
EFFECTES DELS INHIBIDORS DE LA CICLOOXIGENASA EN CÈL·LULES HEPÀTIQUES I EL SEU PAPER EN LA INFLAMACIÓ I FIBROSI HEPÀTICA EXPERIMENTAL

Anna Planagumà Ferrer

Bibliografia

8 BIBLIOGRAFIA

- [1] Bowman WC, Rand MJ. Farmacología. Bases bioquímicas y patológicas, Ed. Interamericana. Inflamación y compuestos antiinflamatorios. México, D.F: Interamericana, 1984;13.
- [2] Lawrence T, Willoughby DA, Gilroy DW. Anti-inflammatory lipid mediators and insights into the resolution of inflammation. *Nature Rev Immunol* 2002;2:787-795.
- [3] Majno G. The healing hand: Man and Wound in the Ancient World. Cambridge: Harvard University Press, 1975.
- [4] Gallin JI, Goldstein IM, Snyderman R, eds. Inflammation: basic principles and clinical correlates. New York: Raven Press, 1988;1.
- [5] Nathan C. Points of control in inflammation. *Nature* 2002;420:846-852.
- [6] Tauber AI, Chernyak L. Metchnikoff and the Origins of Immunology: From Metaphor to Theory. New York: Oxford University Press, 1991.
- [7] Ottonello L, Morone MP, Dapino P, Dallegrì F. Cyclic AMP-elevating agents down-regulate the oxidative burst induced by granulocyte-macrophage colony-stimulating factor (GM-CSF) in adherent neutrophils. *Clin Exp Immunol* 1995;101:502-516.
- [8] Moore AR, Willoughby DA. The role of cAMP regulation in controlling inflammation. *Clin Exp Immunol* 1995;101:387-389.
- [9] Spiegelberg HL. Immunoglobulins. In: Gallin JI, Goldstein IM, Snyderman R, eds. Inflammation: basic principles and clinical correlates. New York: Raven Press, 1988;2:11-19.
- [10] Porter RR. The hydrolysis of rabbit γ -globulin and antibodies with crystalline papain. *Biochem J* 1959;73:119-126.

Bibliografia

- [11] Spiegelberg HL. Biological activities of immunoglobulins of different classes and subclasses. *Adv Immunol* 1974;19:259-294.
- [12] Müller-Eberhard HJ, Goldstein IM, Permenter DH, Colten HR, Fries LF, Frank MM. Complement: Chemistry and Pathways. In: Gallin JI, Goldstein IM, Snyderman R, eds. *Inflammation: basic principles and clinical correlates*. New York: Raven Press, 1988;3:21-53.
- [13] Ward PA, Zvaifler NJ. Complement-derived leukotactic factors in inflammatory synovial fluids of humans. *J Clin Invest* 1971;50:606-616.
- [14] Takematsu H, Tagami H. Eosinophilic pustular folliculitis. Studies on possible chemotactic factors involved in the formation of pustules. *Br J Dermatol* 1986;114:209-215.
- [15] Pinckard RN, Ludwig JC, McManus LM. Platelet-activating factors. In: Gallin JI, Goldstein IM, Snyderman R, eds. *Inflammation: basic principles and clinical correlates*. New York: Raven Press, 1988;10:139-167.
- [16] Dale HH and Laidlaw PP. The physiologic action of b-imidazolylethylamine. *J Physiol* 1911;41:318-344.
- [17] Riley JF, West GB. The presence of histamine in tissue mast cells. *J Physiol* 1953;120:528-537.
- [18] Platshon LF, Kaliner M. The effects of the immunologic release of histamine upon human lung cyclic nucleotide levels and prostaglandin generation. *J Clin Invest* 1978;62:1113-1121.
- [19] White MV, Kaliner MA. Histamine. In: Gallin JI, Goldstein IM, Snyderman R, eds. *Inflammation: basic principles and clinical correlates*. New York: Raven Press, 1988;11:169-193.
- [20] Dinarello CA, Greene WC, Nathan C, Yoshida R Golde DW, Gasson JC. Cytokines: interleukin-1 and tumor necrosis factor. In: Gallin JI, Goldstein IM, Snyderman R, editors. *Inflammation: basic principles and clinical correlates*. New York: Raven Press, 1988;12:195-208.

- [21] Henderson B, Higgs GA. Targets for modulating cytokine responses in inflammatory and infectious diseases. In: Higgs GA i Henderson B eds. Novel Cytokine Inhibitors. Basel: Birkhäuser Verlag AG, 2000:1-8.
- [22] Von der Thusen JH, Kuiper J, van Berkel TJ, Biessen EA. Interleukins in atherosclerosis: molecular pathways and therapeutic potential. *Pharmacol Rev* 2003;55:133-166.
- [23] Morgan BP. The complement system. In: Morgan BP, ed. Complement. Clinical aspects and relevance to disease. London: Academic Press, 1990:1-35.
- [24] Efrat S, Kaempfer R. Control of biologically active interleukin 2 messenger RNA formation in induced human lymphocytes. *Proc Natl Acad Sci U S A* 1984;81:2601-2605.
- [25] Tsudo M, Uchiyama T, Uchino H. Expression of Tac antigen on activated normal human B cells. *J Exp Med* 1984;160:612-617.
- [26] Farrar JJ, Benjamin WR, Hilfiker ML, Howard M, Farrar WL, Fuller-Farrar J. The biochemistry, biology, and role of interleukin 2 in the induction of cytotoxic T cell and antibody-forming B cell responses. *Immunol Rev* 1982;63:129-166.
- [27] Rossi D, Zlotnik A. The biology of chemokines and their receptors. *Annu Rev Immunol* 2000;18:217-242.
- [28] Watanabe K, Koizumi F, Kurashige Y, Tsurufuji S, Nakagawa H. Rat CINC, a member of the interleukin-8 family, is a neutrophil-specific chemoattractant *in vivo*. *Exp Mol Pathol* 1991;55: 30-37.
- [29] Watanabe K, Konishi K, Fujioka M, Kinoshita S, Nakagawa H. The neutrophil chemoattractant produced by the rat kidney epithelioid cell line NRK-53E is a protein related to the KC/gro protein. *J Biol Chem* 1989;264:19559-19563.
- [30] Muller WA. Leukocyte-endothelial cell interactions in the inflammatory response. *Lab Invest* 2002;82:521-533.

