

## 8 Literatur

- Ahn, J., Chung, K. S., Kim, D. U., Won, M., Kim, L., Kim, K. S., Nam, M., Choi, S. J., Kim, H. C., Yoon, M., Chae, S. K. & Hoe, K. L. (2004). Systematic identification of hepatocellular proteins interacting with NS5A of the hepatitis C virus. *J Biochem Mol Biol* **37**, 741-8.
- Alavi, A., Hood, J. D., Frausto, R., Stupack, D. G. & Cheresh, D. A. (2003). Role of Raf in vascular protection from distinct apoptotic stimuli. *Science* **301**, 94-6.
- Alter, H. J., Purcell, R. H., Holland, P. V. & Popper, H. (1978). Transmissible agent in non-A, non-B hepatitis. *Lancet* **1**, 459-63.
- Alter, H. J. & Seeff, L. B. (2000). Recovery, persistence, and sequelae in hepatitis C virus infection: a perspective on long-term outcome. *Semin Liver Dis* **20**, 17-35.
- Andersen, G., Busso, D., Poterszman, A., Hwang, J. R., Wurtz, J. M., Ripp, R., Thierry, J. C., Egly, J. M. & Moras, D. (1997). The structure of cyclin H: common mode of kinase activation and specific features. *Embo J* **16**, 958-67.
- Aoki, H., Hayashi, J., Moriyama, M., Arakawa, Y. & Hino, O. (2000). Hepatitis C virus core protein interacts with 14-3-3 protein and activates the kinase Raf-1. *J Virol* **74**, 1736-41.
- App, H., Hazan, R., Zilberstein, A., Ullrich, A., Schlessinger, J. & Rapp, U. (1991). Epidermal growth factor (EGF) stimulates association and kinase activity of Raf-1 with the EGF receptor. *Mol Cell Biol* **11**, 913-9.
- Appel, N., Pietschmann, T. & Bartenschlager, R. (2005). Mutational analysis of hepatitis C virus nonstructural protein 5A: potential role of differential phosphorylation in RNA replication and identification of a genetically flexible domain. *J Virol* **79**, 3187-94.
- Arima, N., Kao, C. Y., Licht, T., Padmanabhan, R. & Sasaguri, Y. (2001). Modulation of cell growth by the hepatitis C virus nonstructural protein NS5A. *J Biol Chem* **276**, 12675-84.
- Arsura, M., Mercurio, F., Oliver, A. L., Thorgeirsson, S. S. & Sonenshein, G. E. (2000). Role of the I $\kappa$ B kinase complex in oncogenic Ras- and Raf-mediated transformation of rat liver epithelial cells. *Mol Cell Biol* **20**, 5381-91.
- Asabe, S. I., Tanji, Y., Satoh, S., Kaneko, T., Kimura, K. & Shimotohno, K. (1997). The N-terminal region of hepatitis C virus-encoded NS5A is important for NS4A-dependent phosphorylation. *J Virol* **71**, 790-6.
- Ashkenazi, A., Pai, R. C., Fong, S., Leung, S., Lawrence, D. A., Marsters, S. A., Blackie, C., Chang, L., McMurtrey, A. E., Hebert, A., DeForge, L., Koumenis, I. L., Lewis, D., Harris, L., Bussiere, J., Koeppen, H., Shahrokhi, Z. & Schwall, R. H. (1999). Safety and antitumor activity of recombinant soluble Apo2 ligand. *J Clin Invest* **104**, 155-62.
- Aus dem Siepen, M., Lohmann, V., Wiese, M., Ross, S., Roggendorf, M. & Viazov, S. (2005). Nonstructural protein 5A does not contribute to the resistance of hepatitis C virus replication to interferon alpha in cell culture. *Virology* **336**, 131-6.
- Baldwin, E. L. & Osheroff, N. (2005). Etoposide, topoisomerase II and cancer. *Curr Med Chem Anticancer Agents* **5**, 363-72.
- Banner, D. W., D'Arcy, A., Janes, W., Gentz, R., Schoenfeld, H. J., Broger, C., Loetscher, H. & Lesslauer, W. (1993). Crystal structure of the soluble human 55 kd TNF receptor-human TNF beta complex: implications for TNF receptor activation. *Cell* **73**, 431-45.
- Baron, B. W., Anastasi, J., Thirman, M. J., Furukawa, Y., Fears, S., Kim, D. C., Simone, F., Birkenbach, M., Montag, A., Sadhu, A., Zeleznik-Le, N. & McKeithan, T. W. (2002). The human programmed cell death-2 (PDCD2) gene is a target of BCL6 repression: implications for a role of BCL6 in the down-regulation of apoptosis. *Proc Natl Acad Sci USA* **99**, 2860-5.

## Literatur

- Bartenschlager, R. & Lohmann, V. (2000). Replication of hepatitis C virus. *J Gen Virol* **81**, 1631-48.
- Bartosch, B., Dubuisson, J. & Cosset, F. L. (2003). Infectious hepatitis C virus pseudo-particles containing functional E1-E2 envelope protein complexes. *J Exp Med* **197**, 633-42.
- Baserga, R. (1991). Growth regulation of the PCNA gene. *J Cell Sci* **98 ( Pt 4)**, 433-6.
- Baud, V. & Karin, M. (2001). Signal transduction by tumor necrosis factor and its relatives. *Trends Cell Biol* **11**, 372-7.
- Baumert, T. F., Ito, S., Wong, D. T. & Liang, T. J. (1998). Hepatitis C virus structural proteins assemble into viruslike particles in insect cells. *J Virol* **72**, 3827-36.
- Bergametti, F., Denier, C., Labauge, P., Arnoult, M., Boetto, S., Clanet, M., Coubes, P., Echenne, B., Ibrahim, R., Irthum, B., Jacquet, G., Lonjon, M., Moreau, J. J., Neau, J. P., Parker, F., Tremoulet, M. & Tournier-Lasserre, E. (2005). Mutations within the programmed cell death 10 gene cause cerebral cavernous malformations. *Am J Hum Genet* **76**, 42-51.
- Birnboim, H. C. & Doly, J. (1979). A rapid alkaline extraction procedure for screening recombinant plasmid DNA. *Nucleic Acids Res* **7**, 1513-23.
- Biron, C. A. (1999). Initial and innate responses to viral infections--pattern setting in immunity or disease. *Curr Opin Microbiol* **2**, 374-81.
- Biron, C. A., Nguyen, K. B. & Pien, G. C. (2002). Innate immune responses to LCMV infections: natural killer cells and cytokines. *Curr Top Microbiol Immunol* **263**, 7-27.
- Blaschke, S., Mueller, C. A., Markovic-Lipkovski, J., Puch, S., Miosge, N., Becker, V., Mueller, G. A. & Klein, G. (2002). Expression of cadherin-8 in renal cell carcinoma and fetal kidney. *Int J Cancer* **101**, 327-34.
- Blight, K. J., McKeating, J. A., Marcotrigiano, J. & Rice, C. M. (2003). Efficient replication of hepatitis C virus genotype 1a RNAs in cell culture. *J Virol* **77**, 3181-90.
- Blight, K. J., McKeating, J. A. & Rice, C. M. (2002). Highly permissive cell lines for subgenomic and genomic hepatitis C virus RNA replication. *J Virol* **76**, 13001-14.
- Blindenbacher, A., Duong, F. H., Hunziker, L., Stutvoet, S. T., Wang, X., Terracciano, L., Moradpour, D., Blum, H. E., Alonzi, T., Tripodi, M., La Monica, N. & Heim, M. H. (2003). Expression of hepatitis c virus proteins inhibits interferon alpha signaling in the liver of transgenic mice. *Gastroenterology* **124**, 1465-75.
- Block, T. M., Mehta, A. S., Fimmel, C. J. & Jordan, R. (2003). Molecular viral oncology of hepatocellular carcinoma. *Oncogene* **22**, 5093-107.
- Boatright, K. M., Rensatus, M., Scott, F. L., Sperandio, S., Shin, H., Pedersen, I. M., Ricci, J. E., Edris, W. A., Sutherlin, D. P., Green, D. R. & Salvesen, G. S. (2003). A unified model for apical caspase activation. *Mol Cell* **11**, 529-41.
- Boldin, M. P., Goncharov, T. M., Goltsev, Y. V. & Wallach, D. (1996). Involvement of MACH, a novel MORT1/FADD-interacting protease, in Fas/APO-1- and TNF receptor-induced cell death. *Cell* **85**, 803-15.
- Bondzi, C., Grant, S. & Krystal, G. W. (2000). A novel assay for the measurement of Raf-1 kinase activity. *Oncogene* **19**, 5030-3.
- Bradford, M. M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem* **72**, 248-54.
- Brass, V., Bieck, E., Montserret, R., Wolk, B., Hellings, J. A., Blum, H. E., Penin, F. & Moradpour, D. (2002). An amino-terminal amphipathic alpha-helix mediates membrane association of the hepatitis C virus nonstructural protein 5A. *J Biol Chem* **277**, 8130-9.
- Brechot, C. (2004). Pathogenesis of hepatitis B virus-related hepatocellular carcinoma: old and new paradigms. *Gastroenterology* **127**, S56-61.

## Literatur

- Brinster, R. L., Allen, J. M., Behringer, R. R., Gelinas, R. E. & Palmiter, R. D. (1988). Introns increase transcriptional efficiency in transgenic mice. *Proc Natl Acad Sci U S A* **85**, 836-40.
- Bruder, J. T., Heidecker, G. & Rapp, U. R. (1992). Serum-, TPA-, and Ras-induced expression from Ap-1/Ets-driven promoters requires Raf-1 kinase. *Genes Dev* **6**, 545-56.
- Bruns, M., Gessner, A., Lothar, H. & Lehmann-Grube, F. (1988). Host cell-dependent homologous interference in lymphocytic choriomeningitis virus infection. *Virology* **166**, 133-9.
- Bukh, J., Pietschmann, T., Lohmann, V., Krieger, N., Faulk, K., Engle, R. E., Govindarajan, S., Shapiro, M., St Claire, M. & Bartenschlager, R. (2002). Mutations that permit efficient replication of hepatitis C virus RNA in Huh-7 cells prevent productive replication in chimpanzees. *Proc Natl Acad Sci U S A* **99**, 14416-21.
- Burckstümmer, T., Kriegs, M., Lupberger, J., Pauli, E. K., Schmitt, S. & Hildt, E. (2006). Raf-1 kinase associates with Hepatitis C virus NS5A and regulates viral replication. *FEBS Lett* **580**, 575-80.
- Bürkstümmer T. (2005), Identification of cellular targets of Hepatitis C Virus Non-structural Protein 5A. Promotion; *FU Berlin*.
- Castagna, M., Takai, Y., Kaibuchi, K., Sano, K., Kikkawa, U. & Nishizuka, Y. (1982). Direct activation of calcium-activated, phospholipid-dependent protein kinase by tumor-promoting phorbol esters. *J Biol Chem* **257**, 7847-51.
- Cha, S. S., Kim, M. S., Choi, Y. H., Sung, B. J., Shin, N. K., Shin, H. C., Sung, Y. C. & Oh, B. H. (1999). 2.8 Å resolution crystal structure of human TRAIL, a cytokine with selective antitumor activity. *Immunity* **11**, 253-61.
- Chang, H. Y. & Yang, X. (2000). Proteases for cell suicide: functions and regulation of caspases. *Microbiol Mol Biol Rev* **64**, 821-46.
- Chen, D. S., Kuo, G. C., Sung, J. L., Lai, M. Y., Sheu, J. C., Chen, P. J., Yang, P. M., Hsu, H. M., Chang, M. H., Chen, C. J. & et al. (1990). Hepatitis C virus infection in an area hyperendemic for hepatitis B and chronic liver disease: the Taiwan experience. *J Infect Dis* **162**, 817-22.
- Chen, G. & Goeddel, D. V. (2002). TNF-R1 signaling: a beautiful pathway. *Science* **296**, 1634-5.
- Chen, X., Cheung, S. T., So, S., Fan, S. T., Barry, C., Higgins, J., Lai, K. M., Ji, J., Dudoit, S., Ng, I. O., Van De Rijn, M., Botstein, D. & Brown, P. O. (2002). Gene expression patterns in human liver cancers. *Mol Biol Cell* **13**, 1929-39.
- Chinnaiyan, A. M., Tepper, C. G., Seldin, M. F., O'Rourke, K., Kischkel, F. C., Hellbardt, S., Krammer, P. H., Peter, M. E. & Dixit, V. M. (1996). FADD/MORT1 is a common mediator of CD95 (Fas/APO-1) and tumor necrosis factor receptor-induced apoptosis. *J Biol Chem* **271**, 4961-5.
- Chisari, F. V. (1989). Hepatitis B virus gene expression in transgenic mice. *Mol Biol Med* **6**, 143-9.
- Chisari, F. V., Klopchin, K., Moriyama, T., Pasquinelli, C., Dunsford, H. A., Sell, S., Pinkert, C. A., Brinster, R. L. & Palmiter, R. D. (1989). Molecular pathogenesis of hepatocellular carcinoma in hepatitis B virus transgenic mice. *Cell* **59**, 1145-56.
- Chomczynski, P. & Sacchi, N. (1987). Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal Biochem* **162**, 156-9.
- Chong, H., Lee, J. & Guan, K. L. (2001). Positive and negative regulation of Raf kinase activity and function by phosphorylation. *Embo J* **20**, 3716-27.
- Choo, Q. L., Kuo, G., Weiner, A. J., Overby, L. R., Bradley, D. W. & Houghton, M. (1989). Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science* **244**, 359-62.

