani M, Dent P und Grant S (2005). Blockade of histone deacetylase inhibitor-induced RelA/p65 acetylation and NF- $\kappa$ B activation potentiates apoptosis in leukemia cells through a process mediated by oxidative damage, XIAP downregulation and c-Jun N-terminal kinase 1 activation. *Mol Cell Biol* 25: 5429-5444.

**Detjen K**, Murphy D, Welzel M, Farwig K, Wiedenmann B und Rosewicz S (2003). Downregulation of p21(waf/cip-1) mediates apoptosis of human hepatocellular carcinoma cells in response to interferon-gamma. *Exp Cell Research* 282: 78-89.

**Duan H**, Heckman CA und Boxer LM (2005). Histone deacetylase inhibitors down-regulate bcl-2 expression and induce apoptosis in t(14;18) lymphomas. *Mol Cell Biol* 5: 1608-1619.

**Duvic M**, Talpur R, Ni X, Zhang C, Hazaraki P, Kelly C, Chiao JH, Reilly JF, Ricker JL, Richon VM und Frankel SR (2007). Phase 2 trial of oral vorinostat (suberoylanilide hydroxamic acid, SAHA) for refractory cutaneous T-cell lymphoma (CTCL). *Blood* 109: 31-39.

**Erhardt P**, Schremser EJ und Cooper GM (1999). B-Raf inhibits programmed cell death downstream of cytochrome c release from mitochondria by activating the MEK/Erk pathway. *Mol Cell Biol* 19: 5308-5315.

**El-Beltagi HM**, Martens AC, Lelieveld P, Haroun EA und Hagenbeek A (1993). Acetyldinaline: a new oral cytostatic drug with impressive differential activity against leukemic cells and normal stem cells--preclinical studies in a relevant rat model for human acute myelocytic leukemia. *Cancer Res* 53: 3008-3014.

**El Serag HB**, Mason AC und Key C (2001). Trends in survival of patients with hepatocellular carcinoma between 1977 and 1996 in the United States. *Hepatology* 33:62-65

**Eickhoff B**, Ruller S, Laue T, Kohler G, Stahl C, Schlaak M und van der Bosch J (2000). Trichostatin A modulates expression of p21waf1/cip1, Bcl-xL, ID1, ID2, ID3, CRAB2, GATA-2, hsp86 and TFIID/TAFII31 mRNA in human lung adenocarcinoma cells. *Biol Chem* 381: 107–112.

**Eriksson B und Öberg K** (1999). Summing up 15 years of somatostatin analog therapy in neuroendocrine tumors: Future outlook. *Ann Oncol* 10 (Suppl. 2): 31-38

**Esteller M und Herman JG** (2002). Cancer as an epigenetic disease: DNA methylation and chromatin alterations in human tumors. *J Pathol* 196: 1-7.

**Evers BM**, Ishizuka J, Townsend CM Jr. und Thompson JC (1994). The human carcinoid cell line, BON. A model system for the study of carcinoid tumors. *Ann N Y Acad Sci* 15: 393-406.

**Faiss S**, Scherübl H, Riecken EO und Wiedenmann B (1996). Drug therapy in metastatic neuroendocrine tumors of the gastroenteropancreatic system. *Recent Results Cancer Res* 142:193-207.

**Ferlay J**, Bray F, Pisani P und Parkin DM (2004). GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide. *IARC CancerBase No.5, Version 2.0 Lyon, France: IARC Press 2004.*

**Finnin MS**, Donigian JR, Cohen A, Richon VM, Rifkind RA, Marks PA Breslow R und Pavlittich NP (1999). Structures of histone deacetylase homologue bound to the TSA and SAHA inhibitors. *Nature* 401: 188-193.

**Fogh J** (1975). Human tumor cells in vitro. *Plenum Press, New York* 115-159.

**Fottner Ch**, Hoeflich A, Wolf E und Weber MM (2004). Role of insulin-like growth factor system in adrenocortical growth control and carcinogenesis. *Horm Metab Res* 36: 397-405.

**Forero L**, Patnaik A, Hammond A, Tolcher G, Schwartz G und Hidalgo M (2002). Phase I, pharmacokinetic (PK) and biologic study of OSI-774, a selective epidermal growth factor receptor (EGFR) tyrosine kinase (TK) inhibitor in combination with paclitaxel and carboplatin. *Proc Am Soc Clin Oncol* 21.

**Forouzesh B**, Hidalgo M, Takimoto C, DeBono J S, Forero L und Beeram (2002). Phase I, pharmacokinetic (PK), and biological studies of the epidermal growth factor-tyrosine kinase (EGFR-TK) inhibitor OSI-774 in combination with docetaxel. *Proc Am Soc Clin Oncol* 21.

**Fournel M**, Trachy-Bourget MC, Yan PT, Kalita A, Bonfils C, Beaulieu C, Frechette S, Leit S, Abou-Khalil E, Woo SH, Delorme D, MacLeod AR, Besterman JM und Li Z (2002). Sulfonamide anilides, a novel class of histone deacetylase inhibitors, are antiproliferative against human tumors. *Cancer Res* 62: 4325-4330.

**Fribley A**, Qinghua Z und Wang CY (2004). Proteasome inhibitor PS-341 induces apoptosis through induction of endoplasmic reticulum stress-reactive oxygen species in head and neck squamous cell carcinoma cells. *Mol Cell Biol* 24: 9695-9704.

**Fuino L**, Bali P, Wittmann S, Donapaty S, Guo F, Yamaguchi H, Wang HG, Atadja P und Bhalla K (2003). Histone deacetylase inhibitor LAQ824 down-regulates Her-2 and sensitizes human breast cancer cells to trastuzumab, taxotere, gemcitabine, and epothilone B. *Mol Cancer Ther* 2: 971-984.

**Garber K** (2005). IGF-1: Old growth factor shines as new drug target. *J Natl Cancer Inst* 97: 790-793

**Garcia-Echeverria**, Pearson MA, Marti A, Meyer T, Mestan J, Zimmermann J, Gao J, Brueggen, Capraro HG, Cozens R, Evans DB, Fabbro D, Furet P, Porta DG, Liebetanz J, Martiny-Baron G, Ruetz S und Hofmann F (2004). In vivo antitumor activity of NVP-AEW541-A novel, potent, and selective inhibitor of the IGF-IR kinase. *Cancer Cell* 5: 231-239.

**Glassmeier G**, Herzig KH, Höpfner M, Lemmer K, Jansen A, Scherübl H (1998). Expression of functional GABAA receptors in cholecystokininsecreting gut neuroendocrine murine STC-1 cells. *J Physiol* 510: 805-881.