Bibliografia

- [31] Steinhoff M, Vergnolle N, Young SH, Tognetto M, Amadesi S, Ennes HS, Trevisani M, Hollenberg MD, Wallace JL, Caughey GH, Mitchell SE, Williams LM, Geppetti P, Mayer EA, Bunnett NW. Agonists of proteinase-activated receptor 2 induce inflammation by a neurogenic mechanism. *Nat Med* 2000;6:151-158.
- [32] Nathan C, Xie QW, Halbwachs-Mecarelli L, Jin WW. Albumin inhibits neutrophil spreading and hydrogen peroxide release by blocking the shedding of CD43 (sialophorin, leukosialin). *J Cell Biol* 1993;122:243-256.
- [33] Nathan CF. Neutrophil activation on biological surfaces. Massive secretion of hydrogen peroxide in response to products of macrophages and lymphocytes. *J Clin Invest* 1987;80:1550-1560.
- [34] Weiss SJ. Tissue destruction by neutrophils. *N Engl J Med* 1989;320:365-376.
- [35] Morgan JG, Pereira HA, Sukiennicki T, Spitznagel JK, Lerrick JW. Human neutrophil granule cationic protein CAP37 is a specific macrophage chemotaxin that shares homology with inflammatory proteinases. *Adv Exp Med Biol* 1991;305:89-96.
- [36] Yang D, Chertov O, Bykovskaia SN, Chen Q, Buffo MJ, Shogan J, Anderson M, Schroder JM, Wang JM, Howard OM, Oppenheim JJ. Beta-defensins: linking innate and adaptive immunity through dendritic and T cell CCR6. *Science* 1999;286:525-528.
- [37] Robbiani DF, Finch RA, Jager D, Muller WA, Sartorelli AC, Randolph GJ. The leukotriene C(4) transporter MRP1 regulates CCL19 (MIP-3 β , ELC)-dependent mobilization of dendritic cells to lymph nodes. *Cell* 2000;103:757-768.
- [38] Foegh ML, Ramwell PW. The eicosanoids: prostaglandins, thromboxanes, leukotrienes, and related compounds. In: Katzung BG, ed. *Basic and clinical pharmacology*. New York: The McGraw-Hill Companies, 2004;18:298-312.
- [39] Decker K. Biologically active products of stimulated liver macrophages (Kupffer cells). *Eur J Biochem* 1990;192:245-261.
- [40] Balsinde J, Balboa MA, Insel PA, Dennis EA. Regulation and inhibition of phospholipase A₂. *Annu Rev Pharmacol Toxicol* 1999;39:175-189.

- [41] Six DA, Dennis EA. The expanding superfamily of phospholipase A(2) enzymes: classification and characterization. *Biochim Biophys Acta* 2000;1488:1-19.
- [42] Cummings BS, McHowat J, Schnellmann RG. Phospholipase A(2)s in cell injury and death. *J Pharmacol Exp Ther* 2000;294:793-799.
- [43] Chakraborti S. Phospholipase A₂ isoforms: a perspective. *Cell Signal* 2003;15:637-665.
- [44] Cirino G. Multiple controls in inflammation. Extracellular and intracellular phospholipase A2, inducible and constitutive cyclooxygenase, and inducible nitric oxide synthase. *Biochem Pharmacol* 1998;55:105-111.
- [45] Samuelsson B, Dahlen SE, Lindgren JA, Rouzer CA, Serhan CN. Leukotrienes and lipoxins: structures, biosynthesis, and biological effects. *Science* 1987;237:1171-1176.
- [46] Samuelsson B. Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation. *Science* 1983;220:568-575.
- [47] Henderson WR Jr. The role of leukotrienes in inflammation. *Ann Intern Med* 1994;121:684-697.
- [48] Borgeat P, Hamberg M, Samuelsson B. Transformation of arachidonic acid and homo-gamma-linolenic acid by rabbit polymorphonuclear leukocytes. Monohydroxy acids from novel lipoxygenases. *J Biol Chem* 1976;251:7816-7820.
- [49] Brock TG, Paine R 3rd, Peters-Golden M. Localization of 5-lipoxygenase to the nucleus of unstimulated rat basophilic leukemia cells. *J Biol Chem* 1994;269:22059-22066.
- [50] Funk CD, Gunne H, Steiner H, Izumi T, Samuelsson B. Native and mutant 5-lipoxygenase expression in a baculovirus/insect cell system Proc Natl Acad Sci U S A 1989;86:2592-2596.
- [51] Serhan CN, Romano M. Lipoxin biosynthesis and actions: role of the human platelet LX-synthase J Lipid Mediat Cell Signal 1995;12:293-306.
- [52] Dixon RA, Diehl RE, Opas E, Rands E, Vickers PJ, Evans JF, Gillard JW, Miller DK. Requirement of a 5-lipoxygenase-activating protein for leukotriene synthesis. *Nature* 1990;343:282-4.