## Literatur

- Chou, A. H., Tsai, H. F., Wu, Y. Y., Hu, C. Y., Hwang, L. H., Hsu, P. I. & Hsu, P. N. (2005). Hepatitis C virus core protein modulates TRAIL-mediated apoptosis by enhancing Bid cleavage and activation of mitochondria apoptosis signaling pathway. *J Immunol* **174**, 2160-6.
- Chu, Z. L., McKinsey, T. A., Liu, L., Gentry, J. J., Malim, M. H. & Ballard, D. W. (1997). Suppression of tumor necrosis factor-induced cell death by inhibitor of apoptosis c-IAP2 is under NF-kappaB control. *Proc Natl Acad Sci U S A* **94**, 10057-62.
- Chung, K. M., Lee, J., Kim, J. E., Song, O. K., Cho, S., Lim, J., Seedorf, M., Hahm, B. & Jang, S. K. (2000). Nonstructural protein 5A of hepatitis C virus inhibits the function of karyopherin beta3. *J Virol* **74**, 5233-41.
- Chung, Y. L., Sheu, M. L. & Yen, S. H. (2003). Hepatitis C virus NS5A as a potential viral Bcl-2 homologue interacts with Bax and inhibits apoptosis in hepatocellular carcinoma. *Int J Cancer* **107**, 65-73.
- Coito, C., Diamond, D. L., Neddermann, P., Korth, M. J. & Katze, M. G. (2004). High-throughput screening of the yeast kinome: identification of human serine/threonine protein kinases that phosphorylate the hepatitis C virus NS5A protein. *J Virol* **78**, 3502-13.
- Conacci-Sorrell, M., Zhurinsky, J. & Ben-Ze'ev, A. (2002). The cadherin-catenin adhesion system in signaling and cancer. *J Clin Invest* **109**, 987-91.
- Cook, S. J., Rubinfeld, B., Albert, I. & McCormick, F. (1993). RapV12 antagonizes Ras-dependent activation of ERK1 and ERK2 by LPA and EGF in Rat-1 fibroblasts. *Embo J* **12**, 3475-85.
- Daum, G., Eisenmann-Tappe, I., Fries, H. W., Troppmair, J. & Rapp, U. R. (1994). The ins and outs of Raf kinases. *Trends Biochem Sci* **19**, 474-80.
- Dent, P., Reardon, D. B., Morrison, D. K. & Sturgill, T. W. (1995). Regulation of Raf-1 and Raf-1 mutants by Ras-dependent and Ras-independent mechanisms in vitro. *Mol Cell Biol* **15**, 4125-35.
- Deveraux, Q. L., Leo, E., Stennicke, H. R., Welsh, K., Salvesen, G. S. & Reed, J. C. (1999). Cleavage of human inhibitor of apoptosis protein XIAP results in fragments with distinct specificities for caspases. *Embo J* **18**, 5242-51.
- Devin, A., Cook, A., Lin, Y., Rodriguez, Y., Kelliher, M. & Liu, Z. (2000). The distinct roles of TRAF2 and RIP in IKK activation by TNF-R1: TRAF2 recruits IKK to TNF-R1 while RIP mediates IKK activation. *Immunity* **12**, 419-29.
- Devin, A., Lin, Y., Yamaoka, S., Li, Z., Karin, M. & Liu, Z. (2001). The alpha and beta subunits of IkkappaB kinase (IKK) mediate TRAF2-dependent IKK recruitment to tumor necrosis factor (TNF) receptor 1 in response to TNF. *Mol Cell Biol* **21**, 3986-94.
- Dhillon, A. S. & Kolch, W. (2002). Untying the regulation of the Raf-1 kinase. *Arch Biochem Biophys* **404**, 3-9.
- Di Bisceglie, A. M. (2002). Epidemiology and clinical presentation of hepatocellular carcinoma. *J Vasc Interv Radiol* **13**, S169-71.
- Diamond, L., Kruszewski, F., Aden, D. P., Knowles, B. B. & Baird, W. M. (1980). Metabolic activation of benzo[a]pyrene by a human hepatoma cell line. *Carcinogenesis* **1**, 871-5.
- Dimitrova, M., Imbert, I., Kieny, M. P. & Schuster, C. (2003). Protein-protein interactions between hepatitis C virus nonstructural proteins. *J Virol* **77**, 5401-14.
- Ding, W. X. & Yin, X. M. (2004). Dissection of the multiple mechanisms of TNF-alpha-induced apoptosis in liver injury. *J Cell Mol Med* **8**, 445-54.
- Disson, O., Haouzi, D., Desagher, S., Loesch, K., Hahne, M., Kremer, E. J., Jacquet, C., Lemon, S. M., Hibner, U. & Lerat, H. (2004). Impaired clearance of virus-infected hepatocytes in transgenic mice expressing the hepatitis C virus polyprotein. *Gastroenterology* **126**, 859-72.

## Literatur

- Donepudi, M., Mac Sweeney, A., Briand, C. & Grutter, M. G. (2003). Insights into the regulatory mechanism for caspase-8 activation. *Mol Cell* **11**, 543-9.
- Du, C., Fang, M., Li, Y., Li, L. & Wang, X. (2000). Smac, a mitochondrial protein that promotes cytochrome c-dependent caspase activation by eliminating IAP inhibition. *Cell* **102**, 33-42.
- Dumaz, N. & Marais, R. (2005). Raf phosphorylation: one step forward and two steps back. *Mol Cell* **17**, 164-6.
- Earnshaw, W. C., Martins, L. M. & Kaufmann, S. H. (1999). Mammalian caspases: structure, activation, substrates, and functions during apoptosis. *Annu Rev Biochem* **68**, 383-424.
- El-Serag, H. B. (2002). Hepatocellular carcinoma and hepatitis C in the United States. *Hepatology* **36**, S74-83.
- Engels, I. H., Stepczynska, A., Stroh, C., Lauber, K., Berg, C., Schwenzler, R., Wajant, H., Janicke, R. U., Porter, A. G., Belka, C., Gregor, M., Schulze-Osthoff, K. & Wesselborg, S. (2000). Caspase-8/FLICE functions as an executioner caspase in anticancer drug-induced apoptosis. *Oncogene* **19**, 4563-73.
- Enomoto, N., Sakuma, I., Asahina, Y., Kurosaki, M., Murakami, T., Yamamoto, C., Izumi, N., Marumo, F. & Sato, C. (1995). Comparison of full-length sequences of interferon-sensitive and resistant hepatitis C virus 1b. Sensitivity to interferon is conferred by amino acid substitutions in the NS5A region. *J Clin Invest* **96**, 224-30.
- Enomoto, N., Sakuma, I., Asahina, Y., Kurosaki, M., Murakami, T., Yamamoto, C., Ogura, Y., Izumi, N., Marumo, F. & Sato, C. (1996). Mutations in the nonstructural protein 5A gene and response to interferon in patients with chronic hepatitis C virus 1b infection. *N Engl J Med* **334**, 77-81.
- Erhardt, A., Hassan, M., Heintges, T. & Haussinger, D. (2002). Hepatitis C virus core protein induces cell proliferation and activates ERK, JNK, and p38 MAP kinases together with the MAP kinase phosphatase MKP-1 in a HepG2 Tet-Off cell line. *Virology* **292**, 272-84.
- Ezelle, H. J., Balachandran, S., Sicheri, F., Polyak, S. J. & Barber, G. N. (2001). Analyzing the mechanisms of interferon-induced apoptosis using CrmA and hepatitis C virus NS5A. *Virology* **281**, 124-37.
- Fadeel, B., Gleiss, B., Hogstrand, K., Chandra, J., Wiedmer, T., Sims, P. J., Henter, J. I., Orrenius, S. & Samali, A. (1999). Phosphatidylserine exposure during apoptosis is a cell-type-specific event and does not correlate with plasma membrane phospholipid scramblase expression. *Biochem Biophys Res Commun* **266**, 504-11.
- Fattovich, G., Tagger, A., Brollo, L., Giustina, G., Pontisso, P., Realdi, G., Alberti, A. & Ruol, A. (1991). Hepatitis C virus infection in chronic hepatitis B virus carriers. *J Infect Dis* **163**, 400-2.
- Fiers, W. (1991). Tumor necrosis factor. Characterization at the molecular, cellular and in vivo level. *FEBS Lett* **285**, 199-212.
- Fishman, J. R., Gumerlock, P. H., Meyers, F. J. & deVere White, R. W. (1994). Quantitation of NM23 expression in human prostate tissues. *J Urol* **152**, 202-7.
- Fong, T. L., Di Bisceglie, A. M., Waggoner, J. G., Banks, S. M. & Hoofnagle, J. H. (1991). The significance of antibody to hepatitis C virus in patients with chronic hepatitis B. *Hepatology* **14**, 64-7.
- Fontana, R. J. & Lok, A. S. (2002). Noninvasive monitoring of patients with chronic hepatitis C. *Hepatology* **36**, S57-64.
- Fournier, C., Sureau, C., Coste, J., Ducos, J., Pageaux, G., Larrey, D., Domergue, J. & Maurel, P. (1998). In vitro infection of adult normal human hepatocytes in primary culture by hepatitis C virus. *J Gen Virol* **79** ( Pt 10), 2367-74.