**Gillies RJ**, Didier N und Denton M (1986). Determination of cell number in monolayer cultures. *Anal Biochem* 159: 109-113.

**Gilmore AP**, Valentijn AJ, Wang P, Ranger AM, Bundred N, O'Hare MJ, Wakeling A, Korsmeyer SJ und Streuli CH (2002). Activation of BAD by therapeutic inhibition of epidermal growth factor receptor and transactivation by insulin-like growth factor receptor. *J Biol Chem* 277: 27643-27650.

**Gogvadze V**, Robertson JD, Zhivotovsky B und Orrenius S (2001). Cytochrome c release occurs via Ca<sup>2+</sup>-dependent and Ca<sup>2+</sup>-independent mechanisms that are regulated by Bax. *J Biol Chem* 276: 19066-19071

**Gojo I**, Jiemjit A, Trepel JB, Sparreboom A, Figg WD, Rollins S, Tidwell ML, Greer J, Chung EJ, Lee MJ, Gore SD, Sausville EA, Zwiebel J und Karp JE (2007). Phase 1 and pharmacologic study of MS-275, a histone deacetylase inhibitor, in adults with refractory and relapsed acute leukemias. *Blood* 109: 2781-2790.

**Goldstein JC**, Waterhouse NJ, Juin P, Evan GI und Green DR (2000). The coordinate release of cytochrome c during apoptosis is rapid, complete and kinetically invariant. *Nat Cell Biol* 2: 156-162.

**Gores GJ** (2003). Cholangiocarcinoma: current concepts and insights. *Hepatology* 37:961-969

**Gotlieb WH**, Bruchim I, Gu J, Shi Y, Camirand A, Blouin MJ, Zhao Y und Pollak MN (2006). Insulin-like growth factor receptor I targeting in epithelial ovarian cancer. *Gynecol Oncol* 100: 389-396.

**Grignani F**, Matteis S, Nervi C, Tomassoni L, Gelmetti V, Cioce M, Fanelli M, Ruthardt M, Ferrara FF, Zamir I, Seiser C, Grignani F, Lazar MA, Minucci S und Pelicci PG (1998). Fusion protein of retinoic acid receptor-alpha recruits histone deacetylases in promyelocytic leukaemia. *Nature* 391: 815-818.

**Grimberg A und Cohen P** (2000). Role of insulin-like growth factors and their binding proteins in growth control and carcinogenesis. *J Cell Physiol* 183: 1-9.

**Grimberg A** (2003). Mechanisms by which IGF-1 may promote cancer. *Cancer Biol Ther* 2: 630-635.

**Guo F**, Sigua C, Tao J, Bali P, George P, Li Y, Wittmann S, Moscinski L, Atadja P und Bhalla K (2004). Cotreatment with histone deacetylase inhibitor LAQ824 enhances Apo-2L/tumor necrosis factor-related apoptosis inducing ligand-induced death inducing signaling complex activity and apoptosis of human acute leukemia cells. *Cancer Res* 64: 2580-2589.

**Hahn WC und Weinberg RA** (2002). Rules for making human tumor cells. *N Engl J Med* 347: 1593-1603.

**Harari PM** (2004). Epidermal growth factor receptor inhibition strategies in oncology. *Endocr Relat Cancer* 11: 689-708.

**He LZ**, Guidez F, Tribioli C, Peruzzi D, Ruthardt M, Zelent A und Pandolfi PP (1998). Distinct interactions of PML-RARalpha and PLZF-RARalpha with corepressors determine differential responses to RA in APL. *Nat Genet* 18: 126-135

**Henderson C**, Mizzau M, Paroni G, Maestro R, Schneider C und Brancolini C (2003). Role of caspases, Bid, and p53 in the apoptotic response triggered by histone deacetylase inhibitors trichostatin-A (TSA) and suberoylanilide hydroxamic acid (SAHA) *J Biol Chem* 278: 12579-12589.

**Herold C**, Ganslmayer M, Ocker M, Hermann M, Geerts A, Hahn EG und Schuppan D (2002). The histone-deacetylase inhibitor trichostatin A blocks proliferation and triggers apoptotic programs in hepatoma cells. *J Hepatol* 36: 233-240.

**Hess-Stumpp H**, Bracker TU, Henderson D und Politz O (2007). MS-275, a potent orally available inhibitor of histone deacetylases – The development of an anticancer agent. *Int J Biochem Cell Biol* 39: 1388-1405.

**Hofmann F und Garcia-Echeverria C** (2005). Blocking the insulin-like growth factor-I receptor as a strategy for targeting cancer. *Drug Discov Today* 10: 1041-1047.

**Höpfner M**, Sutter AP, Beck NI, Barthel B, Maaser K, Jockers-Scherübl MC, Zeitz M und Scherübl H (2002). Meta-iodobenzylguanidine induces growth inhibition and apoptosis of neuroendocrine gastrointestinal tumor cells. *Int J Cancer* 101: 210-216.

**Höpfner M**, Sutter AP, Huether A, Schuppan D, Zeitz M und Scherübl H (2004). Targeting the epidermal growth factor receptor by gefitinib for treatment of hepatocellular carcinoma. *J Hepatol* 41: 1008-1016.