Bibliografia

- [53] Yang VW. Eicosanoids and inflammatory bowel disease. *Gastroenterol Clin North Am* 1996;25:317-332.
- [54] Devchand PR, Keller H, Peters JM, Vazquez M, Gonzalez FJ, Wahli W. The PPARalpha-leukotriene B4 pathway to inflammation control. *Nature* 1996;384:39-43.
- [55] Capdevila JH, Falck JR, Estabrook RW. Cytochrome P450 and the arachidonate cascade. *FASEB J* 1992;6:731-736.
- [56] Levy GN. Prostaglandin H synthases, nonsteroidal anti-inflammatory drugs, and colon cancer. *FASEB J* 1997;11:234-247.
- [57] Miyamoto T, Ogino N, Yamamoto S, Hayaishi O. Purifications of prostaglandin endoperoxide synthetase from bovine vesicular gland microsomes. *J Biol Chem* 1976; 251:2629-2636.
- [58] DeWitt DL, Smith WL. Primary structure of prostaglandin G/H synthase from sheep vesicular gland determined from complementary DNA sequence. *Proc Natl Acad Sci U S A* 1988; 85:1412-1416.
- [59] Merlie JP, Fagan D, Mudd J, Needleman P. Isolation and characterization of the complementary DNA for sheep seminal vesicle prostaglandin endoperoxide synthase (cyclooxygenase). *J Biol Chem* 1988;263:3550-3553.
- [60] Yokoyama C, Takai T, Tanabe T. Primary structure of sheep prostaglandin endoperoxide synthase deduced from cDNA sequence. *FEBS Lett* 1988;231:347-351.
- [61] Xie W, Chipman JG, Robertson DL, Erikson RL, Simmons DL. Expression of a mitogen-responsive gene encoding prostaglandin synthase is regulated by mRNA splicing. *Proc Natl Acad Sci U S A* 1991;88:2692-2696.
- [62] Hla T, Neilson K. Human cyclooxygenase-2 cDNA. *Proc Natl Acad Sci U S A* 1992; 89:7384-7388.
- [63] Funk CD, Funk LB, Kennedy ME, Pong AS, Fitzgerald GA. Human platelet/erythroleukemia cell prostaglandin G/H synthase: cDNA cloning, expression, and gene chromosomal assignment. *FASEB J* 1991;5:2304-2312.

- [64] Tay A, Squire JA, Goldberg H, Skorecki K. Assignment of the human prostaglandin-endoperoxide synthase 2 (PTGS2) gene to 1q25 by fluorescence in situ hybridization. *Genomics* 1994;23:718-719.
- [65] Vane JR, Bakhle YS, Botting RM. Cyclooxygenases 1 and 2. *Annu Rev Pharmacol Toxicol* 1998;38:97-120.
- [66] Pairet M, Engelhardt G. Distinct isoforms (COX-1 and COX-2) of cyclooxygenase: possible physiological and therapeutic implications. *Fundam Clin Pharmacol* 1996;10:1-17.
- [67] Picot D, Loll P, Garavito M. The X-ray crystal structure of the membrane protein prostaglanind H₂ synthase-1. *Nature* 1994;367:243-249.
- [68] Luong C, Miller A, Barnett J, Chow J, Ramesha C, Browner MF. Flexibility of the NSAID binding site in the structure of human cyclooxygenase-2. *Nat Struct Biol* 1996;3:927-933.
- [69] Kurumbail RG, Stevens AM, Gierse JK, McDonald JJ, Stegeman RA, Pak JY, Gildehaus D, Miyashiro JM, Penning TD, Seibert K, Isakson PC, Stallings WC. Structural basis for selective inhibition of cyclooxygenase-2 by anti-inflammatory agents. *Nature* 1996;384:644-648.
- [70] Meade EA, Smith WL, DeWitt DL. Differential inhibition of prostaglandin endoperoxide synthase (cyclooxygenase) isozymes by aspirin and other non-steroidal anti-inflammatory drugs. *J Biol Chem* 1993;268:6610-6614.
- [71] Romano M, Clària J. Cyclooxygenase-2 and 5-lipoxygenase converging functions on cell proliferation and tumor angiogenesis: implications for cancer therapy. *FASEB J* 2003;17:1986-1995.
- [72] Morita I, Schindler M, Regier MK, Otto JC, Hori T, DeWitt DL, Smith WL. Different intracellular locations for prostaglandin endoperoxide H synthase-1 and -2. *J Biol Chem* 1995;270:10902-10908.
- [73] Smith WL. Prostanoid biosynthesis and the mechanism of action. *Am J Physiol* 1992;263:F118-F191.

Bibliografia

- [74] Otto JC, Smith WL. Prostaglandin endoperoxide synthase-1 and -2. *J Lipid Mediators Cell Signal* 1995;12:139-156.
- [75] Herschman HR. Prostaglandin synthase 2. *Biochim Biophys Acta* 1996;1299:125-140.
- [76] Chandrasekharan NV, Dai H, Roos KL, Evanson NK, Tomsik J, Elton TS, Simmons DL. COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: cloning, structure, and expression. *Proc Natl Acad Sci U S A* 2002;99:13926-13931.
- [77] Warner TD, Mitchell JA. Cyclooxygenase-3 (COX-3): Filling in the gaps toward a COX continuum? *Proc Natl Acad Sci U S A* 2002;99:13371-13373.
- [78] Smith WL, Marnett L. Prostaglandin endoperoxide H synthase: structure and catalysis. *Biochimica et Biophysica Acta* 1991;1083:1-17.
- [79] Lands WE. The biosynthesis and metabolism of prostaglandins. *Annu Rev Physiol* 1979;41:633-652.
- [80] Kikawa Y, Narumiya S, Fukushima M, Wakatsuka H, Hayaishi O. 9-Deoxy-delta 9, delta 12-13,14-dihydroprostaglandin D₂, a metabolite of prostaglandin D₂ formed in human plasma. *Proc Natl Acad Sci U S A* 1984;81:1317-1321.
- [81] Bell-Parikh LC, Ide T, Lawson JA, McNamara P, Reilly M, FitzGerald GA. Biosynthesis of 15-deoxy-delta12,14-PGJ₂ and the ligation of PPARgamma. *J Clin Invest* 2003;112:945-955.
- [82] Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nat New Biol* 1971; 231:232-235.
- [83] Samuelsson B. From studies of biochemical mechanism to novel biological mediators: prostaglandin endoperoxides, thromboxanes, and leukotrienes. *Biosci Rep* 1983;3:791-813.
- [84] Hamberg M, Svensson J, Wakabayashi T, Samuelsson B. Isolation and structure of two prostaglandin endoperoxides that cause platelet aggregation. *Proc Natl Acad Sci U S A* 1974;71:345-349.

