

## 8 LITERATURVERZEICHNIS

- Aden DP, Fogel A, Plotkin S, Damjanov I und Knowles B B (1979)  
Controlled synthesis of HBsAg in a differentiated human liver carcinoma-derived cell line.  
*Nature* 282: 615-616.
- Albanell J, Rojo F und Baselga J (2001)  
Pharmacodynamic studies with the epidermal growth factor receptor tyrosine kinase inhibitor ZD1839.  
*Semin Oncol* 28: 56-66.
- Allgaier HP, Galandi D, Zuber I und Blum H E (2001)  
Radiofrequency thermal ablation of hepatocellular carcinoma.  
*Dig Dis* 19: 301-310.
- Baselga J (2001)  
The EGFR as a target for anticancer therapy-focus on cetuximab.  
*Eur J Cancer* 37 Suppl 4: S16-S22.
- Baserga R (1999)  
The IGF-I receptor in cancer research.  
*Exp Cell Res* 253: 1-6.
- Baxter RC (2000)  
Insulin-like growth factor (IGF)-binding proteins: interactions with IGFs and intrinsic bioactivities.  
*Am J Physiol Endocrinol Metab* 278: 967-976.
- Bishop PC, Myers T, Robey R, Fry D W, Liu E T, Blagosklonny M V und Bates S E (2002)  
Differential sensitivity of cancer cells to inhibitors of the epidermal growth factor receptor family.  
*Oncogene* 21: 119-127.
- Bouillet P und Strasser A (2002)  
BH3-only proteins - evolutionarily conserved proapoptotic Bcl-2 family members essential for initiating programmed cell death.  
*J Cell Sci* 115: 1567-1574.
- Bowman T, Garcia R, Turkson J und Jove R (2000)  
STATs in oncogenesis.  
*Oncogene* 19: 2474-2488.
- Bromberg J und Darnell J E (2000)  
The role of STATs in transcriptional control and their impact on cellular function.  
*Oncogene* 19: 2468-2473.
- Bromberg JF, Horvath C M, Wen Z, Schreiber R D und Darnell J E, Jr. (1996)  
Transcriptionally active Stat1 is required for the antiproliferative effects of both interferon alpha and interferon gamma.  
*Proc Natl Acad Sci U S A* 93: 7673-7678.

- Bruix J, Sherman M, Llovet J M und et al. (2001)  
Clinical management of hepatocellular carcinoma. Conclusions of the Barcelona-2000 EASL Conference.  
*J Hepatol* 35: 421-430.
- Burroughs A, Hochhauser D und Meyer T (2004)  
Systemic treatment and liver transplantation for hepatocellular carcinoma: Two ends of the therapeutic spectrum.  
*Lancet Oncol* 5: 409-418.
- Burtness B (2005)  
The role of cetuximab in the treatment of squamous cell cancer of the head and neck.  
*Expert Opin Biol Ther* 5: 1085-1093.
- Busam KJ, Capodieci P, Motzer R, Kiehn T, Phelan D und Halpern A C (2001)  
Cutaneous side-effects in cancer patients treated with the antiepidermal growth factor receptor antibody C225.  
*Br J Dermatol* 144: 1169-1176.
- Calo V, Migliavacca M, Bazan V, Macaluso M, Buscemi M, Gebbia N und Russo A (2003)  
STAT proteins: From normal control of cellular events to tumorigenesis.  
*J Cell Physiol* 197: 157-168.
- Carter P (2001)  
Improving the efficacy of antibody-based cancer therapies.  
*Nat Rev Cancer* 1: 118-129.
- Chakravarti A, Loeffler J S und Dyson N J (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 kinase mediates the stress-induced activation of mitogen-activated protein kinase cascades.  
*Biochem J* 336 ( Pt 3): 599-609.
- Chang HY und Yang X (2000)  
Proteases for cell suicide: Functions and regulation of caspases.  
*Microbiol Mol Biol Rev* 64: 821-846.
- Chen SC, Chou CK, Wong FH, Chang CM und Hu CP (1991)  
Overexpression of epidermal growth factor and insulin-like growth factor-I receptors and autocrine stimulation in human esophageal carcinoma cells.  
*Cancer Res* 1;51(7):1898-903.
- Cheng M, Sexl V, Sherr C J und Roussel M F (1998)  
Assembly of cyclin D-dependent kinase and titration of p27Kip1 regulated by mitogen-activated protein kinase kinase (MEK1).  
*Proc Natl Acad Sci U S A* 95: 1091-1096.