- Höpfner M**, Sutter AP, Huether A, Baradari V und Scherübl H (2006). Tyrosine kinase of insulin-like growth factor receptor as target for novel treatment and prevention strategies of colorectal cancer. *World J Gastroenterol* 12: 5635-5643.
- Huether A**, Höpfner M, Sutter AP, Schuppan D und Scherübl H. (2005). Erlotinib induces cell cycle arrest and apoptosis in hepatocellular cancer cells and enhances chemosensitivity towards cytostatics. *J Hepatol* 43: 661-669.
- Huether A**, Höpfner M, Sutter AP, Baradari V, Schuppan D und Scherübl H (2006). Signaling pathways involved in the inhibition of epidermal growth factor receptor by erlotinib in hepatocellular cancer. *World J Gastroenterol* 12: 5160-5167.
- Huether A**, Höpfner M, Baradari V, Schuppan D und Scherübl H (2007). Sorafenib alone or as combination therapy for growth control of cholangiocarcinoma. *Biochem Pharmacol*; 73: 1308-1317.
- Hui AM**, Makuuchi M und Li X (1998). Cell cycle regulators and human hepatocarcinogenesis. *Hepatogastroenterology* 45: 1635-1642.
- Insinga A**, Minucci S und Pelicci PG (2005). Mechanisms of selective anticancer action of histone deacetylase inhibitors. *Cell Cycle* 4:741-743.
- Igney FH und Krammer PH** (2002). Death and anti-death: tumor resistance to apoptosis. *Nat Rev Cancer* 2: 277-288
- Jacobson S und Pillus L** (1999). Modifying chromatin and concepts of cancer. *Curr Opin Genet Dev* 9: 175-184.
- Jakobisiak M und Golab J** (2003). Potential antitumor effects of statins. *Int J Oncol* 23: 1055-1069.
- Jenuwein T und Allis CD** (2001). Translating the histone code. *Science* 293:1074-1080
- Jiang Y**, Rom WN, Yie TA, Chi CX und Tchou-Wong KM (1999). Induction of tumor suppression and glandular differentiation of A549 lung carcinoma cells by dominant-negative IGF-I receptor. *Oncogene* 18: 6071-6077.
- Johnson GL und Lapadat R** (2002). Mitogen-activated protein kinase pathways mediated by ERK, JNK, and p38 protein kinases. *Science* 298: 1911-1912.
- Johnstone RW und Licht JD** (2003). Histone deacetylase inhibitors in cancer therapy: is transcription the primary target? *Cancer Cell* 4: 13-18.
- Jones HE**, Goddard L, Gee J, Hiscox S, Rubini M, Barrow D, Knowlden JM, Williams S, Wakeling AE und Nicholson RI (2004). Insulin-like growth factor-I-receptor signalling and acquired resistance to gefitinib (ZD1839; Iressa) in human breast and prostate cancer cells. *Endocr Relat Cancer* 11: 793-814.
- Jung JW**, Cho SD, Ahn NS, Yang SR, Park JS, Jo EH, Hwang JW, Jung JY, Kim SH, Kang KS und Lee YS (2005). Ras/MAP Kinase pathways are involved in Ras specific apoptosis induced by sodium butyrate. *Cancer Lett* 225: 199-206.

**Keller JW**, Franklin JL, Graves-Deal R, Friedmann DB, Whitwell CW und Coffey RJ (2007). Oncogenic KRAS provides a uniquely powerful and variable oncogenic contribution among RAS family members in the colonic epithelium. *J Cell Physiol* 210: 740-749.

**Katso R**, Okkenhaug K, Ahmadi K, White S, Timms J und Waterfield MD (2001). Cellular function of phosphoinositide 3-kinases: implications for development, homeostasis, and cancer. *Annu Rev Cell Dev Biol* 17: 615-675.

**Kellerer M**, Lammers R und Haring HU (1999). Insulin signal transduction: possible mechanism for insulin resistance. *Exp Clin Endocrinol Diabetes* 107: 97-106

**Kelly WK**, Richon VM, O'Connor O, Curley T, Mac-Gregor-Curtelli B, Tong W, Klang M, Schwartz L, Richardson S, Rosa E, Drobnyak M, Cordon-Cordo C, Chiao JH, Rifkind R, Marks PA und Scher H (2003). Phase I clinical trial of histone deacetylase inhibitor: suberoylanilide hydroxamic acid administered intravenously. *Clin Cancer Res* 9: 3578-3588.

**Kelly WK**, O'Connor OA, Krug LM, Chiao JH, Heaney M, Curley T, MacGregore-Cortelli B, Tong W, Secrist JP, Schwartz L, Richardson S, Chu E, Olgac S, Marks PA, Scher H und Richon VM (2005). Phase I study of an oral histone deacetylase inhibitor, suberoylanilide hydroxamic acid, in patients with advanced cancer. *J Clin Oncol* 23: 3923-3931.

**Kerr JF**, Wyllie AH und Currie AR (1972). Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics. *Br J Cancer* 26: 239-257

**Khan SA**, Taylor-Robinson SD, Toledano MB, Beck A, Elliott P und Thomas HC (2002). Changing international trends in mortality rates for liver, biliary and pancreatic tumours. *J Hepatol* 37: 806-813.

**Khan SA**, Thomas HC, Davidson BR und Taylor-Robinson SD (2005). Cholangiocarcinoma. *Lancet* 366: 1303-1314.

**Khandwala HM**, McCutcheon IE, Flyvbjerg A und Friend KE (2000). The effects of insulin-like growth factors on tumorigenesis and neoplastic growth. *Endocrine Reviews* 21: 215-244.

**Kim MS**, Kwon HJ, Lee YM, Baek JH, Jang JE, Lee SW, Moon EJ, Kim HS, Lee SK, Chung HY, Kim CW und Kim KW (2001). Histone deacetylases induce angiogenesis by negative regulation of tumor suppressor genes. *Nat Med* 7: 437-443.

**Kim HS**, Lee JW, Soung YH, Park WS, Kim SY, Lee JH, Park JY, Cho YG, Kim CJ, Jeong SW, Nam SW, Kim SH, Lee JY, Yoo NJ und Lee SH (2003a). Inactivating mutations of caspase-8 gene in colorectal carcinomas. *Gastroenterology* 125: 708-715.

**Kim MS**, Blake M, Baek JH, Kohlhagen G, Pommier Y und Carrier F (2003b). Inhibition of histone deacetylase increases cytotoxicity to anticancer drugs targeting DNA. *Cancer Res* 63: 7921-7300.



**Klausner RD** (2002). The fabric of cancer cell biology – Weaving together the strands. *Cancer Cell* 1: 3-10.

**Kobayashi S**, Nantz R, Kitamura T, Higashikubo R und Horikoshi N (2005). Combined inhibition of extracellular signal-regulated kinases and HSP90 sensitizes human colon carcinoma cells to ionizing radiation. *Oncogene* 23: 3011-3019.

**Kortenhorst MS**, Carducci MA und Shabbeer S (2006). Acetylation and histone deacetylase inhibitors in cancer. *Cell Oncol* 28: 191-222.

**Kountouras J**, Zavos C und Chatzopoulos D (2005). Apoptotic and anti-angiogenic strategies in liver and gastrointestinal malignancies. *J Surg Oncol* 90: 249-259.

**Kouzandes T** (1999). Histone acetylases and deacetylases in cell proliferation. *Curr Opin Genet Dev* 9: 40-48.

**Krämer OH**, Göttlicher M und Heinzel T (2001). Histone deacetylase as a therapeutic target. *Trends Endocrinol Metab* 12: 294-300.

**Kroemer G** (1997). The proto-oncogene Bcl-2 and its role in regulating apoptosis. *Nat Med* 3: 614-620.

**Kubicka S** (2004). Cholangiozelluläres Karzinom und Gallenblasenkarzinom. Cholangiocellular and gallbladder carcinoma. *Z Gastroenterol* 42: 397-340.

**Kullmann F** (2001). Kolorektales Karzinom: Ein vermeidbarer und therapierbarer Krebs. *W. Zuckschwerdt Verlag München* 1-5.