## Literatur

- Foy, E., Li, K., Wang, C., Sumpter, R., Jr., Ikeda, M., Lemon, S. M. & Gale, M., Jr. (2003). Regulation of interferon regulatory factor-3 by the hepatitis C virus serine protease. *Science* **300**, 1145-8.
- Francois, C., Duverlie, G., Rebouillat, D., Khorsi, H., Castelain, S., Blum, H. E., Gatignol, A., Wychowski, C., Moradpour, D. & Meurs, E. F. (2000). Expression of hepatitis C virus proteins interferes with the antiviral action of interferon independently of PKR-mediated control of protein synthesis. *J Virol* **74**, 5587-96.
- Freeman, R. S., Ballantyne, S. M. & Donoghue, D. J. (1991). Meiotic induction by Xenopus cyclin B is accelerated by coexpression with mosXe. *Mol Cell Biol* **11**, 1713-7.
- Frelin, L., Brenndorfer, E. D., Ahlen, G., Weiland, M., Hultgren, C., Alheim, M., Glaumann, H., Rozell, B., Milich, D. R., Bode, J. G. & Sallberg, M. (2006). The hepatitis C virus and immune evasion: non-structural 3/4A transgenic mice are resistant to lethal tumour necrosis factor {alpha} mediated liver disease. *Gut* **55**, 1475-83.
- Frese, M., Barth, K., Kaul, A., Lohmann, V., Schwarzle, V. & Bartenschlager, R. (2003). Hepatitis C virus RNA replication is resistant to tumour necrosis factor-alpha. *J Gen Virol* **84**, 1253-9.
- Frese, M., Pietschmann, T., Moradpour, D., Haller, O. & Bartenschlager, R. (2001). Interferon-alpha inhibits hepatitis C virus subgenomic RNA replication by an MxA-independent pathway. *J Gen Virol* **82**, 723-33.
- Fujioka, Y., Taira, T., Maeda, Y., Tanaka, S., Nishihara, H., Iguchi-Arigo, S. M., Nagashima, K. & Ariga, H. (2001). MM-1, a c-Myc-binding protein, is a candidate for a tumor suppressor in leukemia/lymphoma and tongue cancer. *J Biol Chem* **276**, 45137-44.
- Gale, M., Jr., Blakely, C. M., Kwieciszewski, B., Tan, S. L., Dossett, M., Tang, N. M., Korth, M. J., Polyak, S. J., Gretch, D. R. & Katze, M. G. (1998). Control of PKR protein kinase by hepatitis C virus nonstructural 5A protein: molecular mechanisms of kinase regulation. *Mol Cell Biol* **18**, 5208-18.
- Gale, M. J., Jr., Korth, M. J., Tang, N. M., Tan, S. L., Hopkins, D. A., Dever, T. E., Polyak, S. J., Gretch, D. R. & Katze, M. G. (1997). Evidence that hepatitis C virus resistance to interferon is mediated through repression of the PKR protein kinase by the nonstructural 5A protein. *Virology* **230**, 217-27.
- Gao, L., Aizaki, H., He, J. W. & Lai, M. M. (2004). Interactions between viral nonstructural proteins and host protein hVAP-33 mediate the formation of hepatitis C virus RNA replication complex on lipid raft. *J Virol* **78**, 3480-8.
- Garson, J. A., Brillanti, S., Whitby, K., Foli, M., Deaville, R., Masci, C., Miglioli, M. & Barbara, L. (1995). Analysis of clinical and virological factors associated with response to alpha interferon therapy in chronic hepatitis C. *J Med Virol* **45**, 348-53.
- Geiss, G. K., Carter, V. S., He, Y., Kwieciszewski, B. K., Holzman, T., Korth, M. J., Lazaro, C. A., Fausto, N., Bumgarner, R. E. & Katze, M. G. (2003). Gene expression profiling of the cellular transcriptional network regulated by alpha/beta interferon and its partial attenuation by the hepatitis C virus nonstructural 5A protein. *J Virol* **77**, 6367-75.
- Georgopoulou, U., Caravokiri, K. & Mavromara, P. (2003). Suppression of the ERK1/2 signaling pathway from HCV NS5A protein expressed by herpes simplex recombinant viruses. *Arch Virol* **148**, 237-51.
- Ghosh, A. K., Majumder, M., Steele, R., Meyer, K., Ray, R. & Ray, R. B. (2000a). Hepatitis C virus NS5A protein protects against TNF-alpha mediated apoptotic cell death. *Virus Res* **67**, 173-8.
- Ghosh, A. K., Majumder, M., Steele, R., Ray, R. & Ray, R. B. (2003). Modulation of interferon expression by hepatitis C virus NS5A protein and human homeodomain protein PTX1. *Virology* **306**, 51-9.

## Literatur

- Ghosh, A. K., Majumder, M., Steele, R., Yaciuk, P., Chrivia, J., Ray, R. & Ray, R. B. (2000b). Hepatitis C virus NS5A protein modulates transcription through a novel cellular transcription factor SRCAP. *J Biol Chem* **275**, 7184-8.
- Ghosh, A. K., Steele, R., Meyer, K., Ray, R. & Ray, R. B. (1999). Hepatitis C virus NS5A protein modulates cell cycle regulatory genes and promotes cell growth. *J Gen Virol* **80 ( Pt 5)**, 1179-83.
- Ghosh, S., May, M. J. & Kopp, E. B. (1998). NF-kappa B and Rel proteins: evolutionarily conserved mediators of immune responses. *Annu Rev Immunol* **16**, 225-60.
- Girard, S., Shalhoub, P., Lescure, P., Sabile, A., Misek, D. E., Hanash, S., Brechot, C. & Beretta, L. (2002). An altered cellular response to interferon and up-regulation of interleukin-8 induced by the hepatitis C viral protein NS5A uncovered by microarray analysis. *Virology* **295**, 272-83.
- Girard, S., Vossman, E., Misek, D. E., Podevin, P., Hanash, S., Brechot, C. & Beretta, L. (2004). Hepatitis C virus NS5A-regulated gene expression and signaling revealed via microarray and comparative promoter analyses. *Hepatology* **40**, 708-18.
- Goldstein, J. C., Waterhouse, N. J., Juin, P., Evan, G. I. & Green, D. R. (2000). The coordinate release of cytochrome c during apoptosis is rapid, complete and kinetically invariant. *Nat Cell Biol* **2**, 156-62.
- Gong, G., Waris, G., Tanveer, R. & Siddiqui, A. (2001). Human hepatitis C virus NS5A protein alters intracellular calcium levels, induces oxidative stress, and activates STAT-3 and NF-kappa B. *Proc Natl Acad Sci U S A* **98**, 9599-604.
- Green, D. R. & Evan, G. I. (2002). A matter of life and death. *Cancer Cell* **1**, 19-30.
- Hakem, R., Hakem, A., Duncan, G. S., Henderson, J. T., Woo, M., Soengas, M. S., Elia, A., de la Pompa, J. L., Kagi, D., Khoo, W., Potter, J., Yoshida, R., Kaufman, S. A., Lowe, S. W., Penninger, J. M. & Mak, T. W. (1998). Differential requirement for caspase 9 in apoptotic pathways in vivo. *Cell* **94**, 339-52.
- Hatzakis, A., Katsoulidou, A., Kaklamani, E., Touloumi, G., Koumantaki, Y., Tassopoulos, N. C., Karvountzis, G., Gioustozi, A., Hadziyannis, S. & Trichopoulos, D. (1996). Hepatitis C virus 1b is the dominant genotype in HCV-related carcinogenesis: a case-control study. *Int J Cancer* **68**, 51-3.
- Hayakawa, M., Miyashita, H., Sakamoto, I., Kitagawa, M., Tanaka, H., Yasuda, H., Karin, M. & Kikugawa, K. (2003). Evidence that reactive oxygen species do not mediate NF-kappaB activation. *Embo J* **22**, 3356-66.
- Hayashi, J., Aoki, H., Kajino, K., Moriyama, M., Arakawa, Y. & Hino, O. (2000). Hepatitis C virus core protein activates the MAPK/ERK cascade synergistically with tumor promoter TPA, but not with epidermal growth factor or transforming growth factor alpha. *Hepatology* **32**, 958-61.
- Hazzalin, C. A. & Mahadevan, L. C. (2002). MAPK-regulated transcription: a continuously variable gene switch? *Nat Rev Mol Cell Biol* **3**, 30-40.
- He, Y., Nakao, H., Tan, S. L., Polyak, S. J., Neddermann, P., Vijaysri, S., Jacobs, B. L. & Katze, M. G. (2002). Subversion of cell signaling pathways by hepatitis C virus nonstructural 5A protein via interaction with Grb2 and P85 phosphatidylinositol 3-kinase. *J Virol* **76**, 9207-17.
- He, Y., Tan, S. L., Tareen, S. U., Vijaysri, S., Llangland, J. O., Jacobs, B. L. & Katze, M. G. (2001). Regulation of mRNA translation and cellular signaling by hepatitis C virus nonstructural protein NS5A. *J Virol* **75**, 5090-8.
- Heukeshoven, J. & Dernick, R. (1988). Improved silver staining procedure for fast staining in PhastSystem Development Unit. I. Staining of sodium dodecyl sulfate gels. *Electrophoresis* **9**, 28-32.
- Hildt, E. & Hofschneider, P. H. (1998). The PreS2 activators of the hepatitis B virus: activators of tumour promoter pathways. *Recent Results Cancer Res* **154**, 315-29.