- [85] Goldstein JI. Agents that interfere with arachidonic acid metabolism. In: Gallin JI, Goldstein IM, Snyderman R, eds. *Inflammation: basic principles and clinical correlates*. New York: Raven Press, 1988;52:935-946.
- [86] Clària J, Serhan CN. Aspirin triggers previously unrecognized bioactive eicosanoids by human endothelial cell-leukocyte interaction. *Proc Natl Acad Sci U S A* 1995; 92:9475-9479.
- [87] Serhan CN, Hong S, Gronert K, Colgan SP, Devchand PR, Mirick G, Moussignac RL. Resolvins: a family of bioactive products of omega-3 fatty acid transformation circuits initiated by aspirin treatment that counter proinflammation signals. *J Exp Med* 2002; 196:1025-1037.
- [88] Funk CD. Prostaglandins and leukotrienes: advances in eicosanoid biology. *Science* 2001;294:1871-1875.
- [89] Smith WL, DeWitt DL, Garavito RM. Cyclooxygenases: structural, cellular, and molecular biology. *Annu Rev Biochem* 2000;69:145-182.
- [90] Kliewer SA, Lenhard JM, Willson TM, Patel I, Morris DC, Lehmann JM. A prostaglandin J₂ metabolite binds peroxisome proliferator-activated receptor gamma and promotes adipocyte differentiation. *Cell* 1995;83:813-819.
- [91] Insel PA. Analgesic-antipyretics and antiinflammatory agents; drugs employed in the treatment of rheumatoid arthritis and gout. In: Goodman Gilman A, Rall TW, Nies AS, Taylor P, eds. *Goodman and Gilman's. The pharmacological basis of therapeutics*. New York: McGraw-Hill, 1990;26:638.
- [92] Wagner W, Khanna P, Furst DE. Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, nonopioid analgesics, and drugs used in gout. In: Katzung BG, ed. *Basic and clinical pharmacology*. New York: McGraw-Hill Companies, 2004;36:576-603.
- [93] Ferreira SH, Moncada S, Vane JR. Indomethacin and aspirin abolish prostaglandin release from spleen. *Nature* 1971;231:237-239.

Bibliografia

- [94] Smith JH, Willis AL. Aspirin selectively inhibits prostaglandin production in human platelets. *Nature* 1971;231:235-237.
- [95] FitzGerald GA, Patrono C. The coxibs, selective inhibitors of cyclooxygenase-2. *N Engl J Med* 2001;345:433-442.
- [96] FitzGerald GA. COX-2 and beyond: Approaches to prostaglandin inhibition in human disease. *Nat Rev Drug Discov* 2003;2:879-890.
- [97] Leroux M. Discovery of salicine. *J Chim Med* 1830;6:341.
- [98] Piria R. Recherches sur la salicine et les produits qui en dévirent. *Ann Chim Phys* 1838;69:281-325.
- [99] Weissman G. Aspirin Sci Am 1991;264:84-90.
- [100] Loll PJ, Picot D, and Garavito RM. The structural basis of aspirin activity inferred from the crystal structure of inactivated prostaglandin H₂ synthase. *Nat Struct Biol* 1995;2: 637-643.
- [101] Serhan CN. Lipoxins and novel aspirin-triggered 15-epi-lipoxins (ATL): a jungle of cell-cell interactions or a therapeutic opportunity? *Prostaglandins* 1997;53:107-137.
- [102] Serhan CN. Lipoxins and aspirin-triggered 15-epi-lipoxin biosynthesis: an update and role in anti-inflammation and pro-resolution. *Prostaglandins Other Lipid Mediat* 2002;68-69:433-55.
- [103] Marcus AJ, Hajjar DP. Vascular transcellular signaling. *J Lipid Res* 1993;34:2017-2031.
- [104] Serhan CN. Lipoxin biosynthesis and its impact in inflammatory and vascular events. *Biochim Biophys Acta* 1994;1212:1-25.
- [105] Serhan CN, Hamber M, Samuelsson B. Lipoxins: novel series of biologically active compounds formed from arachidonic acid in human leukocytes. *Proc Natl Acad Sci U S A* 1984;81:5335-5339.