**Kurz EU**, Wilson SE, Leader KB, Sampey BP, Allan WP, Yalowich JC und Kroll DJ (2001). The histone deacetylase inhibitor sodium butyrate induces DNA topoisomerase II $\alpha$  expression and confers hypersensitivity to etoposide in human leukemic cell lines. *Mol Cancer Ther* 1: 121-131.

**Lallemand F**, Courilleau D, Buquet-Fagot C, Atfi A, Montagne MN und Mester J (1999). Sodium butyrate induces G<sub>2</sub> arrest in the human breast cancer cells MDA-MB-231 and renders them competent for DNA rereplication. *Exp Cell Res* 247 432-440.

**Lavoie JN**, L'Allemain G, Brunet A, Muller R und Pouyssegur J (1996). Cyclin D1 expression is regulated positively by the P42/P44MAPK and negatively by the p38/HOGMAPK pathway. *J Biol Chem* 271:20608-20616.

**LeRoith D**, Baserga R, Helman L und Roberts CT (1999). Insulin-like growth factors and cancer. *Ann Intern Med* 122: 54-59.

**LeRoith D und Roberts CT** (2003). The insulin-like growth factor system and cancer. *Cancer Lett* 195:127-137

**Ligensa T** (2002). Identifizierung und Charakterisierung von neuen zytoplasmatischen Interaktionspartnern des IGF-1 Rezeptors. Dissertation aus dem Fachbereich Humanmedizin der Philipps-Universität Marburg.

**Lin RJ**, Nagy L, Inoue S, Shao W, Miller WH Jr. und Evans RM (1998). Role of the histone deacetylase complex in acute promyelocytic leukaemia. *Nature* 391: 811-814.

**Lin HY**, Chen CS, Lin SP, Weng JR und Chen CS (2006). Targeting histone deacetylase in cancer therapy. *Med Res Rev* 26: 397-413.

**Ling YH**, Liebes L, Jiang JD, Holland JF, Elliott PJ, Adams J, Muggia FM und Perez-Soler R (2003). Mechanisms of proteasome inhibitor PS-341-induced G2-M-phase arrest and apoptosis in human non-small cell lung cancer cell lines. *Clin Cancer Res* 9:1145-1154.

**Louis M**, Rosato RR, Brault L, Osbild S, Battaglia E, Yang XH, Grant S und Bagrel D (2004). The histone deacetylase inhibitor sodium butyrate induces breast cancer cell apoptosis through diverse cytotoxic actions including glutathione depletion and oxidative stress. *Int J Oncol* 25: 1701-1711.

**Lowe SW und Lin AW** (2000). Apoptosis in cancer. *Carcinogenesis* 21: 485-495.

**Lu ZL**, Luo DZ und Wen JM (2005). Expression and significance of tumor-related genes in HCC. *World J Gastroenterol* 11: 3850-3854.

**Maaser K**, Höpfner M, Kap H, Sutter AP, Barthel B, von Lampe B, Zeitz M und Scherübl H (2002). Extracellular nucleotides inhibit growth of human esophageal cancer cells via P2Y(2)-receptors. *Br J Cancer* 86: 636-644.

**Maeda T**, Towatari M, Kosugi H und Saito H (2000). Upregulation of costimulatory/adhesion molecules by histone deacetylase inhibitors in acute myeloid leukemia cells. *Blood* 96: 3847-3856.

**Maggio SC**, Rosato RR, Kramer LB, Dai Y, Rahmani M, Paik DS, Czarnik AC, Payne SG, Spiegel S und Grant S (2004). The histone deacetylase inhibitor MS-275 interacts synergistically with fludarabine to induce apoptosis in human leukemia cells. *Cancer Res* 64: 2590-2600.

**Magner WJ**, Kazim AL, Stewart C, Romano MA, Catalano G, Grande C, Kaiser N, Santaniello F und Tomasi TB (2000). Activation of MHC class I, II and CD40 gene expression by histone deacetylase inhibitors. *J Immunol* 165: 7017-7024.

**Marks PA**, Richon VM und Rifkind RA (2000). Histone deacetylase inhibitors: inducers of differentiation or apoptosis of transformed cells. *JNCI Cancer Spectrum* 92: 1210-1216.

**Marks PA**, Richon VM, Breslow R und Rifkind RA (2001a). Histone deacetylase inhibitors as new cancer drugs. *Curr Opin Oncol* 13: 477-483.

**Marks P**, Rifkind RA, Richon VM, Breslow R, Miller T und Kelly WK (2001b). Histone deacetylases and cancer: causes and therapies. *Nat Rev Cancer* 1: 194-202

**Marks PA**, Miller T und Richon VM (2003). Histone deacetylases. *Curr Opin Pharmacol* 3: 344-351.

**Marks PA**, Richon VM, Miller T, Kelly WK (2004). Histone deacetylase inhibitors. *Adv Cancer Res* 91:137-168.

**Mathur A**, Hong Y, Kemp BK, Barrientos AA und Erusalimsky JD (2000). Evaluation of fluorescent dyes for the detection of mitochondrial membrane potential changes in cultured cardiomyocytes. *Cardiovasc Res* 46: 126-138.

**McMillan L**, Butcher SK, Pongracz J und Lord JM (2003). Opposing effects of butyrate and bile acids on apoptosis of human colon adenoma cells: Differential activation of PKC and MAP kinases. *Br J Cancer* 88: 748-753.

**Miller TA**, Witter DJ, Belvedere S (2003). Histone deacetylase inhibitors. *J Med Chem* 46: 5097-5116.

**Minucci S und Pelicci PG** (2006). Histone deacetylase inhibitors and the promise of epigenetic (and more) treatments for cancer. *Nat Rev Cancer* 6: 38-51.

**Mitsiades N**, Mitsiades CS, Poulaki V, Chauhan D, Fanourakis G, Gu X, Bailey C, Joseph M, Libermann TA, Treon SP, Munshi NC, Richardson PG, Hideshima T und Anderson KC (2002). Biologic sequelae of nuclear factor-kappaB blockade in multiple myeloma: therapeutic applications. *Blood* 99: 4079-4086.

**Mitsiades CS**, Mitsiades NS, McMullan CJ, Poulaki V, Shringarpure R, Akiyama M, Hideshima T, Chauhan D, Joseph M, Libermann TA, Garcia-Echeverria C, Pearson MA, Hofmann F, Anderson KC und Kung AL (2004, a). Inhibition of the insulin-like growth factor receptor-1 tyrosine kinase activity as a therapeutic strategy for multiple myeloma, other hematologic malignancies, and solid tumors. *Cancer Cell* 5: 221-230.

**Mitsiades CS**, Mitsiades NS, Mc Mullan CJ, Poulaki V, Shringarpure R, Hideshima T, Akiyama M, Chauhan D, Munshi N, Gu X, Bailey C, Joseph M, Libermann TA, Richon VM, Marks PA und Anderson KC (2004, b). Transcriptional signature of histone deacetylase inhibition in multiple myeloma: biological and clinical implications. *Proc Natl Acad Sci USA* 101: 540-545.