## Literatur

- Hildt, E., Munz, B., Saher, G., Reifenberg, K. & Hofschneider, P. H. (2002). The PreS2 activator MHBs(t) of hepatitis B virus activates c-raf-1/Erk2 signaling in transgenic mice. *Embo J* **21**, 525-35.
- Hirota, M., Satoh, S., Asabe, S., Kohara, M., Tsukiyama-Kohara, K., Kato, N., Hijikata, M. & Shimotohno, K. (1999). Phosphorylation of nonstructural 5A protein of hepatitis C virus: HCV group-specific hyperphosphorylation. *Virology* **257**, 130-7.
- Hoffman, B., Liebermann, D. A., Selvakumaran, M. & Nguyen, H. Q. (1996). Role of c-myc in myeloid differentiation, growth arrest and apoptosis. *Curr Top Microbiol Immunol* **211**, 17-27.
- Honda, A., Arai, Y., Hirota, N., Sato, T., Ikegaki, J., Koizumi, T., Hatano, M., Kohara, M., Moriyama, T., Imawari, M., Shimotohno, K. & Tokuhisa, T. (1999). Hepatitis C virus structural proteins induce liver cell injury in transgenic mice. *J Med Virol* **59**, 281-9.
- Hoofnagle, J. H. (2002). Course and outcome of hepatitis C. *Hepatology* **36**, S21-9.
- Hsu, H., Huang, J., Shu, H. B., Baichwal, V. & Goeddel, D. V. (1996a). TNF-dependent recruitment of the protein kinase RIP to the TNF receptor-1 signaling complex. *Immunity* **4**, 387-96.
- Hsu, H., Shu, H. B., Pan, M. G. & Goeddel, D. V. (1996b). TRADD-TRAF2 and TRADD-FADD interactions define two distinct TNF receptor 1 signal transduction pathways. *Cell* **84**, 299-308.
- Huang, L., Hwang, J., Sharma, S. D., Hargittai, M. R., Chen, Y., Arnold, J. J., Raney, K. D. & Cameron, C. E. (2005). Hepatitis C virus nonstructural protein 5A (NS5A) is an RNA-binding protein. *J Biol Chem* **280**, 36417-28.
- Huser, M., Lockett, J., Chiloeches, A., Mercer, K., Iwobi, M., Giblett, S., Sun, X. M., Brown, J., Marais, R. & Pritchard, C. (2001). MEK kinase activity is not necessary for Raf-1 function. *Embo J* **20**, 1940-51.
- Huynh, H., Nguyen, T. T., Chow, K. H., Tan, P. H., Soo, K. C. & Tran, E. (2003). Over-expression of the mitogen-activated protein kinase (MAPK) kinase (MEK)-MAPK in hepatocellular carcinoma: its role in tumor progression and apoptosis. *BMC Gastroenterol* **3**, 19.
- Hymowitz, S. G., Christinger, H. W., Fuh, G., Ultsch, M., O'Connell, M., Kelley, R. F., Ashkenazi, A. & de Vos, A. M. (1999). Triggering cell death: the crystal structure of Apo2L/TRAIL in a complex with death receptor 5. *Mol Cell* **4**, 563-71.
- Iizuka, N., Oka, M., Noma, T., Nakazawa, A., Hirose, K. & Suzuki, T. (1995). NM23-H1 and NM23-H2 messenger RNA abundance in human hepatocellular carcinoma. *Cancer Res* **55**, 652-7.
- Itoh, N. & Nagata, S. (1993). A novel protein domain required for apoptosis. Mutational analysis of human Fas antigen. *J Biol Chem* **268**, 10932-7.
- Jiang, Y., Woronicz, J. D., Liu, W. & Goeddel, D. V. (1999). Prevention of constitutive TNF receptor 1 signaling by silencer of death domains. *Science* **283**, 543-6.
- Jones, E. Y., Stuart, D. I. & Walker, N. P. (1989). Structure of tumour necrosis factor. *Nature* **338**, 225-8.
- Jorns, J., Mangold, U., Neumann, U., Van Damme, E. J., Peumans, W. J., Pfuller, U. & Schumacher, U. (2003). Lectin histochemistry of the lymphoid organs of the chicken. *Anat Embryol (Berl)* **207**, 85-94.
- Kaizu, H., Cho, D., Matsuki, A., Ohkoshi, S., Nomoto, M. & Asakura, H. (2000). Gamma-ray induced hepatocarcinogenesis in p53-deficient mice. *Anticancer Res* **20**, 1545-9.
- Kalkeri, G., Khalap, N., Garry, R. F., Fermin, C. D. & Dash, S. (2001). Hepatitis C virus protein expression induces apoptosis in HepG2 cells. *Virology* **282**, 26-37.
- Kamada, S., Washida, M., Hasegawa, J., Kusano, H., Funahashi, Y. & Tsujimoto, Y. (1997). Involvement of caspase-4(-like) protease in Fas-mediated apoptotic pathway. *Oncogene* **15**, 285-90.



## Literatur

- Kaneko, T., Tanji, Y., Satoh, S., Hijikata, M., Asabe, S., Kimura, K. & Shimotohno, K. (1994). Production of two phosphoproteins from the NS5A region of the hepatitis C viral genome. *Biochem Biophys Res Commun* **205**, 320-6.
- Karpinich, N. O., Tafani, M., Rothman, R. J., Russo, M. A. & Farber, J. L. (2002). The course of etoposide-induced apoptosis from damage to DNA and p53 activation to mitochondrial release of cytochrome c. *J Biol Chem* **277**, 16547-52.
- Kato, N., Lan, K. H., Ono-Nita, S. K., Shiratori, Y. & Omata, M. (1997). Hepatitis C virus nonstructural region 5A protein is a potent transcriptional activator. *J Virol* **71**, 8856-9.
- Kato, T., Miyamoto, M., Date, T., Yasui, K., Taya, C., Yonekawa, H., Ohue, C., Yagi, S., Seki, E., Hirano, T., Fujimoto, J., Shirai, T. & Wakita, T. (2003). Repeated hepatocyte injury promotes hepatic tumorigenesis in hepatitis C virus transgenic mice. *Cancer Sci* **94**, 679-85.
- Katoh, M. (2004). Identification and characterization of PDZRN3 and PDZRN4 genes in silico. *Int J Mol Med* **13**, 607-13.
- Katze, M. G., Kwieciszewski, B., Goodlett, D. R., Blakely, C. M., Neddermann, P., Tan, S. L. & Aebersold, R. (2000). Ser(2194) is a highly conserved major phosphorylation site of the hepatitis C virus nonstructural protein NS5A. *Virology* **278**, 501-13.
- Kaufmann, S. H., Desnoyers, S., Ottaviano, Y., Davidson, N. E. & Poirier, G. G. (1993). Specific proteolytic cleavage of poly(ADP-ribose) polymerase: an early marker of chemotherapy-induced apoptosis. *Cancer Res* **53**, 3976-85.
- Kawakami, T., Furukawa, Y., Sudo, K., Saito, H., Takami, S., Takahashi, E. & Nakamura, Y. (1995). Isolation and mapping of a human gene (PDCD2) that is highly homologous to Rp8, a rat gene associated with programmed cell death. *Cytogenet Cell Genet* **71**, 41-3.
- Kelliher, M. A., Grimm, S., Ishida, Y., Kuo, F., Stanger, B. Z. & Leder, P. (1998). The death domain kinase RIP mediates the TNF-induced NF-kappaB signal. *Immunity* **8**, 297-303.
- Kim, C. M., Koike, K., Saito, I., Miyamura, T. & Jay, G. (1991). HBx gene of hepatitis B virus induces liver cancer in transgenic mice. *Nature* **351**, 317-20.
- Kim, J., Lee, D. & Choe, J. (1999). Hepatitis C virus NS5A protein is phosphorylated by casein kinase II. *Biochem Biophys Res Commun* **257**, 777-81.
- Kimberley, F. C. & Screaton, G. R. (2004). Following a TRAIL: update on a ligand and its five receptors. *Cell Res* **14**, 359-72.
- Kipreos, E. T. & Pagano, M. (2000). The F-box protein family. *Genome Biol* **1**, REVIEWS3002.
- Kisseljov, F. L. (2000). Virus-associated human tumors: cervical carcinomas and papilloma viruses. *Biochemistry (Mosc)* **65**, 68-77.
- Klein, N. P. & Schneider, R. J. (1997). Activation of Src family kinases by hepatitis B virus HBx protein and coupled signaling to Ras. *Mol Cell Biol* **17**, 6427-36.
- Koch, J. O. & Bartenschlager, R. (1999). Modulation of hepatitis C virus NS5A hyperphosphorylation by nonstructural proteins NS3, NS4A, and NS4B. *J Virol* **73**, 7138-46.
- Koike, K. (2002). Hepatocarcinogenesis in hepatitis viral infection: lessons from transgenic mouse studies. *J Gastroenterol* **37 Suppl 13**, 55-64.
- Koike, T., Wang, X., Unoki, H., Liang, J., Ichikawa, T., Kitajima, S., Watanabe, T. & Fan, J. (2002). Increased expression of lipoprotein lipase in transgenic rabbits does not lead to abnormalities in skeletal and heart muscles. *Muscle Nerve* **26**, 823-7.
- Kolch, W. (2000). Meaningful relationships: the regulation of the Ras/Raf/MEK/ERK pathway by protein interactions. *Biochem J* **351 Pt 2**, 289-305.

## Literatur

- Kolch, W., Heidecker, G., Kochs, G., Hummel, R., Vahidi, H., Mischak, H., Finkenzeller, G., Marme, D. & Rapp, U. R. (1993). Protein kinase C alpha activates RAF-1 by direct phosphorylation. *Nature* **364**, 249-52.
- Korkaya, H., Jameel, S., Gupta, D., Tyagi, S., Kumar, R., Zafrullah, M., Mazumdar, M., Lal, S. K., Xiaofang, L., Sehgal, D., Das, S. R. & Sahal, D. (2001). The ORF3 protein of hepatitis E virus binds to Src homology 3 domains and activates MAPK. *J Biol Chem* **276**, 42389-400.
- Krammer, P. H. (2000). CD95's deadly mission in the immune system. *Nature* **407**, 789-95.
- Krieger, N., Lohmann, V. & Bartenschlager, R. (2001). Enhancement of hepatitis C virus RNA replication by cell culture-adaptive mutations. *J Virol* **75**, 4614-24.
- Laack, E., Nikbakht, H., Peters, A., Kugler, C., Jasiewicz, Y., Edler, L., Hossfeld, D. K. & Schumacher, U. (2002). Lectin histochemistry of resected adenocarcinoma of the lung: helix pomatia agglutinin binding is an independent prognostic factor. *Am J Pathol* **160**, 1001-8.
- Laemmli, U. K. (1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* **227**, 680-5.
- Lan, K. H., Sheu, M. L., Hwang, S. J., Yen, S. H., Chen, S. Y., Wu, J. C., Wang, Y. J., Kato, N., Omata, M., Chang, F. Y. & Lee, S. D. (2002). HCV NS5A interacts with p53 and inhibits p53-mediated apoptosis. *Oncogene* **21**, 4801-11.
- Lau, J. Y., Xie, X., Lai, M. M. & Wu, P. C. (1998). Apoptosis and viral hepatitis. *Semin Liver Dis* **18**, 169-76.
- LeBlanc, H., Lawrence, D., Varfolomeev, E., Totpal, K., Morlan, J., Schow, P., Fong, S., Schwall, R., Sinicropi, D. & Ashkenazi, A. (2002). Tumor-cell resistance to death receptor--induced apoptosis through mutational inactivation of the proapoptotic Bcl-2 homolog Bax. *Nat Med* **8**, 274-81.
- Lehmann-Grube, F (1971), Lymphocytic choriomeningitis virus. *Virology Monographs*
- Lehmann-Grube, F., Assmann, U., Loliger, C., Moskophidis, D. & Lohler, J. (1985). Mechanism of recovery from acute virus infection. I. Role of T lymphocytes in the clearance of lymphocytic choriomeningitis virus from spleens of mice. *J Immunol* **134**, 608-15.
- Leist, M., Gantner, F., Bohlinger, I., Germann, P. G., Tiegs, G. & Wendel, A. (1994). Murine hepatocyte apoptosis induced in vitro and in vivo by TNF-alpha requires transcriptional arrest. *J Immunol* **153**, 1778-88.
- Leong, K. G. & Karsan, A. (2000). Signaling pathways mediated by tumor necrosis factor alpha. *Histol Histopathol* **15**, 1303-25.
- Lerat, H., Honda, M., Beard, M. R., Loesch, K., Sun, J., Yang, Y., Okuda, M., Gosert, R., Xiao, S. Y., Weinman, S. A. & Lemon, S. M. (2002). Steatosis and liver cancer in transgenic mice expressing the structural and nonstructural proteins of hepatitis C virus. *Gastroenterology* **122**, 352-65.
- Levrero, M. (2006). Viral hepatitis and liver cancer: the case of hepatitis C. *Oncogene* **25**, 3834-47.
- Li, H., Zhu, H., Xu, C. J. & Yuan, J. (1998). Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis. *Cell* **94**, 491-501.
- Li, S. & Sedivy, J. M. (1993). Raf-1 protein kinase activates the NF-kappa B transcription factor by dissociating the cytoplasmic NF-kappa B-I kappa B complex. *Proc Natl Acad Sci U S A* **90**, 9247-51.
- Liang, Y., Kang, C. B. & Yoon, H. S. (2006). Molecular and structural characterization of the domain 2 of hepatitis C virus non-structural protein 5A. *Mol Cells* **22**, 13-20.
- Lin, L. Y., Li, S. C. & Lu, S. L. (2003). [Hepatitis C virus nonstructural 5A protein inhibits tumor necrosis factor alpha mediated apoptosis of HepG2 cells]. *Zhonghua Nei Ke Za Zhi* **42**, 392-5.