Chomczynski P und Sacchi N (1987)  
Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction.  
*Anal Biochem* 162: 156-159.

Ciardiello F (2000)  
Epidermal growth factor receptor tyrosine kinase inhibitors as anticancer agents.  
*Drugs* 60 Suppl 1: 25-32.

Ciardiello F, Caputo R, Bianco R, Damiano V, Pomatico G, De Placido S, Bianco A R und Tortora G (2000)  
Antitumor effect and potentiation of cytotoxic drugs activity in human cancer cells by ZD-1839 (Iressa), an epidermal growth factor receptor-selective tyrosine kinase inhibitor.  
*Clin Cancer Res* 6: 2053-2063.

Ciardiello F und Tortora G (2001)  
A novel approach in the treatment of cancer: Targeting the epidermal growth factor receptor.  
*Clin Cancer Res* 7: 2958-2970.

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

Cunningham D, Humblet Y, Siena S, Khayat D, Bleiberg H, Santoro A, Bets D, Mueser M, Harstrick A, Verslype C, Chau I und Van Cutsem E (2004)  
Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer.  
*N Engl J Med* 351: 337-345.

Daveau M, Scotte M, Francois A, Coulouarn C, Ros G, Tallet Y, Hiron M, Hellot M F und Salier J P (2003)  
Hepatocyte growth factor, transforming growth factor alpha, and their receptors as combined markers of prognosis in hepatocellular carcinoma.  
*Molecular Carcinogenesis* 36: 130-141.

Eichhorst ST (2005)  
Modulation of apoptosis as a target for liver disease.  
*Expert Opin Ther Targets* 9: 83-99.

El Deiry WS, Harper J W, O'Connor P M, Velculescu V E, Canman C E, Jackman J, Pietenpol J A, Burrell M, Hill D E und Wang Y (1994)  
WAF1/CIP1 is induced in p53-mediated G1 arrest and apoptosis.  
*Cancer Res* 54: 1169-1174.

Engelman JA und Janne P A (2005)  
Factors predicting response to EGFR tyrosine kinase inhibitors.  
*Semin Respir Crit Care Med* 26: 314-322.

Erhardt P, Schremser E J und Cooper G M (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.

Fachinformation Erbitux<sup>TM</sup> (2004)  
Merck KGaA, 64271 Darmstadt, D.

Fachinformation Iressa<sup>TM</sup> (2004)  
AstraZeneca AG, 6301 Zug, CH.

Fachinformation Tarceva<sup>TM</sup> (2004)  
OSI Pharmaceuticals and Genentech, NY, USA.

Ferlay J, Bray F, Pisani P und Parkin DM (2004)  
GLOBOCAN 2002. Cancer incidence, mortality and prevalence worldwide.  
*IARC Cancer Base No 5 Version 2 0 Lyon, France: IARCP*ress; 2004.

Fischer OM, Hart S, Gschwind A und Ullrich A (2003)  
EGFR signal transactivation in cancer cells.  
*Biochem Soc Trans* 31: 1203-1208.

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

Garcia R, Bowman T L, Niu G, Yu H, Minton S, Muro-Cacho C A, Cox C E, Falcone R, Fairclough R, Parsons S, Laudano A, Gazit A, Levitzki A, Kraker A und Jove R (2001)  
Constitutive activation of Stat3 by the Src and JAK tyrosine kinases participates in growth regulation of human breast carcinoma cells.  
*Oncogene* 20: 2499-2513.

Giaccone G, Gonzalez-Larriba J L, van Oosterom A T, Alfonso R, Smit E F, Martens M, Peters G J, van der Vijgh W J, Smith R, Averbuch S und Fandi A (2004a)  
Combination therapy with gefitinib, an epidermal growth factor receptor tyrosine kinase inhibitor, gemcitabine and cisplatin in patients with advanced solid tumors.  
*Ann Oncol* 15: 831-838.

Giaccone G, Herbst R S, Manegold C, Scagliotti G, Rosell R, Miller V, Natale R B, Schiller J H, von Pawel J, Pluzanska A, Gatzemeier U, Grous J, Ochs J S, Averbuch S D, Wolf M K, Rennie P, Fandi A und Johnson D H (2004b)  
Gefitinib in combination with gemcitabine and cisplatin in advanced non-small-cell lung cancer: a phase III trial--INTACT 1.  
*J Clin Oncol* 22: 777-784.