**Mitsui H**, Takuwa N, Maruyama T, Maekawa H, Hirayama M, Sawatari T, Hashimoto N, Takuwa Y, Kimura S (2001). The MEK-1-ERK map kinase pathway and the PI 3-kinase-Akt pathway independently mediate anti-apoptotic signals in HepG2 liver cancer cells. *Int J Cancer* 92: 55-62.

**Mohan S und Baylink DJ** (2002). IGF-binding proteins are multifunctional and act via IGF-dependent and -independent mechanisms. *J Endocrinol* 175: 19-31.

**Morgan DO** (1995). Principles of CDK regulation. *Nature* 374: 131-134.

**Morgillo F**, Kim WY, Kim, ES, Ciardiello F, Hong WK und Lee HY (2007). Implication of the insulin-like growth factor-IR pathway in the resistance of non-small cell lung cancer cells to treatment of gefitinib. *Clin Cancer Res* 13: 2795-2803.

**Mori Y**, Selaru FM, Sato F, Yin J, Simms LA, Xu Y, Oлару A, Deacu E, Wang S, Taylor JM, Young J, Leggett B, Jass JR, Abraham JM, Shibata D und Meltzer SJ (2003). The impact of microsatellite instability on the molecular phenotype of colorectal tumors. *Cancer Res* 63: 4577-4582.

**Nakabayashi H**, Taketa K, Miyano K, Yamane T und Sato J (1982). Growth of human hepatoma cells lines with differentiated functions in chemically defined medium. *Cancer Res* 42: 3858-3863.

**Natoni F**, Diolordi L, Santoni C und Gilardini Montani MS (2005). Sodium butyrate sensitises human pancreatic cancer cells to both the intrinsic and the extrinsic apoptotic pathways. *Biochim Biophys Acta* 1745: 318-329.

**Neuenschwander S**, Roberts CT Jr. und LeRoith D (1995). Growth inhibition of MCF-7 breast cancer cells by stable expression of an insulin-like growth factor I receptor antisense ribonucleic acid. *Endocrinology* 136: 4298-4303.

**Newmark HL**, Lupton JR und Young CW (1994). Butyrate as a differentiating agent: pharmacokinetics, analogues and current status. *Cancer Lett* 78: 1-5.

**Nicholson RI**, Gee JM, Harper ME (2001). EGFR and cancer prognosis. *Eur J Cancer* 37(Suppl. 4): 9-15.

**Noh EJ und Lee JS** (2003). Functional interplay between modulation of histone deacetylase activity and its regulatory role in G<sub>2</sub>-M transition. *Biochem Biophys Res Commun* 310: 267-273

**Öberg K** (1994). Expression of growth factors and their receptors in neuroendocrine gut and pancreatic tumors, and prognostic factors for survival. *Ann N Y Acad Sci* 733:46-55.

**Öberg K** (1996). Neuroendocrine gastrointestinal tumours. *Ann Oncol* 7: 453-463

**Öberg K** (2001). Chemotherapy and biotherapy in the treatment of neuroendocrine tumours. *Ann Oncol* 12 (Suppl. 2):111-114.

**O'Connell JB**, Maggard MA und Ko CY (2004). Colon cancer survival rates with the new American Joint Committee on Cancer sixth edition staging. *J Natl Cancer Inst* 96:1420-1425.

**Ouban A**, Muraca P, Yeatman T, Coppola D (2003). Expression and distribution of insulin-like growth factor-1 receptor in human carcinomas. *Hum Pathol* 34: 803-808.

**Paragh G**, Kertai P, Kovacs P, Paragh Jr G, Fulop P und Foris G (2003). HMG CoA reductase inhibitor fluvastatin arrests the development of implanted hepatocarcinoma in rats. *Anticancer Res* 23: 3949-3954.

**Parizzas M**, Gazit A, Levitzki A, Wertheimer E und LeRoith D (1997). Specific inhibition of insulin-like growth factor-1 and insulin receptor tyrosine kinase activity and biological function by tyrphostins. *Endocrinology* 138: 1427-1433.

**Parkin DM** (2001). Global cancer statistics in the year 2000. *Lancet Oncol* 2:533-543.

- Patel T** (2006). Cholangiocarcinoma. *Nat Clin Pract Gastroenterol Hepatol* 3: 33-42.
- Peart MJ**, Tainton KM, Ruefli AA, Dear AE, Sedelies KA, O'Reilly LA, Waterhouse NJ, Trapani JA und Johnstone RW (2003). Novel mechanisms of apoptosis induced by histone deacetylase inhibitors. *Cancer Res* 63: 4460-4471.
- Pei XY**, Dai Y und Grant S (2004). Synergistic induction of oxidative injury and apoptosis in human multiple myeloma cells by the proteasome inhibitor bortezomib and histone deacetylase inhibitors. *Clin Cancer Res* 10: 3839-3852.
- Pietrzkowski Z**, Mulholland G, Gomella L, Jameson BA, Wernicke D und Baserga R (1993). Inhibition of growth of prostatic cancer cell lines by peptide analogues of insulin-like growth factor 1. *Cancer Res* 53: 1102-1106.
- Pollak MN**, Schernhammer ES und Hankinson SE (2004). Insulin-like growth factors and neoplasia. *Nat Rev Cancer* 4: 505- 518
- Ponder BA** (2001). Cancer genetics. *Nature* 411: 336-341.
- Porter AG** (1999). Protein translocation in apoptosis. *Trends Cell Biol* 9: 394-401
- Prager D**, Li HL, Asa S und Melmed S (1994). Dominant negative inhibition of tumorigenesis in vivo by human insulin-like growth factor I receptor mutant. *Proc Natl Acad Sci* 91: 2181-2185.
- Pratesi G**, Perego P und Zunino F (2001). Role of Bcl-2 and its post-transcriptional modification in response to antitumor therapy. *Biochem Pharmacol* 61: 381-386.
- Prokop A**, Wieder T, Sturm I, Essmann F, Seeger K, Wuchter C, Ludwig WD, Henze G, Dorken B und Daniel PT (2000). Relapse in childhood acute lymphoblastic leukemia is associated with a decrease of the Bax/Bcl-2 ratio and loss of spontaneous caspase-3 processing in vivo. *Leukemia* 14: 1606-1613.
- Rampino N**, Yamamoto H, Ionov Y, Li Y, Sawai H, Reed JC und Perucho M (1997). Somatic frameshift mutations in the BAX gene in colon cancers of the microsatellite mutator phenotype. *Science* 275: 967-969.
- Rasheed WK**, Johnstone RW und Prince HM (2007). Histone deacetylase inhibitors in cancer therapy. *Expert Opin Investig Drugs* 16:659-678.
- Ratain MJ**, George CM, Janisch L, Kindler HL, Ryan C, Wood DL, Nadler PI und Vokes EE (2002). Phase I trial of erlotinib (OSI-774) in combination with gemcitabine (G) and cisplatin (P) in patients with advanced solid tumors. *Proc Am Soc Clin Oncol* 21.
- Resnicoff M**, Burgaud JL, Rotman HL, Abraham D und Baserga R (1995). Correlation between apoptosis, tumorigenesis, and levels of insulin-like growth factor I receptors. *Cancer Res* 55: 3739-3741.
- Richon VM**, Emiliani S, Verdin E, Webb Y, Breslow R, Rifkind RA und Marks PA (1998). A class of hybrid polar inducers of transformed cell differentiation inhibits histone deacetylases. *Proc Natl Acad Sci USA* 95: 3003-3007.