## Literatur

- Lin, Y., Devin, A., Rodriguez, Y. & Liu, Z. G. (1999). Cleavage of the death domain kinase RIP by caspase-8 prompts TNF-induced apoptosis. *Genes Dev* **13**, 2514-26.
- Lindenbach, B. D., Evans, M. J., Syder, A. J., Wolk, B., Tellinghuisen, T. L., Liu, C. C., Maruyama, T., Hynes, R. O., Burton, D. R., McKeating, J. A. & Rice, C. M. (2005). Complete replication of hepatitis C virus in cell culture. *Science* **309**, 623-6.
- Littlewood, T. D. & Evan, G. I. (1990). The role of myc oncogenes in cell growth and differentiation. *Adv Dent Res* **4**, 69-79.
- Locksley, R. M., Killeen, N. & Lenardo, M. J. (2001). The TNF and TNF receptor superfamilies: integrating mammalian biology. *Cell* **104**, 487-501.
- Lohmann, V., Hoffmann, S., Herian, U., Penin, F. & Bartenschlager, R. (2003). Viral and cellular determinants of hepatitis C virus RNA replication in cell culture. *J Virol* **77**, 3007-19.
- Lohmann, V., Korner, F., Dobierzewska, A. & Bartenschlager, R. (2001). Mutations in hepatitis C virus RNAs conferring cell culture adaptation. *J Virol* **75**, 1437-49.
- Lohmann, V., Korner, F., Koch, J., Herian, U., Theilmann, L. & Bartenschlager, R. (1999). Replication of subgenomic hepatitis C virus RNAs in a hepatoma cell line. *Science* **285**, 110-3.
- Lu, X., Lee, M., Tran, T. & Block, T. (2005). High level expression of apoptosis inhibitor in hepatoma cell line expressing Hepatitis B virus. *Int J Med Sci* **2**, 30-35.
- Ludwig, L., Kessler, H., Wagner, M., Hoang-Vu, C., Dralle, H., Adler, G., Bohm, B. O. & Schmid, R. M. (2001). Nuclear factor-kappaB is constitutively active in C-cell carcinoma and required for RET-induced transformation. *Cancer Res* **61**, 4526-35.
- Luo, X., Budihardjo, I., Zou, H., Slaughter, C. & Wang, X. (1998). Bid, a Bcl2 interacting protein, mediates cytochrome c release from mitochondria in response to activation of cell surface death receptors. *Cell* **94**, 481-90.
- Macdonald, A., Chan, J. K. & Harris, M. (2005). Perturbation of epidermal growth factor receptor complex formation and Ras signalling in cells harbouring the hepatitis C virus subgenomic replicon. *J Gen Virol* **86**, 1027-33.
- Macdonald, A., Crowder, K., Street, A., McCormick, C. & Harris, M. (2004). The hepatitis C virus NS5A protein binds to members of the Src family of tyrosine kinases and regulates kinase activity. *J Gen Virol* **85**, 721-9.
- Macdonald, A., Crowder, K., Street, A., McCormick, C., Saksela, K. & Harris, M. (2003). The hepatitis C virus non-structural NS5A protein inhibits activating protein-1 function by perturbing ras-ERK pathway signaling. *J Biol Chem* **278**, 17775-84.
- Macdonald, A. & Harris, M. (2004). Hepatitis C virus NS5A: tales of a promiscuous protein. *J Gen Virol* **85**, 2485-502.
- MacEwan, D. J. (2002). TNF ligands and receptors--a matter of life and death. *Br J Pharmacol* **135**, 855-75.
- Machida, K., Tsukiyama-Kohara, K., Seike, E., Tone, S., Shibasaki, F., Shimizu, M., Takahashi, H., Hayashi, Y., Funata, N., Taya, C., Yonekawa, H. & Kohara, M. (2001). Inhibition of cytochrome c release in Fas-mediated signaling pathway in transgenic mice induced to express hepatitis C viral proteins. *J Biol Chem* **276**, 12140-6.
- Maga, G. & Hubscher, U. (2003). Proliferating cell nuclear antigen (PCNA): a dancer with many partners. *J Cell Sci* **116**, 3051-60.
- Magnuson, N. S., Beck, T., Vahidi, H., Hahn, H., Smola, U. & Rapp, U. R. (1994). The Raf-1 serine/threonine protein kinase. *Semin Cancer Biol* **5**, 247-53.
- Major, M. E. & Feinstone, S. M. (1997). The molecular virology of hepatitis C. *Hepatology* **25**, 1527-38.
- Major, M. E., Mihalik, K., Fernandez, J., Seidman, J., Kleiner, D., Kolykhalov, A. A., Rice, C. M. & Feinstone, S. M. (1999). Long-term follow-up of chimpanzees inoculated with the first infectious clone for hepatitis C virus. *J Virol* **73**, 3317-25.

## Literatur

- Majumder, M., Ghosh, A. K., Steele, R., Ray, R. & Ray, R. B. (2001). Hepatitis C virus NS5A physically associates with p53 and regulates p21/waf1 gene expression in a p53-dependent manner. *J Virol* **75**, 1401-7.
- Majumder, M., Ghosh, A. K., Steele, R., Zhou, X. Y., Phillips, N. J., Ray, R. & Ray, R. B. (2002). Hepatitis C virus NS5A protein impairs TNF-mediated hepatic apoptosis, but not by an anti-FAS antibody, in transgenic mice. *Virology* **294**, 94-105.
- Majumder, M., Steele, R., Ghosh, A. K., Zhou, X. Y., Thornburg, L., Ray, R., Phillips, N. J. & Ray, R. B. (2003). Expression of hepatitis C virus non-structural 5A protein in the liver of transgenic mice. *FEBS Lett* **555**, 528-32.
- Maniatis, T. (1997). Catalysis by a multiprotein IkappaB kinase complex. *Science* **278**, 818-9.
- Mariani, S. M. & Krammer, P. H. (1998). Differential regulation of TRAIL and CD95 ligand in transformed cells of the T and B lymphocyte lineage. *Eur J Immunol* **28**, 973-82.
- Martinez-Hernandez, A. & Amenta, P. S. (1993). The hepatic extracellular matrix. II. Ontogenesis, regeneration and cirrhosis. *Virchows Arch A Pathol Anat Histopathol* **423**, 77-84.
- Marusawa, H., Hijikata, M., Chiba, T. & Shimotohno, K. (1999). Hepatitis C virus core protein inhibits Fas- and tumor necrosis factor alpha-mediated apoptosis via NF-kappaB activation. *J Virol* **73**, 4713-20.
- Mason, C. S., Springer, C. J., Cooper, R. G., Superti-Furga, G., Marshall, C. J. & Marais, R. (1999). Serine and tyrosine phosphorylations cooperate in Raf-1, but not B-Raf activation. *Embo J* **18**, 2137-48.
- Masumi, A., Aizaki, H., Suzuki, T., DuHadaway, J. B., Prendergast, G. C., Komuro, K. & Fukazawa, H. (2005). Reduction of hepatitis C virus NS5A phosphorylation through its interaction with amphiphysin II. *Biochem Biophys Res Commun* **336**, 572-8.
- Medema, J. P., Scaffidi, C., Kischkel, F. C., Shevchenko, A., Mann, M., Krammer, P. H. & Peter, M. E. (1997). FLICE is activated by association with the CD95 death-inducing signaling complex (DISC). *Embo J* **16**, 2794-804.
- Meier, P., Finch, A. & Evan, G. (2000). Apoptosis in development. *Nature* **407**, 796-801.
- Mercer, D. F., Schiller, D. E., Elliott, J. F., Douglas, D. N., Hao, C., Rinfret, A., Addison, W. R., Fischer, K. P., Churchill, T. A., Lakey, J. R., Tyrrell, D. L. & Kneteman, N. M. (2001). Hepatitis C virus replication in mice with chimeric human livers. *Nat Med* **7**, 927-33.
- Miller, R. H. & Purcell, R. H. (1990). Hepatitis C virus shares amino acid sequence similarity with pestiviruses and flaviviruses as well as members of two plant virus supergroups. *Proc Natl Acad Sci U S A* **87**, 2057-61.
- Miller, W. E. & Raab-Traub, N. (1999). The EGFR as a target for viral oncoproteins. *Trends Microbiol* **7**, 453-8.
- Miltenberger, R. J., Cortner, J. & Farnham, P. J. (1993). An inhibitory Raf-1 mutant suppresses expression of a subset of v-raf-activated genes. *J Biol Chem* **268**, 15674-80.
- Miyasaka, Y., Enomoto, N., Kurosaki, M., Sakamoto, N., Kanazawa, N., Kohashi, T., Ueda, E., Maekawa, S., Watanabe, H., Izumi, N., Sato, C. & Watanabe, M. (2003). Hepatitis C virus nonstructural protein 5A inhibits tumor necrosis factor-alpha-mediated apoptosis in Huh7 cells. In *J Infect Dis*, pp. 1537-44.
- Mongkolsapaya, J., Grimes, J. M., Chen, N., Xu, X. N., Stuart, D. I., Jones, E. Y. & Screaton, G. R. (1999). Structure of the TRAIL-DR5 complex reveals mechanisms conferring specificity in apoptotic initiation. *Nat Struct Biol* **6**, 1048-53.
- Moradpour, D., Brass, V., Bieck, E., Friebe, P., Gosert, R., Blum, H. E., Bartenschlager, R., Penin, F. & Lohmann, V. (2004). Membrane association of the RNA-dependent RNA polymerase is essential for hepatitis C virus RNA replication. *J Virol* **78**, 13278-84.