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

- Grunwald V und Hidalgo M (2003)  
Developing inhibitors of the epidermal growth factor receptor for cancer treatment.  
*J Natl Cancer Inst* 95: 851-867.
- Haddad R, Morrow A D, Plass C und Held W A (2000)  
Restriction landmark genomic scanning of mouse liver tumors for gene amplification:  
Overexpression of cyclin A2.  
*Biochem Biophys Res Commun* 274: 188-196.
- Harari PM (2004)  
Epidermal growth factor receptor inhibition strategies in oncology.  
*Endocr Relat Cancer* 11: 689-708.
- Herbst RS, Giaccone G, Schiller J H, Natale R B, Miller V, Manegold C, Scagliotti G, Rosell R, Oliiff I, Reeves J A, Wolf M K, Krebs A D, Averbuch S D, Ochs J S, Grous J, Fandi A und Johnson D H (2004)  
Gefitinib in combination with paclitaxel and carboplatin in advanced non-small-cell lung cancer: a Phase III trial--INTACT 2.  
*J Clin Oncol* 22: 785-794.
- Herbst RS, Prager D, Hermann R, Fehrenbacher L, Johnson B E, Sandler A, Kris M G, Tran H T, Klein P, Li X, Ramies D, Johnson D H und Miller V A (2005)  
TRIBUTE: A phase III trial of erlotinib hydrochloride (OSI-774) combined with carboplatin and paclitaxel chemotherapy in advanced non-small-cell lung cancer.  
*J Clin Oncol* 23(25):5892-9.
- Höpfner M, Sutter A P, Beck N I, Barthel B, Maaser K, Jockers-Scherübl M C, Zeitz M und Scherübl H (2002)  
Meta-iodobenzylguanidine induces growth inhibition and apoptosis of neuroendocrine gastrointestinal tumor cells.  
*Int J Cancer* 20;101: 210-216.
- Höpfner M, Sutter A P, Gerst B, Zeitz M und Scherübl H (2003)  
A novel approach in the treatment of neuroendocrine gastrointestinal tumours. Targeting the epidermal growth factor receptor by gefitinib (ZD1839).  
*Br J Cancer* 89: 1766-1775.
- Höpfner M, Sutter A P, 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.
- Huang S, Armstrong E A, Benavente S, Chinnaian P und Harari P M (2004)  
Dual-agent molecular targeting of the epidermal growth factor receptor (EGFR): Combining anti-EGFR antibody with tyrosine kinase inhibitor.  
*Cancer Res* 64: 5355-5362.
- Huang SM, Bock J M und Harari P M (1999)  
Epidermal growth factor receptor blockade with C225 modulates proliferation, apoptosis, and radiosensitivity in squamous cell carcinomas of the head and neck.  
*Cancer Res* 59: 1935-1940.

- Huang SM und Harari P M (1999)  
Epidermal growth factor receptor inhibition in cancer therapy: Biology, rationale and preliminary clinical results.  
*Invest New Drugs* 17: 259-269.
- Hui AM, Makuuchi M und Li X (1998)  
Cell cycle regulators and human hepatocarcinogenesis.  
*Hepatogastroenterology* 45: 1635-1642.
- Israels LG und Israels E D (1999)  
Apoptosis.  
*Oncologist* 4: 332-339.
- Ito Y, Takeda T, Sakon M, Tsujimoto M, Higashiyama S, Noda K, Miyoshi E, Monden M und Matsuura N (2001)  
Expression and clinical significance of erb-B receptor family in hepatocellular carcinoma.  
*British Journal of Cancer* 84: 1377-1383.
- Jackson PE, Qian G S, Friesen M D, Zhu Y R, Lu P, Wang J B, Wu Y, Kensler T W, Vogelstein B und Groopman J D (2001)  
Specific p53 mutations detected in plasma and tumors of hepatocellular carcinoma patients by electrospray ionization mass spectrometry.  
*Cancer Res* 61: 33-35.
- Johnson GL und Lapadat R (2002)  
Mitogen-activated protein kinase pathways mediated by ERK, JNK, and p38 protein kinases.  
*Science* 298: 1911-1912.
- Kaufmann SH und Hengartner M O (2001)  
Programmed cell death: Alive and well in the new Millennium.  
*Trends Cell Biol* 11: 526-534.
- Kawata S, Yamasaki E, Nagase T, Inui Y, Ito N, Matsuda Y, Inada M, Tamura S, Noda S, Imai Y und Matsuzawa Y (2001)  
Effect of pravastatin on survival in patients with advanced hepatocellular carcinoma. A randomized controlled trial.  
*Br J Cancer* 84: 886-891.
- Kerr JF, Wyllie A H und Currie A R (1972)  
Apoptosis: A basic biological phenomenon with wide-ranging implications in tissue kinetics.  
*Br J Cancer* 26: 239-257.
- Kim ES, Khuri F R und Herbst R S (2001)  
Epidermal growth factor receptor biology (IMC-C225).  
*Curr Opin Oncol* 13: 506-513.
- Kira S, Nakanishi T, Suemori S, Kitamoto M, Watanabe Y und Kajiyama G (1997)  
Expression of transforming growth factor alpha and epidermal growth factor receptor in human hepatocellular carcinoma.  
*Liver* 17: 177-182.