**Richon VM**, Sandhoff TW, Rifkind RA und Marks PA (2000). Histone deacetylase inhibitor selectively induces p21WAF1 expression and gene-associated histone acetylation. *Proc Natl Acad Sci USA* 97:10014-10019.

**Roccaro AM**, Hideshima T, Richardson PG, Russo D, Ribatti D, Vacca A, Dammacco F und Anderson KC (2006). Bortezomib as an antitumor agent. *Curr Pharm Biotech* 7:441-448.

**Roh MS**, Kim CW, Park BS, Kim GC, Jeong JH, Kwon HC, Suh DJ, Cho KH, Yee SB und Yoo YH (2004). Mechanism of histone deacetylase inhibitor trichostatin A induced apoptosis in human osteosarcoma cells. *Apoptosis* 9: 583-589.

**Rosato RR**, Almenara JA und Grant S (2003). The histone deacetylase inhibitor MS-275 promotes differentiation or apoptosis in human leukemia cells through a process regulated by generation of reactive oxygen species and induction of p21CIP1/WAF1. *Cancer Res* 63: 3637-3645.

**Rosato RR und Grant S** (2003). Histone deacetylase inhibitors in cancer therapy. *Cancer Biol Ther* 2: 30-37.

**Roudabush FL**, Pierce KL, Maudsley S, Khan KD und Luttrell LM (2000). Transactivation of the EGF receptor mediates IGF-I-stimulated shc phosphorylation and ERK1/2 activation in COS-7 cells. *J Biol Chem* 275: 22583-22589.

**Rubin R und Baserga R** (1995). Biology of disease. Insulin-like growth factor-I receptor. Its role in cell proliferation, apoptosis, and tumorigenicity. *Lab Invest* 73: 311-331.

**Rubinfeld H und Seger R** (2005). The ERK cascade: A prototype of MAPK signaling. *Mol Biotechnol* 31: 151-174.

**Ryan QC**, Headlee D, Acharya M, Sparreboom A, Trepel JB, Ye J, Figg WD, Hwang K, Chung EJ, Murgo A, Melillo G, Elsayed Y, Monga M, Kalnitskiy M, Zwiebel J und Sausville EA (2005). Phase I and pharmacokinetic study of MS-275, a histone deacetylase inhibitor, in patients with advanced and refractory solid tumors or lymphoma. *J Clin Oncol* 23: 3912-3922.

**Ryu JK**, Lee WJ, Lee KH, Hwang JH, Kim YT, Yoon YB und Kim CY (2006). SK-7041, a new histone deacetylase inhibitor, induces G2-M cell cycle arrest and apoptosis in pancreatic cancer cell lines. *Cancer Lett* 237: 143-154.

**Saijyo S**, Kudo T, Suzuki M, Katayose Y, Shinoda M, Mutor T, Fukuhara K, Suzuki T und Matsuno S (1995). Establishment of a new extrahepatic bile duct carcinoma cell line, TFK-1. *Tohoku J Exp Med* 177: 61-71.

**Saiki RK**, Scharf S, Faloona F, Mullis KB, Horn GT, Erlich HA und Arnheim N (1985). Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia. *Science* 230: 1350-1354.

**Saito A**, Yamashita T, Mariko Y, Nosaka Y, Tsuchiya K, Ando T, Suzuki T, Tsuruo T und Nakanishi O (1999). A synthetic inhibitor of histone deacetylase, MS-27-275, with marked in vivo antitumor activity against human tumors. *PNAS* 96: 4592-4597.

**Sawa H**, Murakami H, Ohshima Y, Sugino T., Nakajyo T, Kisanuki T, Tamura Y, Satone A, Ide W, Hashimoto I und Kamada H (2001). Histone deacetylase inhibitors such as sodium butyrate and trichostatin A induce apoptosis through an increase of the bcl-2-related protein Bad. *Brain Tumor Pathol* 18: 109-114.

**Scharf JG und Braulke T** (2003). The role of the IGF axis in hepatocarcinogenesis. *Horm Metab Res* 35: 685-693.

**Scherdin G**, Garbrecht M, Klouche M et al. (1987). In vitro interaction of á-difluoromethylornithine (DFMO) and human recombinant interferon- $\alpha$  (rIFN- $\alpha$ ) on human cancer cell lines. *Immunobiology* 1987; 175: 1-143 (Abstract).

**Schurr R**, Stölzel U, Schuppan D, Schwertner C, Steinberg J und Scherübl H (2006). Zunahme des hepatozellulären und des intrahepatischen cholangiozellulären Karzinoms im Nordosten Deutschlands. Increased incidence of hepatocellular and intrahepatic cholangiocellular cancer in the Northeast of Germany. *Dtsch Med Wochenschr* 131:1649-1655.

**Schutte B und Ramaekers FC** (2000). Molecular switches that govern the balance between proliferation and apoptosis. *Prog Cell Cycle Res* 4: 207-217

**Scotlandi K**, Manara MC, Nicoletti G, Lollini PL, Lukas S, Benini S, Croci S, Perdichizzi S, Zambelli D, Serra M, Garcia-Echeverria C, Hofmann F und Picci P (2005). Antitumor activity of the insulin-like growth factor-I receptor kinase inhibitor NVP-AEW541 in musculoskeletal tumors. *Cancer Res* 65: 3868-3876.

**Shaib YH**, El Serag HB, Davila JA, Morgan R und McGlynn KA (2005). Risk factors of intrahepatic cholangiocarcinoma in the United States: a case-control study. *Gastroenterology* 128: 620-626.

**Singh TR**, Shankar S und Srivastava RK (2005). HDAC inhibitors enhance the apoptosis-inducing potential of TRAIL in breast carcinoma. *Oncogene* 24: 4609-4623.