## Literatur

- Moradpour, D., Brass, V. & Penin, F. (2005). Function follows form: the structure of the N-terminal domain of HCV NS5A. *Hepatology* **42**, 732-5.
- Moriya, K., Fujie, H., Shintani, Y., Yotsuyanagi, H., Tsutsumi, T., Ishibashi, K., Matsuura, Y., Kimura, S., Miyamura, T. & Koike, K. (1998). The core protein of hepatitis C virus induces hepatocellular carcinoma in transgenic mice. *Nat Med* **4**, 1065-7.
- Morrison, D. K., Heidecker, G., Rapp, U. R. & Copeland, T. D. (1993). Identification of the major phosphorylation sites of the Raf-1 kinase. *J Biol Chem* **268**, 17309-16.
- Moss, M. L., Jin, S. L., Milla, M. E., Bickett, D. M., Burkhart, W., Carter, H. L., Chen, W. J., Clay, W. C., Didsbury, J. R., Hassler, D., Hoffman, C. R., Kost, T. A., Lambert, M. H., Leesnitzer, M. A., McCauley, P., McGeehan, G., Mitchell, J., Moyer, M., Pahel, G., Rocque, W., Overton, L. K., Schoenen, F., Seaton, T., Su, J. L., Becherer, J. D. & et al. (1997). Cloning of a disintegrin metalloproteinase that processes precursor tumour-necrosis factor-alpha. *Nature* **385**, 733-6.
- Muller, M., Strand, S., Hug, H., Heinemann, E. M., Walczak, H., Hofmann, W. J., Stremmel, W., Krammer, P. H. & Galle, P. R. (1997). Drug-induced apoptosis in hepatoma cells is mediated by the CD95 (APO-1/Fas) receptor/ligand system and involves activation of wild-type p53. *J Clin Invest* **99**, 403-13.
- Muratori, L. & Gibellini, D. (2001). A new route to apoptosis in hepatitis C virus infection. *J Hepatol* **35**, 814-5.
- Muzio, M., Chinnaiyan, A. M., Kischkel, F. C., O'Rourke, K., Shevchenko, A., Ni, J., Scaffidi, C., Bretz, J. D., Zhang, M., Gentz, R., Mann, M., Krammer, P. H., Peter, M. E. & Dixit, V. M. (1996). FLICE, a novel FADD-homologous ICE/CED-3-like protease, is recruited to the CD95 (Fas/APO-1) death--inducing signaling complex. *Cell* **85**, 817-27.
- Muzio, M., Stockwell, B. R., Stennicke, H. R., Salvesen, G. S. & Dixit, V. M. (1998). An induced proximity model for caspase-8 activation. *J Biol Chem* **273**, 2926-30.
- Nagata, S. (1997). Apoptosis by death factor. *Cell* **88**, 355-65.
- Nakabayashi, H., Taketa, K., Miyano, K., Yamane, T. & Sato, J. (1982). Growth of human hepatoma cells lines with differentiated functions in chemically defined medium. *Cancer Res* **42**, 3858-63.
- Nakanishi, F., Ohkawa, K., Ishida, H., Hosui, A., Sato, A., Hiramatsu, N., Ueda, K., Takehara, T., Kasahara, A., Sasaki, Y., Hori, M. & Hayashi, N. (2005). Alteration in gene expression profile by full-length hepatitis B virus genome. *Intervirology* **48**, 77-83.
- Nakano, H., Shindo, M., Sakon, S., Nishinaka, S., Mihara, M., Yagita, H. & Okumura, K. (1998). Differential regulation of IkappaB kinase alpha and beta by two upstream kinases, NF-kappaB-inducing kinase and mitogen-activated protein kinase/ERK kinase kinase-1. *Proc Natl Acad Sci U S A* **95**, 3537-42.
- Neddermann, P., Clementi, A. & De Francesco, R. (1999). Hyperphosphorylation of the hepatitis C virus NS5A protein requires an active NS3 protease, NS4A, NS4B, and NS5A encoded on the same polyprotein. *J Virol* **73**, 9984-91.
- Neddermann, P., Quintavalle, M., Di Pietro, C., Clementi, A., Cerretani, M., Altamura, S., Bartholomew, L. & De Francesco, R. (2004). Reduction of hepatitis C virus NS5A hyperphosphorylation by selective inhibition of cellular kinases activates viral RNA replication in cell culture. *J Virol* **78**, 13306-14.
- Nita, M. E., Alves, V. A., Carrilho, F. J., Ono-Nita, S. K., Mello, E. S. & Gama-Rodrigues, J. J. (2002). Molecular aspects of hepatic carcinogenesis. *Rev Inst Med Trop Sao Paulo* **44**, 39-48.
- Nomura-Takigawa, Y., Nagano-Fujii, M., Deng, L., Kitazawa, S., Ishido, S., Sada, K. & Hotta, H. (2006). Non-structural protein 4A of Hepatitis C virus accumulates on

## Literatur

- mitochondria and renders the cells prone to undergoing mitochondria-mediated apoptosis. *J Gen Virol* **87**, 1935-45.
- Nunez, G., Benedict, M. A., Hu, Y. & Inohara, N. (1998). Caspases: the proteases of the apoptotic pathway. *Oncogene* **17**, 3237-45.
- O'Brien, V. (1998). Viruses and apoptosis. *J Gen Virol* **79** ( Pt 8), 1833-45.
- Obaya, A. J., Mateyak, M. K. & Sedivy, J. M. (1999). Mysterious liaisons: the relationship between c-Myc and the cell cycle. *Oncogene* **18**, 2934-41.
- Ozes, O. N., Mayo, L. D., Gustin, J. A., Pfeffer, S. R., Pfeffer, L. M. & Donner, D. B. (1999). NF-kappaB activation by tumour necrosis factor requires the Akt serine-threonine kinase. *Nature* **401**, 82-5.
- Pagano, M. (1997). Cell cycle regulation by the ubiquitin pathway. *Faseb J* **11**, 1067-75.
- Pan, G., O'Rourke, K., Chinnaiyan, A. M., Gentz, R., Ebner, R., Ni, J. & Dixit, V. M. (1997). The receptor for the cytotoxic ligand TRAIL. *Science* **276**, 111-3.
- Panteva, M., Korkaya, H. & Jameel, S. (2003). Hepatitis viruses and the MAPK pathway: is this a survival strategy? *Virus Res* **92**, 131-40.
- Papageorge, A., Lowy, D. & Scolnick, E. M. (1982). Comparative biochemical properties of p21 ras molecules coded for by viral and cellular ras genes. *J Virol* **44**, 509-19.
- Park, K. J., Choi, S. H., Choi, D. H., Park, J. M., Yie, S. W., Lee, S. Y. & Hwang, S. B. (2003). Hepatitis C virus NS5A protein modulates c-Jun N-terminal kinase through interaction with tumor necrosis factor receptor-associated factor 2. *J Biol Chem* **278**, 30711-8.
- Pascu, M., Martus, P., Hohne, M., Wiedenmann, B., Hopf, U., Schreier, E. & Berg, T. (2004). Sustained virological response in hepatitis C virus type 1b infected patients is predicted by the number of mutations within the NS5A-ISDR: a meta-analysis focused on geographical differences. *Gut* **53**, 1345-51.
- Pasquinelli, C., Shoenberger, J. M., Chung, J., Chang, K. M., Guidotti, L. G., Selby, M., Berger, K., Lesniewski, R., Houghton, M. & Chisari, F. V. (1997). Hepatitis C virus core and E2 protein expression in transgenic mice. *Hepatology* **25**, 719-27.
- Patterson, S. D., Spahr, C. S., Dugas, E., Susin, S. A., Irinopoulou, T., Koehler, C. & Kroemer, G. (2000). Mass spectrometric identification of proteins released from mitochondria undergoing permeability transition. *Cell Death Differ* **7**, 137-44.
- Pavlovic, D., Neville, D. C., Argaud, O., Blumberg, B., Dwek, R. A., Fischer, W. B. & Zitzmann, N. (2003). The hepatitis C virus p7 protein forms an ion channel that is inhibited by long-alkyl-chain iminosugar derivatives. *Proc Natl Acad Sci U S A* **100**, 6104-8.
- Pawley, J.B. (1995). Handbook of Biological Confocal Microscopy (2nd edition). *Plenum Press, New York*.
- Pawlotsky, J. M. & Germanidis, G. (1999). The non-structural 5A protein of hepatitis C virus. *J Viral Hepat* **6**, 343-56.
- Penin, F., Brass, V., Appel, N., Ramboarina, S., Montserret, R., Ficheux, D., Blum, H. E., Bartenschlager, R. & Moradpour, D. (2004a). Structure and function of the membrane anchor domain of hepatitis C virus nonstructural protein 5A. *J Biol Chem* **279**, 40835-43.
- Penin, F., Dubuisson, J., Rey, F. A., Moradpour, D. & Pawlotsky, J. M. (2004b). Structural biology of hepatitis C virus. *Hepatology* **39**, 5-19.
- Peyssonnaux, C. & Eychene, A. (2001). The Raf/MEK/ERK pathway: new concepts of activation. *Biol Cell* **93**, 53-62.
- Pflugheber, J., Fredericksen, B., Sumpter, R., Jr., Wang, C., Ware, F., Sodora, D. L. & Gale, M., Jr. (2002). Regulation of PKR and IRF-1 during hepatitis C virus RNA replication. *Proc Natl Acad Sci U S A* **99**, 4650-5.

## Literatur

- Pietschmann, T., Lohmann, V., Kaul, A., Krieger, N., Rinck, G., Rutter, G., Strand, D. & Bartenschlager, R. (2002). Persistent and transient replication of full-length hepatitis C virus genomes in cell culture. *J Virol* **76**, 4008-21.
- Pietschmann, T., Lohmann, V., Rutter, G., Kurpanek, K. & Bartenschlager, R. (2001). Characterization of cell lines carrying self-replicating hepatitis C virus RNAs. *J Virol* **75**, 1252-64.
- Pinkert, C. A., Ornitz, D. M., Brinster, R. L. & Palmiter, R. D. (1987). An albumin enhancer located 10 kb upstream functions along with its promoter to direct efficient, liver-specific expression in transgenic mice. *Genes Dev* **1**, 268-76.
- Pober, J. S. (1998). Activation and injury of endothelial cells by cytokines. *Pathol Biol (Paris)* **46**, 159-63.
- Polyak, S. J., Khabar, K. S., Paschal, D. M., Ezelle, H. J., Duverlie, G., Barber, G. N., Levy, D. E., Mukaida, N. & Gretch, D. R. (2001). Hepatitis C virus nonstructural 5A protein induces interleukin-8, leading to partial inhibition of the interferon-induced antiviral response. *J Virol* **75**, 6095-106.
- Postel, E. H., Berberich, S. J., Flint, S. J. & Ferrone, C. A. (1993). Human c-myc transcription factor PuF identified as nm23-H2 nucleoside diphosphate kinase, a candidate suppressor of tumor metastasis. *Science* **261**, 478-80.
- Pousset, D., Piller, V., Bureaud, N., Monsigny, M. & Piller, F. (1997). Increased alpha2,6 sialylation of N-glycans in a transgenic mouse model of hepatocellular carcinoma. *Cancer Res* **57**, 4249-56.
- Prikhod'ko, E. A., Prikhod'ko, G. G., Siegel, R. M., Thompson, P., Major, M. E. & Cohen, J. I. (2004). The NS3 protein of hepatitis C virus induces caspase-8-mediated apoptosis independent of its protease or helicase activities. *Virology* **329**, 53-67.
- Qadri, I., Iwahashi, M. & Simon, F. (2002). Hepatitis C virus NS5A protein binds TBP and p53, inhibiting their DNA binding and p53 interactions with TBP and ERCC3. *Biochim Biophys Acta* **1592**, 193-204.
- Qin, L. X. & Tang, Z. Y. (2002). The prognostic molecular markers in hepatocellular carcinoma. *World J Gastroenterol* **8**, 385-92.
- Quintavalle, M., Sambucini, S., Di Pietro, C., De Francesco, R. & Neddermann, P. (2006). The {alpha}-isoform of protein kinase CKI is responsible for Hepatitis C Virus NS5A hyperphosphorylation. *J Virol*.
- Racanelli, V. & Rehmann, B. (2003). Hepatitis C virus infection: when silence is deception. *Trends Immunol* **24**, 456-64.
- Rapp, U. R., Goldsborough, M. D., Mark, G. E., Bonner, T. I., Groffen, J., Reynolds, F. H., Jr. & Stephenson, J. R. (1983). Structure and biological activity of v-raf, a unique oncogene transduced by a retrovirus. *Proc Natl Acad Sci U S A* **80**, 4218-22.
- Realdon, S., Gerotto, M., Dal Pero, F., Marin, O., Granato, A., Basso, G., Muraca, M. & Alberti, A. (2004). Proapoptotic effect of hepatitis C virus CORE protein in transiently transfected cells is enhanced by nuclear localization and is dependent on PKR activation. *J Hepatol* **40**, 77-85.
- Rebouillat, D. & Hovanessian, A. G. (1999). The human 2',5'-oligoadenylate synthetase family: interferon-induced proteins with unique enzymatic properties. *J Interferon Cytokine Res* **19**, 295-308.
- Reding, G. R. & Ennis, B. (1964). Treatment of the Couple by a Couple. *Br J Med Psychol* **37**, 325-30.
- Reed, K. E., Xu, J. & Rice, C. M. (1997). Phosphorylation of the hepatitis C virus NS5A protein in vitro and in vivo: properties of the NS5A-associated kinase. *J Virol* **71**, 7187-97.