Koshy M, Esiashvili N, Landry J C, Thomas C R, Jr. und Matthews R H (2004)  
Multiple management modalities in esophageal cancer: Epidemiology, presentation and progression, work-up, and surgical approaches.  
*Oncologist* 9: 137-146.

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

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

Kultz D, Madhani S und Burg M B (1998)  
Hyperosmolality causes growth arrest of murine kidney cells. Induction of GADD45 and GADD153 by osmosensing via stress-activated protein kinase 2.  
*J Biol Chem* 273: 13645-13651.

Las Alas MM, Christen R D, Gately D P, Weiner D E, Benbatoul K, Kirmani S, D'Agostino H R, Plaxe S C, Darrah D, McClay E F, Aebi S, Howell S B und Los G (2000)  
Increase in tumor GADD153 mRNA level following treatment correlates with response to paclitaxel.  
*Cancer Chemother Pharmacol* 45: 381-388.

Lavoie JN, L'Allemand 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.

Lawen A (2003)  
Apoptosis-an introduction.  
*Bioessays* 25: 888-896.

Lee TK, Lau T C und Ng I O (2002)  
Doxorubicin-induced apoptosis and chemosensitivity in hepatoma cell lines.  
*Cancer Chemother Pharmacol* 49: 78-86.

Levine AJ (1997)  
P53, the cellular gatekeeper for growth and division.  
*Cell* 88: 323-331.

Liebermann DA und Hoffman B (2002)  
Myeloid differentiation (MyD)/growth arrest DNA damage (GADD) genes in tumor suppression, immunity and inflammation.  
*Leukemia* 16: 527-541.

Lin SB, Hsieh SH, Hsu H L, Lai M Y, Kan L S und Au L C (1997)  
Antisense oligodeoxynucleotides of IGF-II selectively inhibit growth of human hepatoma cells overproducing IGF-II.  
*J Biochem (Tokyo)* 122: 717-722.

- Liu YC, Leu CM, Wong FH, Fong WS, Chen SC, Chang C und Hu CP (2002)  
Autocrine stimulation by insulin-like growth factor I is involved in the growth, tumorigenicity and chemoresistance of human esophageal carcinoma cells. *J Biomed Sci* 9(6 Pt 2):665-74.
- Lodisch H, Berk A, Zipurski S L, Matsudaira P, Baltimore D und Darnell J E (2001)  
Molekulare Zellbiologie.  
*Spektrum Akademischer Verlag*. Heidelberg; Berlin.
- Los G, Benbatoul K, Gately D P, Barton R, Christen R, Robbins K T, Vicario D, Kirmani S, Orloff L A, Weisman R und Howell S B (1999)  
Quantitation of the change in GADD153 messenger RNA level as a molecular marker of tumor response in head and neck cancer.  
*Clin Cancer Res* 5: 1610-1618.
- Lowe SW, Ruley H E, Jacks T und Housman D E (1993)  
P53-dependent apoptosis modulates the cytotoxicity of anticancer agents.  
*Cell* 74: 957-967.
- Lu ZL, Luo D Z und Wen J M (2005)  
Expression and significance of tumor-related genes in HCC.  
*World J Gastroenterol* 11: 3850-3854.
- Lynch TJ, Bell D W, Sordella R, Gurubhagavatula S, Okimoto R A, Brannigan B W, Harris P L, Haserlat S M, Supko J G, Haluska F G, Louis D N, Christiani D C, Settleman J und Haber D A (2004)  
Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib.  
*N Engl J Med* 350: 2129-2139.
- Maaser K, Höpfner M, Kap H, Sutter A P, 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.
- Magne N, Fischel J L, Dubreuil A, Formento P, Poupon M F, Laurent-Puig P und Milano G (2002)  
Influence of epidermal growth factor receptor (EGFR), p53 and intrinsic MAP kinase pathway status of tumour cells on the antiproliferative effect of ZD1839 ("Iressa").  
*Br J Cancer* 86: 1518-1523.
- Matar P, Rojo F, Cassia R, Moreno-Bueno G, Di Cosimo S, Tabernero J, Guzman M, Rodriguez S, Arribas J, Palacios J und Baselga J (2004)  
Combined epidermal growth factor receptor targeting with the tyrosine kinase inhibitor gefitinib (ZD1839) and the monoclonal antibody cetuximab (IMC-C225): Superiority over single-agent receptor targeting.  
*Clin Cancer Res* 10: 6487-6501.
- Mathur A, Hong Y, Kemp B K, Barrientos A A und Erusalimsky J D (2000)  
Evaluation of fluorescent dyes for the detection of mitochondrial membrane potential changes in cultured cardiomyocytes.  
*Cardiovasc Res* 46: 126-138.