- [106] Lefer AM, Stahl GL, Lefer DJ, Brezinski ME, Nicolaou KC, Veale CA, Abe Y, Smith JB. Lipoxins A₄ and B₄: comparison of icosanoids having bronchoconstrictor and vasodilator actions but lacking platelet aggregatory activity. Proc Natl Acad Sci U S A 1988;85:8340-8344.
- [107] Dahlen SE, Franzen L, Raud J, Serhan CN, Westlund P, Wikstrom E, Bjorck T, Matsuda H, Webber SE, Veale CA, Puustinen T, Haeggstrom J, Nicolau KC, Samuelsson B. Actions of lipoxin A₄ and related compounds in smooth muscle preparations and on the microcirculation in vivo. Adv Exp Med Biol 1988;229:107-130.
- [108] Titos E, Chiang N, Serhan CN, Romano M, Gaya J, Pueyo G, Clària J. Hepatocytes are a rich source of novel aspirin-triggered 15-epi-lipoxin A₄. Am J Physiol 1999;277: C870-C877.
- [109] Fiore S, Serhan CN. Formation of lipoxins and leukotrienes during receptor-mediated interactions of human platelets and recombinant human granulocyte/macrophage colony-stimulating factor-primed neutrophils. J Exp Med 1990;172:1451-1457.
- [110] Serhan CN, Sheppard KA. Lipoxin formation during human neutrophil-platelet interactions. Evidence for the transformation of leukotriene A₄ by platelet 12-lipoxygenase in vitro. J Clin Invest 1990;85:772-780.
- [111] Otto JC, Smith WL. The orientation of prostaglandin endoperoxide synthases-1 and -2 in the endoplasmic reticulum. J Biol Chem 1994;269:19868-19875.
- [112] Clària J, Lee MH, Serhan CN. Aspirin-triggered lipoxins (15-epi-LX) are generated by the human lung adenocarcinoma cell line (A549)-neutrophil interactions and are potent inhibitors of cell proliferation. Mol Med 1996;2:583-596.
- [113] Savage MP, Goldberg S, Bove AA, Deutsch E, Vetrovec G, Macdonald RG, Bass T, Margolis JR, Whitworth HB, Taussig A. Effect of thromboxane A2 blockade on clinical outcome and restenosis after successful coronary angioplasty. Multi-Hospital Eastern Atlantic Restenosis Trial (M-HEART II) Circulation 1995;92:3194-3200.
- [114] Giovannucci E, Egan KM, Hunter DJ, Stampfer MJ, Colditz GA, Willett WC, Speizer FE. Aspirin and the risk of colorectal cancer in women. N Engl J Med 1995;333:609-614.

Bibliografia

- [115] Takano T, Fiore S, Maddox JF, Brady HR, Petasis NA, Serhan CN. Aspirin-triggered 15-epi-lipoxin A₄ (LXA₄) and LXA₄ stable analogues are potent inhibitors of acute inflammation: evidence for anti-inflammatory receptors. *J Exp Med* 1997;185:1693-1704.
- [116] Simmons DL, Botting RM, Hla T. Cyclooxygenase isozymes: the biology of prostaglandin synthesis and inhibition. *Pharmacol Rev* 2004;56:387-437.
- [117] Marnett LJ, Kalgutkar AS. Design of selective inhibitors of cyclooxygenase-2 as nonulcerogenic anti-inflammatory agents. *Curr Opin Chem Biol* 1998;2:482-490.
- [118] Selinsky BS, Gupta K, Sharkey CT, Loll PJ. Structural analysis of NSAID binding by prostaglandin H₂ synthase: time-dependent and time-independent inhibitors elicit identical enzyme conformations. *Biochemistry* 2001;40:5172-5180.
- [119] Smith CJ, Zhang Y, Koboldt CM, Muhammad J, Zweifel BS, Shaffer A, Talley JJ, Masferrer JL, Seibert K, Isakson PC. Pharmacological analysis of cyclooxygenase-1 in inflammation. *Proc Natl Acad Sci U S A* 1998;95:13313-13318.
- [120] Masferrer JL, Zweifel BS, Manning PT, Hauser SD, Leahy KM, Smith WG, Isakson PC, Seibert K. Selective inhibition of inducible cyclooxygenase 2 in vivo is antiinflammatory and nonulcerogenic. *Proc Natl Acad Sci U S A* 1994;91:3228-3232.
- [121] Clària J. Cyclooxygenase-2 biology. *Curr Pharm Des* 2003;9:2177-2190.
- [122] Flower RJ. The development of COX-2 inhibitors. *Nature Reviews Drug Discovery* 2003;2:179-191.
- [123] Smith HS, Baird W. Meloxicam and selective COX-2 inhibitors in the management of pain in the palliative care population. *Am J Hosp Palliat Care* 2003;20:297-306.
- [124] Hunt RH, Harper S, Watson DJ, Yu C, Quan H, Lee M, Evans JK, Oxenius B. The gastrointestinal safety of the COX-2 selective inhibitor etoricoxib assessed by both endoscopy and analysis of upper gastrointestinal events. *Am J Gastroenterol* 2003;98:1725-1733.
- [125] Ding C, Jones G. Lumiracoxib (Novartis). *IDrugs* 2002;5:1168-1172.