## Literatur

- Renatus, M., Stennicke, H. R., Scott, F. L., Liddington, R. C. & Salvesen, G. S. (2001). Dimer formation drives the activation of the cell death protease caspase 9. *Proc Natl Acad Sci USA* **98**, 14250-5.
- Reyes, G. R. (2002). The nonstructural NS5A protein of hepatitis C virus: an expanding, multifunctional role in enhancing hepatitis C virus pathogenesis. *J Biomed Sci* **9**, 187-97.
- Rodriguez, J. & Lazebnik, Y. (1999). Caspase-9 and APAF-1 form an active holoenzyme. *Genes Dev* **13**, 3179-84.
- Rosenberg, S. (2001). Recent advances in the molecular biology of hepatitis C virus. *J Mol Biol* **313**, 451-64.
- Rothe, M., Wong, S. C., Henzel, W. J. & Goeddel, D. V. (1994). A novel family of putative signal transducers associated with the cytoplasmic domain of the 75 kDa tumor necrosis factor receptor. *Cell* **78**, 681-92.
- Rumin, S., Berthillon, P., Tanaka, E., Kiyosawa, K., Trabaud, M. A., Bizollon, T., Guillat, C., Gripon, P., Guguen-Guillouzo, C., Inchauspe, G. & Trepo, C. (1999). Dynamic analysis of hepatitis C virus replication and quasispecies selection in long-term cultures of adult human hepatocytes infected in vitro. *J Gen Virol* **80** ( Pt 11), 3007-18.
- Sainz, B., Jr. & Chisari, F. V. (2006). Production of infectious hepatitis C virus by well-differentiated, growth-arrested human hepatoma-derived cells. *J Virol* **80**, 10253-7.
- Sambrook, J., Fritsch, E.F., Maniatis, T. (1989). Molecular cloning: A Laboratory Manual. 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. *A. Photochem. Photobiol.* **65**, 750-758.
- Sames, K., Schumacher, U., Halata, Z., Van Damme, E. J., Peumans, W. J., Asmus, B., Moll, R. & Moll, I. (2001). Lectin and proteoglycan histochemistry of Merkel cell carcinomas. *Exp Dermatol* **10**, 100-9.
- Samuel, C. E. (2001). Antiviral actions of interferons. *Clin Microbiol Rev* **14**, 778-809, table of contents.
- Sanger, F., Nicklen, S. & Coulson, A. R. (1977). DNA sequencing with chain-terminating inhibitors. *Proc Natl Acad Sci USA* **74**, 5463-7.
- Sansonno, D., Cornacchiulo, V., Iacobelli, A. R., Di Stefano, R., Lospalluti, M. & Dammacco, F. (1995a). Localization of hepatitis C virus antigens in liver and skin tissues of chronic hepatitis C virus-infected patients with mixed cryoglobulinemia. *Hepatology* **21**, 305-12.
- Sansonno, D., Iacobelli, A. R., Cornacchiulo, V., Distasi, M. & Dammacco, F. (1995b). Immunohistochemical detection of hepatitis C virus-related proteins in liver tissue. *Clin Exp Rheumatol* **13 Suppl 13**, S29-32.
- Sarcar, B., Ghosh, A. K., Steele, R., Ray, R. & Ray, R. B. (2004). Hepatitis C virus NS5A mediated STAT3 activation requires co-operation of Jak1 kinase. *Virology* **322**, 51-60.
- Satoh, S., Hirota, M., Noguchi, T., Hijikata, M., Handa, H. & Shimotohno, K. (2000). Cleavage of hepatitis C virus nonstructural protein 5A by a caspase-like protease(s) in mammalian cells. *Virology* **270**, 476-87.
- Schaeffer, H. J. & Weber, M. J. (1999). Mitogen-activated protein kinases: specific messages from ubiquitous messengers. *Mol Cell Biol* **19**, 2435-44.
- Schiappa, D. A., Mittal, C., Brown, J. A. & Mika, B. P. (2002). Relationship of hepatitis C genotype 1 NS5A sequence mutations to early phase viral kinetics and interferon effectiveness. *J Infect Dis* **185**, 868-77.
- Schneider, P., Thome, M., Burns, K., Bodmer, J. L., Hofmann, K., Kataoka, T., Holler, N. & Tschopp, J. (1997). TRAIL receptors 1 (DR4) and 2 (DR5) signal FADD-dependent apoptosis and activate NF-kappaB. *Immunity* **7**, 831-6.



## Literatur

- Schulze-Osthoff, K., Ferrari, D., Los, M., Wesselborg, S. & Peter, M. E. (1998). Apoptosis signaling by death receptors. *Eur J Biochem* **254**, 439-59.
- Schumacher, U., Adam, E., Flavell, D. J., Boehm, D., Brooks, S. A. & Leathem, A. J. (1994). Glycosylation patterns of the human colon cancer cell line HT-29 detected by Helix pomatia agglutinin and other lectins in culture, in primary tumours and in metastases in SCID mice. *Clin Exp Metastasis* **12**, 398-404.
- Schwenzer, R., Siemienski, K., Liptay, S., Schubert, G., Peters, N., Scheurich, P., Schmid, R. M. & Wajant, H. (1999). The human tumor necrosis factor (TNF) receptor-associated factor 1 gene (TRAF1) is up-regulated by cytokines of the TNF ligand family and modulates TNF-induced activation of NF-kappaB and c-Jun N-terminal kinase. *J Biol Chem* **274**, 19368-74.
- Sell, S. (2002). Cellular origin of hepatocellular carcinomas. *Semin Cell Dev Biol* **13**, 419-24.
- Serrano, M., Hannon, G. J. & Beach, D. (1993). A new regulatory motif in cell-cycle control causing specific inhibition of cyclin D/CDK4. *Nature* **366**, 704-7.
- Sheridan, J. P., Marsters, S. A., Pitti, R. M., Gurney, A., Skubatch, M., Baldwin, D., Ramakrishnan, L., Gray, C. L., Baker, K., Wood, W. I., Goddard, A. D., Godowski, P. & Ashkenazi, A. (1997). Control of TRAIL-induced apoptosis by a family of signaling and decoy receptors. *Science* **277**, 818-21.
- Shimizu, K., Goldfarb, M., Suard, Y., Perucho, M., Li, Y., Kamata, T., Feramisco, J., Stavnezer, E., Fogh, J. & Wigler, M. H. (1983). Three human transforming genes are related to the viral ras oncogenes. *Proc Natl Acad Sci U S A* **80**, 2112-6.
- Siavoshian, S., Abraham, J. D., Thumann, C., Kieny, M. P. & Schuster, C. (2005). Hepatitis C virus core, NS3, NS5A, NS5B proteins induce apoptosis in mature dendritic cells. *J Med Virol* **75**, 402-11.
- Siegel, R. M. (2006). Caspases at the crossroads of immune-cell life and death. *Nat Rev Immunol* **6**, 308-17.
- Soguero, C., Joo, M., Chianese-Bullock, K. A., Nguyen, D. T., Tung, K. & Hahn, Y. S. (2002). Hepatitis C virus core protein leads to immune suppression and liver damage in a transgenic murine model. *J Virol* **76**, 9345-54.
- Soldani, C., Lazze, M. C., Bottone, M. G., Tognon, G., Biggiogera, M., Pellicciari, C. E. & Scovassi, A. I. (2001). Poly(ADP-ribose) polymerase cleavage during apoptosis: when and where? *Exp Cell Res* **269**, 193-201.
- Soldani, C. & Scovassi, A. I. (2002). Poly(ADP-ribose) polymerase-1 cleavage during apoptosis: an update. *Apoptosis* **7**, 321-8.
- Sporn, M. B. & Roberts, A. B. (1986). Peptide growth factors and inflammation, tissue repair, and cancer. *J Clin Invest* **78**, 329-32.
- Srinivasan, A., Li, F., Wong, A., Kodandapani, L., Smidt, R., Jr., Krebs, J. F., Fritz, L. C., Wu, J. C. & Tomaselli, K. J. (1998). Bcl-xL functions downstream of caspase-8 to inhibit Fas- and tumor necrosis factor receptor 1-induced apoptosis of MCF7 breast carcinoma cells. *J Biol Chem* **273**, 4523-9.
- Srinivasula, S. M., Ahmad, M., Fernandes-Alnemri, T. & Alnemri, E. S. (1998). Autoactivation of procaspase-9 by Apaf-1-mediated oligomerization. *Mol Cell* **1**, 949-57.
- Stancovski, I. & Baltimore, D. (1997). NF-kappaB activation: the I kappaB kinase revealed? *Cell* **91**, 299-302.
- Stockl, L., Berting, A., Malkowski, B., Foerste, R., Hofschneider, P. H. & Hildt, E. (2003). Integrity of c-Raf-1/MEK signal transduction cascade is essential for hepatitis B virus gene expression. *Oncogene* **22**, 2604-10.
- Stoker, M. G. (1974). Effects of tumour viruses on cell growth. *J Clin Pathol Suppl (R Coll Pathol)* **7**, 60-4.