Maytin EV, Ubeda M, Lin J C und Habener J F (2001)  
Stress-inducible transcription factor CHOP/Gadd153 induces apoptosis in mammalian cells via p38 kinase-dependent and -independent mechanisms.  
*Exp Cell Res* 267: 193-204.

McMillan L, Butcher S K, Pongracz J und Lord J M (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.

Mendelsohn J (2001)  
The epidermal growth factor receptor as a target for cancer therapy.  
*Endocr Relat Cancer* 8: 3-9.

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

Moore M J, Goldstein D, Hamm J, Kotecha J, Gallinger S, Au H J, Nomikos D. und Parulekar W (2005)  
Erlotinib improves survival when added to gemcitabine in patients with advanced pancreatic cancer. A phase III trial of the National Cancer Institute of Canada clinical trials group (NCIC-CTG).

*Gastrointestinal Cancers Symposium*

Moyer JD, Barbacci E G, Iwata K K, Arnold L, Boman B, Cunningham A, DiOrio C, Doty J, Morin M J, Moyer M P, Neveu M, Pollack V A, Pustilnik L R, Reynolds M M, Sloan D, Theleman A und Miller P (1997)  
Induction of apoptosis and cell cycle arrest by CP-358,774, an inhibitor of epidermal growth factor receptor tyrosine kinase.  
*Cancer Res* 57: 4838-4848.

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.

Nakabayashi H, Taketa K, Yamane T, Miyazaki M, Miyano K und Sato J (1984)  
Phenotypical stability of a human hepatoma cell line, Huh-7, in long-term culture with chemically defined medium.  
*Gann* 75: 151-158.

Neuman MG (2001)  
Apoptosis in diseases of the liver.  
*Crit Rev Clin Lab Sci* 38: 109-166.

O'Connor R (2003)  
Regulation of IGF-I receptor signaling in tumor cells.  
*Horm Metab Res* 35: 771-777.