- [126] Gierse JK, McDonald JJ, Hauser SD, Rangwala SH, Koboldt CM, Seibert K. A single amino acid difference between cyclooxygenase-1 (COX-1) and -2 (COX-2) reverses the selectivity of COX-2 specific inhibitors. *J Bio Chem* 1996; 271:15810-15814.
- [127] Penning TD, Talley JJ, Bertenshaw SR, Carter JS, Collins PW, Docter S, Graneto MJ, Lee LF, Malecha JW, Miyashiro JM, Rogers RS, Rogier DJ, Yu SS, Anderson GD, Burton EG, Cogburn JN, Gregory SA, Koboldt CM, Perkins WE, Seibert K, Veenhuizen AW, Zhang YY, Isakson PC. Synthesis and biological evaluation of the 1,5-diarylpyrazole class of cyclooxygenase-2 inhibitors: identification of 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (SC-58635, celecoxib). *J Med Chem* 1997;40:1347-1365.
- [128] Castaño E, Bartrons R, Gil J. Inhibition of cyclooxygenase-2 decreases DNA synthesis induced by platelet-derived growth factor in Swiss 3T3 fibroblasts. *J Pharmacol Exp Ther* 2000; 293:509-513.
- [129] Petersen C, Petersen S, Milas L, Lang FF i Tofilon PJ. Enhancement of intrinsic tumor cell radiosensitivity induced by a selective cyclooxygenase-2 inhibitor. *Clin Cancer Res* 2000;6:2513-2520.
- [130] Masferrer JL, Koki A, Seibert K. COX-2 inhibitors. A new class of antiangiogenic agents. *Ann N Y Acad Sci* 1999;889:84-86.
- [131] Friedman SL. Liver fibrosis -- from bench to bedside. *J Hepatol* 2003;38 Suppl 1:S38-53.
- [132] Laskin DL. Nonparenchymal cells and hepatotoxicity. *Semin Liver Dis* 1990;10:293-304.
- [133] Friedman SL. Molecular regulation of hepatic fibrosis, an integrated cellular response to tissue injury. *J Biol Chem* 2000;275:2247-2250.
- [134] Wake K. Perisinusoidal stellate cells (fat-storing cells, interstitial cells, lipocytes) their related structure in and around liver sinusoids, and vitamin A storing cells in extrahepatic organs. *Int Rev Cytol* 1980;66:303-353.
- [135] Friedman SL, Roll FJ, Boyles J, Bissell DM. Hepatic lipocytes: the principal collagen-producing cells of normal rat liver. *Proc Natl Acad Sci U S A* 1985;82:8681-8685.

Bibliografia

- [136] Brenner DA, Waterboer T, Choi SK, Linquist JN, Stefanovic B, Burchardt E, Yamauchi M, Guillan A i Rippe RA. New aspects of hepatic fibrosis. *J Hepatol* 2000;32:32-38.
- [137] Kupffer K. Ueber Sternzellen der Leber. Briefliche Mitteilung an Profesor Waldeyer. *Arch Mikr Anat* 1876;12:353-358.
- [138] Clària J, Titos E. La célula de Kupffer. *Gastroenterol Hepatol* 2004;27:264-273.
- [139] Wisse E. Observations on the fine structure and peroxidase cytochemistry of normal rat liver Kupffer cells. *J Ultrastruct Res* 1974;46:393-426.
- [140] Marugg RA, Gehr P, de Leeuw M. Secondary lysosomes as an integral part of the cytoskeleton: a morphological study in rat Kupffer cells. *J Struct Biol* 1990;105:146-153.
- [141] Sun WB, Han BL, Peng ZM, Li K, Ji Q, Chen J, Wang HZ, Ma RL. Effect of aging on cytoskeleton system of Kupffer cell and its phagocytic capacity. *World J Gastroenterol* 1998;4:77-79.
- [142] Wisse E. Ultrastructure and function of Kupffer cells and other sinusoidal cells in the liver. In: Wisse E, Knook DL, eds. *Kupffer cells and other sinusoidal cells*. Amsterdam: Elsevier, 1977:33-60.
- [143] Hoedemakers RM, Morselt HW, Scherphof GL, Daemen T. Heterogeneity in secretory responses of rat liver macrophages of different size. *Liver* 1995;15:313-319.
- [144] Dijkstra CD, Dopp EA, Joling P, Kraal G. The heterogeneity of mononuclear phagocytes in lymphoid organs: distinct macrophage subpopulations in the rat recognized by monoclonal antibodies ED1, ED2 and ED3. *Immunology* 1985;54:589-599.
- [145] Fox ES, Broitman SA, Thomas P. Bacterial endotoxins and the liver. *Lab Invest* 1990;63:733-741.
- [146] Van Bossuyt H, Wisse E. Cultured Kupffer cells, isolated from human and rat liver biopsies, ingest endotoxin. *J Hepatol* 1988;7:45-56.
- [147] Rogoff TM, Lipsky PE. Role of the Kupffer cells in local and systemic immune responses. *Gastroenterology* 1981;80:854-860.

- [148] Schuurman B, Heuff G, Beelen RH, Meyer S. Enhanced human Kupffer cell-mediated cytotoxicity after activation of the effector cells and modulation of the target cells by interferon-gamma: a mechanistic study at the cellular level. *Cell Immunol* 1995;165:141-147.
- [149] Decker K. Eicosanoids, signal molecules of liver cells. *Semin Liver Dis* 1985;5:175-190.
- [150] Winwood PJ, Arthur MJ. Kupffer cells: their activation and role in animal models of liver injury and human liver disease. *Semin Liver Dis* 1993;13:50-59.
- [151] Eyhorn S, Schlayer HJ, Henninger HP, Dieter P, Hermann R, Woort-Menker M, Becker H, Schaefer HE, Decker K. Rat hepatic sinusoidal endothelial cells in monolayer culture. Biochemical and ultrastructural characteristics. *J Hepatol* 1988;6:23-35.
- [152] Rieder H, Ramadori G, Allmann KH, Meyer zum Buschenfelde KH. Prostanoid release of cultured liver sinusoidal endothelial cells in response to endotoxin and tumor necrosis factor. Comparison with umbilical vein endothelial cells. *J Hepatol* 1990;11:359-366.
- [153] Efsen E, Bonacchi A, Pastacaldi S, Valente AJ, Wenzel UO, Tosti-Guerra C, Pinzani M, Laffi G, Abboud HE, Gentilini P, Marra F. Agonist-specific regulation of monocyte chemoattractant protein-1 expression by cyclooxygenase metabolites in hepatic stellate cells. *Hepatology* 2001;33:713-721.
- [154] Mallat A, Gallois C, Tao J, Habib A, Maclouf J, Mavier P, Preaux AM, Lotersztajn S. Platelet-derived growth factor- β and thrombin generate positive and negative signals for human hepatic stellate cell proliferation. Role of a prostaglandin/cyclic AMP pathway and cross-talk with endothelin receptors. *J Biol Chem* 1998;273:27300-27305.
- [155] Gallois C, Habib A, Tao J, Moulin S, Maclouf J, Mallat A, Lotersztajn S. Role of NF-kappaB in the antiproliferative effect of endothelin-1 and tumor necrosis factor-alpha in human hepatic stellate cells. Involvement of cyclooxygenase-2. *J Biol Chem* 1998;273:23183-23190.
- [156] Athari A, Hanecke K, Jungermann K. Prostaglandin F2 alpha and D2 release from primary Ito cell cultures after stimulation with noradrenaline and ATP but not adenosine. *Hepatology* 1994;20:142-148.