**Sherr CJ und Roberts JM** (1999). CDK inhibitors: positive and negative regulators of G1-phase progression. *Gene Dev* 13:1501-1512.

**Sherr CJ** (2000). The Peczoller lecture: cancer cell cycles revisited. *Cancer Res* 60: 3689-3695.

**Shukla R**, Pooja B, Radhika S, Nijhawan R und Rajwanshi A (2005). Fine-needle aspiration cytology of extramammary neoplasms metastatic to the breast. *Diagn Cytopathol* 32: 193-197.

**Skolnik EY**, Margolis B, Mohammadi M, Lowenstein E, Fischer R, Drepps A, Ullrich A, Schlessinger J (1991). Cloning of PI3 kinase-associated p85 utilizing a novel method for expression/cloning of target proteins for receptor tyrosine kinases. *Cell* 65: 83-90.

**Smith PK**, Krohn RI, Hermanson GT, Mallia AK, Gartner FH, Provenzano MD, Fujimoto E K, Goeke N M, Olson B J und Klenk D C (1985). Measurement of protein using bicinchoninic acid. *Anal Biochem* 150: 76-85.

**Sridhar SS**, Hedley D und Siu LL (2005). Raf kinase as a target for anticancer therapeutics. *Mol Cancer Ther* 4: 677-685.

**Stephenson BM**, Finan PJ, Gascoyne J, Garbett F, Murday VA und Bishop DT (1991). Frequency of familial colorectal cancer. *Br J Surg* 78:1162-1166.

**Stewart CE und Rotwein P** (1996). Growth, differentiation, and survival: multiple physiological functions for insulin-like growth factors. *Physiol Rev* 76: 1005-1026.

**Sutter AP**, Maaser K, Barthel B und Scherübl H (2003). Ligands of the peripheral benzodiazepine receptor induce apoptosis and cell cycle arrest in oesophageal cancer cells: involvement of the p38MAPK signalling pathway. *Br J Cancer* 89: 564-572.

**Sutter AP**, Maaser K, Grabowski P, Bradacs G, Vormbrock K, Höpfner M, Krahn A, Heine B, Stein H, Somasundaram R, Schuppan D, Zeitz M und Scherübl H (2004). Peripheral benzodiazepine receptor ligands induce apoptosis and cell cycle arrest in human hepatocellular carcinoma cells and enhance chemosensitivity to paclitaxel, docetaxel, doxorubicin and the Bcl-2 inhibitor HA14-1. *J Hepatol* 41: 799-807.

**Sutter AP**, Maaser K, Höpfner M, Huether A, Schuppan D und Scherübl H (2005). Cell cycle arrest and apoptosis induction in hepatocellular carcinoma cells by HMG-CoA reductase inhibitors. Synergistic antiproliferative action with ligands of the peripheral benzodiazepine receptor. *J Hepatol* 43: 808-816.

**Sutter AP**, Höpfner M, Huether A, Maaser K und Scherübl H (2006). Targeting the epidermal growth factor receptor by erlotinib (Tarceva) for the treatment of esophageal cancer. *Int J Cancer* 118: 1814-1822.

**Suzuki T**, Ando T, Tsuchiya K, Fukazawa N, Saito A, Mariko Y, Yamashita T und Nakanishi O. (1999). Synthesis and histone deacetylase inhibitory activity of new benzamide derivatives. *J Med Chem* 42: 3001-3003.

**Suzuki T**, Yokozaki H, Kuniyasu H, Hayashi K, Naka K, Ono S, Ishikawa T, Tahara E und Yasui W (2000). Effect of Trichostatin A on cell growth and expression of cell cycle- and apoptosis related molecules in human gastric and oral carcinoma cell lines. *Int J Cancer* 88: 992-997.

**Suzuki H**, Gabrielson E, Chen W, Anbazhagan R, van Engeland M, Weijnenberg MP, Herman JG und Baylin SB (2002). A genomic screen for genes upregulated by demethylation and histone deacetylase inhibition in human colorectal cancer. *Nat Genet* 31: 141-149.

**Takahashi M**, Saito H, Okuyama T, Miyashita T, Kosuga M, Sumisa F, Yamada M, Ebinuma H und Ishii H (1999). Overexpression of Bcl-2 protects human hepatoma cells from Fas-antibody-mediated apoptosis. *J Hepatol* 31: 315-322.



**Takai N**, Desmond JC, Kumagai T, Gui D, Said JW, Whittaker S, Miyakawa I und Koeffler HP (2004). Histone deacetylase inhibitors have a profound antigrowth activity in endometrial cancer cells. *Clin Cancer Res* 10: 1141-1149.

**Tanno B**, Mancini C, Vitali R, Mancuso M, McDowell HP, Dominici C und Raschella G (2006). Down-regulation of insulin-like growth factor I receptor activity by NVP-AEW541 has an antitumor effect on neuroblastoma cells in vitro and in vivo. *Clin Cancer Res* 12: 6772-6780.

**Taylor-Robinson SD**, Toledano MB, Arora S, Keegan TJ, Hargreaves S, Beck A, Khan SA, Elliott P und Thomas HC (2001). Increase in mortality rates from intrahepatic cholangiocarcinoma in England and Wales 1968-1998. *Gut* 48: 816-820.

**Tazzari PL**, Tabellini G, Bortul R, Papa V, Evangelisti C, Grafone T, Martinelli G, McCubrey JA und Martelli AM (2007). The insulin-like growth factor-I receptor kinase inhibitor NVP-AEW541 induces apoptosis in acute myeloid leukemia cells exhibiting autocrine insulin-like growth factor-I secretion. *Leukemia* 21: 886-898.

**Thompson CB** (1995). Apoptosis in the pathogenesis and treatment of disease. *Science* 267: 1456-1462.

**Trojan J**, Blossey BK, Johnson TR, Rudin SD, Tykocinski M, Ilan J und Ilan J (1992). Loss of tumorigenicity of rat glioblastoma directed by episome-based antisense cDNA transcription of insulin-like growth factor I. *Proc Natl Acad Sci* 89: 4874-4878.

**Trojan J**, Johnson TR, Rudin SD, Ilan J, Tykocinski M und Ilan J (1993). Treatment and prevention of rat glioblastoma by immunogenic C6 cells expressing antisense insulin-like growth factor I RNA. *Science* 259: 94-97.

**Vanhaesebroeck B**, Leever SJ, Panayotou G und Waterfield MD (1997). Phosphoinositide 3-kinases: a conserved family of signal transducers. *Trends Biochem Sci* 22: 267-272.

**Van Lint C**, Emiliani S und Verdin E (1996). The expression of a small fraction of cellular gene is changed in response to histone hyperacetylation. *Gene Expr* 5: 245-254.