- Oh-Hashi K, Maruyama W und Isobe K (2001)  
Peroxynitrite induces GADD34, 45, and 153 via p38 MAPK in human neuroblastoma SH-SY5Y Cells.  
*Free Radic Biol Med* 30: 213-221.
- Ozturk M (1999)  
Genetic aspects of hepatocellular carcinogenesis.  
*Semin Liver Dis* 19: 235-242.
- Paez JG, Janne P A, Lee J C, Tracy S, Greulich H, Gabriel S, Herman P, Kaye F J, Lindeman N, Boggon T J, Naoki K, Sasaki H, Fujii Y, Eck M J, Sellers W R, Johnson B E und Meyerson M (2004)  
EGFR mutations in lung cancer: Correlation with clinical response to gefitinib therapy.  
*Science* 304: 1497-1500.
- Parkin DM (2001)  
Global cancer statistics in the year 2000.  
*Lancet Oncol* 2: 533-543.
- Piret JP, Arnould T, Fuks B, Chatelain P, Remacle J und Michiels C (2004)  
Mitochondria permeability transition-dependent tert-butyl hydroperoxide-induced apoptosis in hepatoma HepG2 cells.  
*Biochem Pharmacol* 67: 611-620.
- Porter AG (1999)  
Protein translocation in apoptosis.  
*Trends Cell Biol* 9: 394-401.
- 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.
- Prewett M, Rockwell P, Rockwell R F, Giorgio N A, Mendelsohn J, Scher H I und Goldstein N I (1996)  
The biologic effects of C225, a chimeric monoclonal antibody to the EGFR, on human prostate carcinoma.  
*Journal of Immunotherapy* 19: 419-427.
- Raoul JL, Guyader D, Bretagne J F, Duvaufier R, Bourguet P, Bekhechi D, Deugnier Y M und Gosselin M (1994)  
Randomized controlled trial for hepatocellular carcinoma with portal vein thrombosis: intra-arterial iodine-131-iodized oil versus medical support.  
*J Nucl Med* 35: 1782-1787.
- Ratain M J, George C M, Janisch L, Kindler H L, Ryan C, Wood D L, Nadler P I und Vokes E. E. (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
- Rieder CL und Khodjakov A (1997)  
Mitosis and checkpoints that control progression through mitosis in vertebrate somatic cells.  
*Prog Cell Cycle Res* 3: 301-312.

Rubin R und Baserga R (1995)

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.

Saiki RK, Scharf S, Faloona F, Mullis K B, Horn G T, Erlich H A 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.

Salomon DS, Brandt R, Ciardiello F und Normanno N (1995)

Epidermal growth factor-related peptides and their receptors in human malignancies. *Crit Rev Oncol Hematol* 19: 183-232.

Savill J (1996)

Phagocyte recognition of apoptotic cells.

*Biochem Soc Trans* 24: 1065-1069.

Scharf JG und Braulke T (2003)

The role of the IGF axis in hepatocarcinogenesis.

*Horm Metab Res* 35: 685-693.

Scharf JG, Schmidt-Sandte W, Pahernik S A, Ramadori G, Braulke T und Hartmann H (1998)

Characterization of the insulin-like growth factor axis in a human hepatoma cell line (PLC).

*Carcinogenesis* 19: 2121-2128.

Schurr R, Schuppan D, Stölzel U und Scherübl H (2005)

Zunahme des HCCs und des intrahepatischen cholangiozellulären Karzinoms im Nordosten Deutschlands.

*DMW*, im Druck

Schutte B und Ramaekers F C (2000)

Molecular switches that govern the balance between proliferation and apoptosis.

*Prog Cell Cycle Res* 4: 207-217.

Sherman M (2005)

Hepatocellular carcinoma: Epidemiology, risk factors, and screening.

*Semin Liver Dis* 25: 143-154.

Shimada Y, Imamura M, Wagata T, Yamaguchi N und Tobe T (1992)

Characterization of 21 newly established esophageal cancer cell lines.

*Cancer* 69: 277-284.

Shimizu Y, Zhu J J, Han F, Ishikawa T und Oda H (1999)

Different frequencies of p53 codon-249 hot-spot mutations in hepatocellular carcinomas in Jiang-Su province of China.

*Int J Cancer* 82: 187-190.

Singh R, Pervin S und Chaudhuri G (2002)  
Caspase-8-mediated BID cleavage and release of mitochondrial cytochrome c during nomega-hydroxy-L-arginine-induced apoptosis in MDA-MB-468 cells. antagonistic effects of L-ornithine.  
*J Biol Chem* 277: 37630-37636.

Smith PK, Krohn R I, Hermanson G T, Mallia A K, Gartner F H, Provenzano M D, 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.

Steele RJ und Lane D P (2005)  
P53 in cancer: A paradigm for modern management of cancer.  
*Surgeon* 3: 197-205.

Sun L, Gong R, Wan B, Huang X, Wu C, Zhang X, Zhao S und Yu L (2003)  
GADD45gamma, down-regulated in 65% hepatocellular carcinoma (HCC) from 23 chinese patients, inhibits cell growth and induces cell cycle G2/M arrest for hepatoma Hep-G2 cell lines.  
*Mol Biol Rep* 30: 249-253.

Sutter A P, Höpfner M, Huether A, Maaser K und Scherübl H (2005)  
Targeting the epidermal growth factor receptor by erlotinib (Tarceva<sup>TM</sup>) for the treatment of esophageal cancer.  
*Int J Cancer*, im Druck.

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.

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.