Bibliografia

- [157] Pestel S, Jungermann K, Gotze O, Schieferdecker HL. Inhibition by prostaglandin E(2) of anaphylatoxin C5a- but not zymosan-induced prostanoid release from rat Kupffer cells. *Lab Invest* 2002;82:463-471.
- [158] Schieferdecker HL, Pestel S, Rothermel E, Puschel GP, Gotze O, Jungermann K. Stimulation by anaphylatoxin C5a of glycogen phosphorylase in rat hepatocytes via prostanoid release from hepatic stellate cells but not sinusoidal endothelial cells. *FEBS Lett* 1998;434:245-250.
- [159] Martín-Sanz P, Callejas NA, Casado M, Díaz-Guerra MJ, Boscá L. Expression of cyclooxygenase-2 in fetal rat hepatocytes stimulated with lipopolysaccharide and pro-inflammatory cytokines. *Br J Pharmacol* 1998;125:1313-1319.
- [160] Keppler D, Huber M, Baumert T. Leukotrienes as mediators in diseases of the liver. *Semin Liver Dis* 1988;8:357-866.
- [161] Pérez HD, Roll FJ, Bissell DM, Shak S, Goldstein IM. Production of chemotactic activity for polymorphonuclear leukocytes by cultured rat hepatocytes exposed to ethanol. *J Clin Invest* 1984;74:1350-1357.
- [162] Roll FJ, Bissell DM, Perez HD. Human hepatocytes metabolizing ethanol generate a non-polar chemotactic factor for human neutrophils. *Biochem Biophys Res Commun* 1986;137:688-694.
- [163] Shirley MA, Reidhead CT, Murphy RC. Chemotactic LTB4 metabolites produced by hepatocytes in the presence of ethanol. *Biochem Biophys Res Commun* 1992;185:604-610.
- [164] Titos E, Clària J, Bataller R, Bosch-Marce M, Ginès P, Jiménez W, Arroyo V, Rivera F, Rodés J. Hepatocyte-derived cysteinyl leukotrienes modulate vascular tone in experimental cirrhosis. *Gastroenterology* 2000;119:794-805.
- [165] Titos E, Clària J, Planagumà A, López-Parra M, Villamor N, Párrizas M, Carrió A, Miquel R, Jiménez W, Arroyo V, Rivera F, Rodés J. Inhibition of 5-lipoxygenase induces cell growth arrest and apoptosis in rat Kupffer cells: implications for liver fibrosis. *FASEB J* 2003;17:1745-1747.

- [166] Shimada K, Navarro J, Goeger DE, Mustafa SB, Weigel PH, Weinman SA. Expression and regulation of leukotriene-synthesis enzymes in rat liver cells. *Hepatology* 1998;28:1275-1281.
- [167] Scoggan KA, Jakobsson PJ, Ford-Hutchinson AW. Production of leukotriene C₄ in different human tissues is attributable to distinct membrane bound biosynthetic enzymes. *J Biol Chem* 1997;272:10182-10187.
- [168] Fukai F, Suzuki Y, Ohtaki H, Katayama T. Rat hepatocytes generate peptide leukotrienes from leukotriene A₄. *Arch Biochem Biophys* 1993;305:378-384.
- [169] Fukai F, Suzuki Y, Nishizawa Y, Katayama T. Transcellular biosynthesis of cysteinyl leukotrienes by Kupffer cell-hepatocyte cooperation in rat liver. *Cell Biol Int* 1996;20:423-428.
- [170] Wheelan P, Murphy RC, Simon FR. Gas chromatographic/mass spectrometric analysis of oxo and chain-shortened leukotriene B4 metabolites. Leukotriene B4 metabolism in Ito cells. *J Mass Spectrom* 1996;31:236-246.
- [171] Clària J, Titos E. *Medicas UIS* 2003;17:115-122.
- [172] Kawada N, Mizoguchi Y, Kobayashi K, Morisawa S, Monna T, Yamamoto S. Interferon gamma modulates production of interleukin 1 and tumor necrosis factor by murine Kupffer cells. *Liver* 1991;11:42-47.
- [173] Stachura J, Tarnawski A, Ivey KJ, Mach T, Bogdal J, Szczudrawa J, klimczyk B. Prostaglandin protection of carbon tetrachloride-induced liver cell necrosis in the rat. *Gastroenterology* 1981;81:211-217.
- [174] Crafa F, Gugenheim J, Saint-Paul MC, Cavanel C, Lapalus F, Ouzan D, Militerno G, Mouiel J. Protective effects of prostaglandin E1 on normothermic liver ischemia. *Eur Surg Res* 1991;23:278-284.
- [175] Arai M, Peng XX, Currin RT, Thurman RG, Lemasters JJ. Protection of sinusoidal endothelial cells against storage/reperfusion injury by prostaglandin E2 derived from Kupffer cells. *Transplantation* 199;68:440-445.