**Vauthey JN und Blumgart LH** (1994). Recent advances in the management of cholangiocarcinomas. *Semin Liver Dis* 14:109-114.

**Velazquez OC und Rombeau JL** (1997). Butyrate. Potential role in colon cancer prevention and treatment. *Adv Exp Med Biol* 427: 169-181.

**Vergarajauregui S**, San Miguel A und Puertollano R (2006). Activation of p38 mitogen-activated protein kinase promotes epidermal growth factor receptor internalization. *Traffic* 7: 686-698.

**Vindelov L und Christensen IJ** (1990). An integrated set of methods for routine flow cytometric DNA analysis. *Methods Cell Biol* 33: 127-137

**Vigushin DM**, Ali S, Pace PE, Mirsaidi N, Ito K, Adcock I und Coombes RC (2001). Trichostatin A is a histone deacetylase inhibitor with potent antitumor activity against breast cancer in vivo. *Clin Cancer Res* 2001 7: 971-976.

**Vogelstein B und Gillespie D** (1979). Preparative and analytical purification of DNA from agarose. *Proc Natl Acad Sci USA* 76: 615-619.

**Vogelstein B und Kinzler KW** (2001). Achilles' heel of cancer? *Nature* 412: 865-866.

**von Wichert G**, Jehle PM, Hoeflich A, Koschnick S, Dralle H, Wolf E, Wiedenmann B, Boehm BO, Adler G und Seufferlein T (2000). Insulin-like growth factor-I is an autocrine regulator of chromogranin A secretion and growth in human neuroendocrine tumor cells. *Cancer Res* 60: 4573-4581.

**Vousden KH und Lu X** (2002). Live or let die: the cell's response to p53. *Nat Rev Cancer* 2: 594-604.

**Walczak H und Krammer PH** (2000). The CD95 (APO-1/Fas) and the TRAIL (Apo-2L) apoptosis systems. *Exp Cell Res* 256: 58-66.

**Wang HG und Reed JC** (1998). Mechanisms of Bcl-2 protein function. *Histol Histopathol* 13: 521-530.

**Wang Y und Sun Y** (2002). Insulin-like growth factor receptor-1 as an anticancer target: blocking transformation and inducing apoptosis. *Curr Cancer Drug Targets* 2: 191-207.

**Wang Z**, Ruan YB, Guan Y und Liu SH (2003). Expression of IGF-II in early experimental hepatocellular carcinomas and its significance in early diagnosis. *World J Gastroenterol* 9: 267-270.

**Weckbecker G**, Raulf F, Tolcsvai L und Bruns C (1996). Potentiation of the anti-proliferative effects of anti-cancer drugs by octreotide in vitro and in vivo. *Digestion* 57, (Suppl. 1): 22-28.

**Weidle UH und Grossmann A** (2000). Inhibition of histone deacetylases: a new strategy to target epigenetic modifications for anticancer treatment. *Anticancer Res* 20: 1471-1485.

**Weinstein-Oppenheimer CR**, Henriquez-Roldan CF, Davis JM, Navolanic PM, Saleh OA, Steelman LS, Franklin RA, Robinson PJ, McMahon M und McCubrey JA (2001). Role of the Raf signal transduction cascade in the in vitro resistance to the anticancer drug doxorubicin. *Clin Cancer Res* 7: 2898-2907.

**Wilhelm S und Chien DS** (2002). BAY 42-9006: preclinical data. *Curr Pharm Des* 8: 2255-2257.

**Wilkinson MG und Millar JB** (2000). Control of the eukaryotic cell cycle by MAP kinase signaling pathways. *FASEB J* 14: 2147-2157.

**Wong WW**, Tan MM, Xia Z, Dimitroulakos J, Minden MD und Penn LZ (2001). Cerivastatin triggers tumor-specific apoptosis with higher efficacy than lovastatin. *Clin Cancer Res* 7: 2067-2075

**Wu J und Grunstein M** (2000). 25 years after the chromosome model: chromatin modifications. *Trends Biochem Sci* 25: 619-623

**Wulbrand U**, Remmert G, Zofel P, Wied M, Arnold R und Fehm HC (2000). mRNA expression patterns of insulin-like growth factor system components in human neuroendocrine tumours. *Eur J Clin Invest* 30: 729-739.

**Yamamoto K**, Altschuler D, Wood E, Horlick K, Jacobs S und Lapetina EG (1992). Association of phosphorylated insulin-like growth factor-I receptor with the SH2 domains of phosphatidylinositol 3-kinase p85. *J Biol Chem* 267: 11337-11343.

**Yamashita Y**, Shimada M, Harimoto N, Rikimaru T, Shirabe K, Tanaka S und Sugimachi K (2003). Histone deacetylase inhibitor trichostatin A induces cell-cycle arrest/apoptosis and hepatocyte differentiation in human hepatoma cells. *Int J Cancer* 103: 572-576

**Yarden Y und Sliwkowski MX** (2001). Untangling the ErbB signalling network. *Nat Rev Mol Cell Biol* 2: 127-137.

**Yao X**, Hu JF, Daniels M, Yien H, Lu H, Sharan H, Zhou X, Zeng Z, Li T, Yang Y und Hoffman AR (2003). A novel orthotopic tumor model to study growth factors and oncogenes in hepatocarcinogenesis. *Clin Cancer Res* 9: 2719-2726.

**Yu H und Rohan T** (2000). Role of the insulin-like growth factor family in cancer development and progression. *J Natl Cancer Inst* 92: 1472-1489.

**Yu C**, Rahmani M, Conrad D, Subler M, Dent P und Grant S (2003). The proteasome inhibitor bortezomib interacts synergistically with histone deacetylase inhibitors to induce apoptosis in Bcr/Abl<sup>+</sup> cells sensitive and resistant to STI571. *Blood* 12: 3765-3774.

**Zamzami N**, Susin S A, Marchetti P, Hirsch T, Gomez-Monterrey I, Castedo M und Kroemer G (1996). Mitochondrial control of nuclear apoptosis. *J Exp Med* 183: 1533-1544.

**Zhu P**, Martin E, Mengwasser J, Schlag P, Janssen KP und Göttlicher M (2004a). Induction of HDAC2 expression upon loss of APC in colorectal tumorigenesis. *Cancer Cell* 5: 455-463.

**Zhu H**, Zhang L, Wu S, Teraishi F, Davis JJ, Jacob D und Fang B (2004b). Induction of S-phase arrest and p21 overexpression by a small molecule 2[[3-(2,3-dichlorophenoxy)propyl] amino]ethanol in correlation with activation of ERK. *Oncogene* 23: 4984-4992.