## Literatur

- Street, A., Macdonald, A., Crowder, K. & Harris, M. (2004). The Hepatitis C virus NS5A protein activates a phosphoinositide 3-kinase-dependent survival signaling cascade. *J Biol Chem* **279**, 12232-41.
- Street, A., Macdonald, A., McCormick, C. & Harris, M. (2005). Hepatitis C virus NS5A-mediated activation of phosphoinositide 3-kinase results in stabilization of cellular beta-catenin and stimulation of beta-catenin-responsive transcription. *J Virol* **79**, 5006-16.
- Su, F & Schneider, R J (1997). Hepatitis B virus HBx protein sensitizes cells to apoptotic killing by tumor necrosis factor alpha. *Proc Natl Acad Sci U S A* **94**, 8744-9.
- Su, F, Theodosis, C, N & Schneider, R, J (2001). Role of NF-kappaB and myc proteins in apoptosis induced by hepatitis B virus HBx protein. *J Virol* **75**, 215-25.
- Subramanian, C., Cotter, M. A., 2nd & Robertson, E. S. (2001). Epstein-Barr virus nuclear protein EBNA-3C interacts with the human metastatic suppressor Nm23-H1: a molecular link to cancer metastasis. *Nat Med* **7**, 350-5.
- Sumpter, R., Jr., Loo, Y. M., Foy, E., Li, K., Yoneyama, M., Fujita, T., Lemon, S. M. & Gale, M., Jr. (2005). Regulating intracellular antiviral defense and permissiveness to hepatitis C virus RNA replication through a cellular RNA helicase, RIG-I. *J Virol* **79**, 2689-99.
- Takeuchi, M., Rothe, M. & Goeddel, D. V. (1996). Anatomy of TRAF2. Distinct domains for nuclear factor-kappaB activation and association with tumor necrosis factor signaling proteins. *J Biol Chem* **271**, 19935-42.
- Tan, S. L. & Katze, M. G. (2001). How hepatitis C virus counteracts the interferon response: the jury is still out on NS5A. *Virology* **284**, 1-12.
- Tan, S. L., Nakao, H., He, Y., Vijaysri, S., Neddermann, P., Jacobs, B. L., Mayer, B. J. & Katze, M. G. (1999). NS5A, a nonstructural protein of hepatitis C virus, binds growth factor receptor-bound protein 2 adaptor protein in a Src homology 3 domain/ligand-dependent manner and perturbs mitogenic signaling. *Proc Natl Acad Sci U S A* **96**, 5533-8.
- Tanaka, M., Nagano-Fujii, M., Deng, L., Ishido, S., Sada, K. & Hotta, H. (2006). Single-point mutations of hepatitis C virus NS3 that impair p53 interaction and anti-apoptotic activity of NS3. *Biochem Biophys Res Commun* **340**, 792-9.
- Tang, D., Lahti, J. M. & Kidd, V. J. (2000). Caspase-8 activation and bid cleavage contribute to MCF7 cellular execution in a caspase-3-dependent manner during staurosporine-mediated apoptosis. *J Biol Chem* **275**, 9303-7.
- Tanji, Y., Kaneko, T., Satoh, S. & Shimotohno, K. (1995). Phosphorylation of hepatitis C virus-encoded nonstructural protein NS5A. *J Virol* **69**, 3980-6.
- Tartaglia, L. A., Ayres, T. M., Wong, G. H. & Goeddel, D. V. (1993). A novel domain within the 55 kd TNF receptor signals cell death. *Cell* **74**, 845-53.
- Tassan, J. P., Jaquenoud, M., Fry, A. M., Frutiger, S., Hughes, G. J. & Nigg, E. A. (1995). In vitro assembly of a functional human CDK7-cyclin H complex requires MAT1, a novel 36 kDa RING finger protein. *Embo J* **14**, 5608-17.
- Taylor, D. R., Shi, S. T., Romano, P. R., Barber, G. N. & Lai, M. M. (1999). Inhibition of the interferon-inducible protein kinase PKR by HCV E2 protein. *Science* **285**, 107-10.
- Tellinghuisen, T. L., Marcotrigiano, J., Gorbalenya, A. E. & Rice, C. M. (2004). The NS5A protein of hepatitis C virus is a zinc metalloprotein. *J Biol Chem* **279**, 48576-87.
- Tellinghuisen, T. L., Marcotrigiano, J. & Rice, C. M. (2005). Structure of the zinc-binding domain of an essential component of the hepatitis C virus replicase. *Nature* **435**, 374-9.
- Terrault, N. A. (2002). Sexual activity as a risk factor for hepatitis C. *Hepatology* **36**, S99-105.

## Literatur

- Thomas, D. L. (2002). Hepatitis C and human immunodeficiency virus infection. *Hepatology* **36**, S201-9.
- Thompson, C. B. (1995). Apoptosis in the pathogenesis and treatment of disease. *Science* **267**, 1456-62.
- Toubi, E., Kessel, A., Goldstein, L., Slobodin, G., Sabo, E., Shmuel, Z. & Zuckerman, E. (2001). Enhanced peripheral T-cell apoptosis in chronic hepatitis C virus infection: association with liver disease severity. *J Hepatol* **35**, 774-80.
- Towbin, H., Staehelin, T. & Gordon, J. (1992). Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications. 1979. *Biotechnology* **24**, 145-9.
- Tracey, K. J. & Cerami, A. (1993). Tumor necrosis factor, other cytokines and disease. *Annu Rev Cell Biol* **9**, 317-43.
- Troppmair, J. & Rapp, U. R. (2003). Raf and the road to cell survival: a tale of bad spells, ring bearers and detours. *Biochem Pharmacol* **66**, 1341-5.
- Tu, H., Gao, L., Shi, S. T., Taylor, D. R., Yang, T., Mircheff, A. K., Wen, Y., Gorbalenya, A. E., Hwang, S. B. & Lai, M. M. (1999). Hepatitis C virus RNA polymerase and NS5A complex with a SNARE-like protein. *Virology* **263**, 30-41.
- van Horsen, R., Ten Hagen, T. L. & Eggermont, A. M. (2006). TNF-alpha in cancer treatment: molecular insights, antitumor effects, and clinical utility. *Oncologist* **11**, 397-408.
- Vandenabeele, P., Declercq, W., Beyaert, R. & Fiers, W. (1995). Two tumour necrosis factor receptors: structure and function. *Trends Cell Biol* **5**, 392-9.
- Verhagen, A. M., Ekert, P. G., Pakusch, M., Silke, J., Connolly, L. M., Reid, G. E., Moritz, R. L., Simpson, R. J. & Vaux, D. L. (2000). Identification of DIABLO, a mammalian protein that promotes apoptosis by binding to and antagonizing IAP proteins. *Cell* **102**, 43-53.
- Wakita, T., Pietschmann, T., Kato, T., Date, T., Miyamoto, M., Zhao, Z., Murthy, K., Habermann, A., Krausslich, H. G., Mizokami, M., Bartenschlager, R. & Liang, T. J. (2005). Production of infectious hepatitis C virus in tissue culture from a cloned viral genome. *Nat Med* **11**, 791-6.
- Walczak, H., Miller, R. E., Ariail, K., Gliniak, B., Griffith, T. S., Kubin, M., Chin, W., Jones, J., Woodward, A., Le, T., Smith, C., Smolak, P., Goodwin, R. G., Rauch, C. T., Schuh, J. C. & Lynch, D. H. (1999). Tumoricidal activity of tumor necrosis factor-related apoptosis-inducing ligand in vivo. *Nat Med* **5**, 157-63.
- Wang, C. Y., Mayo, M. W., Korneluk, R. G., Goeddel, D. V. & Baldwin, A. S., Jr. (1998). NF-kappaB antiapoptosis: induction of TRAF1 and TRAF2 and c-IAP1 and c-IAP2 to suppress caspase-8 activation. *Science* **281**, 1680-3.
- Wang, X. (2001). The expanding role of mitochondria in apoptosis. *Genes Dev* **15**, 2922-33.
- Waris, G., Livolsi, A., Imbert, V., Peyron, J. F. & Siddiqui, A. (2003). Hepatitis C virus NS5A and subgenomic replicon activate NF-kappaB via tyrosine phosphorylation of IkappaBalpha and its degradation by calpain protease. *J Biol Chem* **278**, 40778-87.
- Wieder, T., Essmann, F., Prokop, A., Schmelz, K., Schulze-Osthoff, K., Beyaert, R., Dorken, B. & Daniel, P. T. (2001). Activation of caspase-8 in drug-induced apoptosis of B-lymphoid cells is independent of CD95/Fas receptor-ligand interaction and occurs downstream of caspase-3. *Blood* **97**, 1378-87.
- Windisch, M. P., Frese, M., Kaul, A., Trippler, M., Lohmann, V. & Bartenschlager, R. (2005). Dissecting the interferon-induced inhibition of hepatitis C virus replication by using a novel host cell line. *J Virol* **79**, 13778-93.
- Wood, K. W., Sarnecki, C., Roberts, T. M. & Blenis, J. (1992). ras mediates nerve growth factor receptor modulation of three signal-transducing protein kinases: MAP kinase, Raf-1, and RSK. *Cell* **68**, 1041-50.

## Literatur

- Woods, K. M. & Chapes, S. K. (1993). Three distinct cell phenotypes of induced-TNF cytotoxicity and their relationship to apoptosis. *J Leukoc Biol* **53**, 37-44.
- Wright, T. L. (2002). Treatment of patients with hepatitis C and cirrhosis. *Hepatology* **36**, S185-94.
- Wu, X. Z. & Chen, D. (2006). Origin of hepatocellular carcinoma: role of stem cells. *J Gastroenterol Hepatol* **21**, 1093-8.
- Xu, J., Rockow, S., Kim, S., Xiong, W. & Li, W. (1994). Interferons block protein kinase C-dependent but not-independent activation of Raf-1 and mitogen-activated protein kinases and mitogenesis in NIH 3T3 cells. *Mol Cell Biol* **14**, 8018-27.
- Xu, Z., Choi, J., Yen, T. S., Lu, W., Strohecker, A., Govindarajan, S., Chien, D., Selby, M. J. & Ou, J. (2001). Synthesis of a novel hepatitis C virus protein by ribosomal frameshift. *Embo J* **20**, 3840-8.
- You, J. & Pickart, C. M. (2001). A HECT domain E3 enzyme assembles novel polyubiquitin chains. *J Biol Chem* **276**, 19871-8.
- Zech, B., Kurtenbach, A., Krieger, N., Strand, D., Blencke, S., Morbitzer, M., Salassidis, K., Cotten, M., Wissing, J., Obert, S., Bartenschlager, R., Herget, T. & Daub, H. (2003). Identification and characterization of amphiphysin II as a novel cellular interaction partner of the hepatitis C virus NS5A protein. *J Gen Virol* **84**, 555-60.
- Zein, N. N., Poterucha, J. J., Gross, J. B., Jr., Wiesner, R. H., Therneau, T. M., Gossard, A. A., Wendt, N. K., Mitchell, P. S., Germer, J. J. & Persing, D. H. (1996). Increased risk of hepatocellular carcinoma in patients infected with hepatitis C genotype 1b. *Am J Gastroenterol* **91**, 2560-2.
- Zheng, C. F. & Guan, K. L. (1994). Activation of MEK family kinases requires phosphorylation of two conserved Ser/Thr residues. *Embo J* **13**, 1123-31.
- Zhong, J., Gastaminza, P., Cheng, G., Kapadia, S., Kato, T., Burton, D. R., Wieland, S. F., Uprichard, S. L., Wakita, T. & Chisari, F. V. (2005). Robust hepatitis C virus infection in vitro. *Proc Natl Acad Sci U S A* **102**, 9294-9.
- Zhu, H., Wang, Y., Chen, J., Cheng, G. & Xue, J. (2004). Transgenic mice expressing hepatitis B virus X protein are more susceptible to carcinogen induced hepatocarcinogenesis. *Exp Mol Pathol* **76**, 44-50.
- Zhu, N., Khoshnan, A., Schneider, R., Matsumoto, M., Dennert, G., Ware, C. & Lai, M. M. (1998). Hepatitis C virus core protein binds to the cytoplasmic domain of tumor necrosis factor (TNF) receptor 1 and enhances TNF-induced apoptosis. *J Virol* **72**, 3691-7.

### Internetseiten:

- <http://jaxmice.jax.org/strain/001800.html> (02/2007)
- <http://expasy.org/sprot> (02/2007)
- <http://www.genomics.uni-freiburg.de> (02/2007)
- [http://www.molecular-virology.uni-hd.de/rsr/area\\_hcv.htm](http://www.molecular-virology.uni-hd.de/rsr/area_hcv.htm) (02/2007)
- <http://www.ncbi.nlm.nih.gov/entrez> (02/2007)
- <http://www.hepatitis-c.de/alleshep.htm> (02/2007)
- <http://www.who.int/mediacentre/factsheets/fs164/en/index.html> (02/2007)
- <https://www.expasy.ch> (02/2007)