Takaoka M, Harada H, Andl C D, Oyama K, Naomoto Y, Dempsey K L, Klein-Szanto A J, el Deiry W S, Grimberg A und Nakagawa H (2004)  
Epidermal growth factor receptor regulates aberrant expression of insulin-like growth factor-binding protein 3.  
*Cancer Res* 64: 7711-7723.

Tanaka H, Shibagaki I, Shimada Y, Wagata T, Imamura M und Ishizaki K (1996)  
Characterization of p53 gene mutations in esophageal squamous cell carcinoma cell lines: Increased frequency and different spectrum of mutations from primary tumors.  
*Int J Cancer* 65: 372-376.

Tannapfel A und Wittekind C (2002)  
Genes involved in hepatocellular carcinoma: Dereulation in cell cycling and apoptosis.  
*Virchows Arch* 440: 345-352.

- Toyoda H, Komurasaki T, Uchida D und Morimoto S (1997)  
Distribution of mRNA for human epiregulin, a differentially expressed member of the  
epidermal growth factor family.  
*Biochem J* 326: 69-75.
- Vairapandi M, Balliet A G, Fornace A J, Jr., Hoffman B und Liebermann D A (1996)  
The differentiation primary response gene MyD118, related to GADD45, encodes for a  
nuclear protein which interacts with PCNA and p21WAF1/CIP1.  
*Oncogene* 12: 2579-2594.
- Vander Heiden MG, Chandel N S, Schumacker P T und Thompson C B (1999)  
Bcl-XL prevents cell death following growth factor withdrawal by facilitating mitochondrial  
ATP/ADP exchange.  
*Mol Cell* 3: 159-167.
- Vindelov L und Christensen I J (1990)  
An integrated set of methods for routine flow cytometric DNA analysis.  
*Methods Cell Biol* 33: 127-137.
- Vogelstein B und Gillespie D (1979)  
Preparative and analytical purification of DNA from agarose.  
*Proc Natl Acad Sci U S A* 76: 615-619.
- Wang HG und Reed J C (1998)  
Mechanisms of Bcl-2 protein function.  
*Histol Histopathol* 13: 521-530.
- Watanabe J, Kushihata F, Honda K, Sugita A, Tateishi N, Mominoki K, Matsuda S und  
Kobayashi N (2004)  
Prognostic significance of Bcl-XL in human hepatocellular carcinoma.  
*Surgery* 135: 604-612.
- Watanabe T, Shintani A, Nakata M, Shing Y, Folkman J, Igarashi K und Sasada R (1994)  
Recombinant human betacellulin. Molecular structure, biological activities, and receptor  
interaction.  
*J Biol Chem* 269: 9966-9973.
- Wells A (1999)  
EGF receptor.  
*Int J Biochem Cell Biol* 31: 637-643.
- Wilkinson MG und Millar J B (2000)  
Control of the eukaryotic cell cycle by MAP kinase signaling pathways.  
*FASEB J* 14: 2147-2157.
- Woodburn JR (1999)  
The epidermal growth factor receptor and its inhibition in cancer therapy.  
*Pharmacol Ther* 82: 241-250.
- Yarden Y und Sliwkowski M X (2001)  
Untangling the ErbB signalling network.  
*Nat Rev Mol Cell Biol* 2: 127-137.

- 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.
- Zhan Q, Bae I, Kastan M B und Fornace A J, Jr. (1994a)  
The p53-dependent gamma-ray response of GADD45.  
*Cancer Res* 54: 2755-2760.
- Zhan Q, Lord K A, Alamo I, Jr., Hollander M C, Carrier F, Ron D, Kohn K W, Hoffman B, Liebermann D A und Fornace A J, Jr. (1994b)  
The Gadd and MyD genes define a novel set of mammalian genes encoding acidic proteins that synergistically suppress cell growth.  
*Mol Cell Biol* 14: 2361-2371.
- Zhou Q, He Q und Liang L J (2003)  
Expression of p27, cyclin E and cyclin A in hepatocellular carcinoma and its clinical significance.  
*World J Gastroenterol* 9: 2450-2454.
- Zhu H, Zhang L, Wu S, Teraishi F, Davis J J, Jacob D und Fang B (2004)  
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.
- Zwick E, Hackel P O, Prenzel N und Ullrich A (1999)  
The EGF receptor as central transducer of heterologous signalling systems.  
*Trends Pharmacol Sci* 20: 408-412.