Bibliografia

- [176] Quiroga J, Prieto J. Liver cytoprotection by prostaglandins. *Pharmacol Ther* 993;58:67-91.
- [177] Enomoto N, Ikejima K, Yamashina S, Enomoto A, Nishiura T, Nishimura T, Brenner DA, Schemmer P, Bradford BU, Rivera CA, Zhong Z, Thurman RG. Kupffer cell-derived prostaglandin E(2) is involved in alcohol-induced fat accumulation in rat liver. *Am J Physiol Gastrointest Liver Physiol* 2000;279:G100-G106.
- [178] Harbrecht BG, McClure EA, Simmons RL, Billiar TR. Prostanoids inhibit Kupffer cell nitric oxide synthesis. *J Surg Res* 1995;58:625-629.
- [179] Karck U, Peters T, Decker K. The release of tumor necrosis factor from endotoxin-stimulated rat Kupffer cells is regulated by prostaglandin E2 and dexamethasone. *J Hepatol* 1988;7:352-361.
- [180] Kuiper J, De Rijke YB, Zijlstra FJ, Van Waas MP, Van Berkel TJ. The induction of glycogenolysis in the perfused liver by platelet activating factor is mediated by prostaglandin D2 from Kupffer cells. *Biochem Biophys Res Commun* 1988;157:1288-1295.
- [181] Iwai M, Jungermann K. Leukotrienes increase glucose and lactate output and decrease flow in perfused rat liver. *Biochem Biophys Res Commun* 1988;151:283-290.
- [182] Ruf G, Mappes HJ, Koch H, Baumgartner U, Hagmann W, Farthmann EH. Aminoterminal propeptide of type III procollagen: a marker of hepatic fibrosis after bile duct obstruction in the monkey. *Hepatogastroenterology* 1996;43:121-126.
- [183] Gressner AM, Haarmann R. Regulation of hyaluronate synthesis in rat liver fat storing cell cultures by Kupffer cells. *J Hepatol* 1988;7:310-318.
- [184] Friedman SL. Mechanisms of hepatic fibrosis and therapeutic implications. *Nature Clinical Practice in Gastroenterology and Hepatology* 2004;1:98-105.
- [185] Brenner DA, Waterboer T, Choi SK, Lindquist JN, Stefanovic B, Burchardt E, Yamauchi M, Gillan A, Rippe RA. New aspects of hepatic fibrosis. *J Hepatol* 2000;32:32-38.

- [186] Bataller R, Brenner DA. Liver fibrosis. *J Clin Invest* 2005;115:209-218.
- [187] Bataller R, Ginés P. Nuevas perspectivas terapéuticas de la fibrosis hepática: bases patogénicas. *Med Clin (Barc)* 2002;118:339-346.
- [188] de Leeuw AM, McCarthy SP, Geerts A, Knook DL. Purified rat liver fat-storing cells in culture divide and contain collagen. *Hepatology* 1984;4:392-403.
- [189] Iredale JP, Benyon RC, McCullen PM, Northrop M, Pawley S, Hovell C, Arthur MJP. Mechanisms of spontaneous resolution of rat liver fibrosis. *J Clin Invest* 1998;102:538-549.
- [190] Duffield JS, Forbes SJ, Constandinou CM, Clay S, Partolina M, Vuthoori S, Wu S, Lang R, Iredale JP. Selective depletion of macrophages reveals distinct, opposing roles during liver injury and repair. *J Clin Invest* 2005;115:56-65.
- [191] Friedman SL. Mac the knife? Macrophages-the double-edged sword of hepatic fibrosis. *J Clin Invest* 2005;115:29-32.
- [192] Geerts A, Schellinck P, Bouwens L, Wisse E. Cell population kinetics of Kupffer cells during the onset of fibrosis in rat liver by chronic carbon tetrachloride administration. *J Hepatol* 1988;6:50-56.
- [193] Thompson WD, Jack AS, Patrick RS. The possible role of macrophages in transient hepatic fibrogenesis induced by acute carbon tetrachloride injury. *J Pathol* 1980;130:65-73.
- [194] Luckey SW, Petersen DR. Activation of Kupffer cells during the course of carbon tetrachloride-induced liver injury and fibrosis in rats. *Exp Mol Pathol* 2001;71:226-240.
- [195] Alric L, Orfila C, Carrere N, Beraud M, Carrera G, Lepert JC, Duffaut M, Pipy B, Vinel JP. Reactive oxygen intermediates and eicosanoid production by kupffer cells and infiltrated macrophages in acute and chronic liver injury induced in rats by CCl_4 . *Inflamm Res* 2000;49:700-707.

Bibliografia

- [196] Matsuoka M, Tsukamoto H. Stimulation of hepatic lipocyte collagen production by Kupffer cell-derived transforming growth factor beta: implication for a pathogenetic role in alcoholic liver fibrogenesis. *Hepatology* 1990;11:599-605.
- [197] Shiratori Y, Geerts A, Ichida T, Kawase T, Wisse E. Kupffer cells from CCl₄-induced fibrotic livers stimulate proliferation of fat-storing cells. *J Hepatol* 1986;3:294-303.
- [198] Friedman SL, Arthur MJ. Activation of cultured rat hepatic lipocytes by Kupffer cell conditioned medium. Direct enhancement of matrix synthesis and stimulation of cell proliferation via induction of platelet-derived growth factor receptors. *J Clin Invest* 1989;84:1780-1785.
- [199] Gressner AM, Zerbe O. Kupffer cell-mediated induction of synthesis and secretion of proteoglycans by rat liver fat-storing cells in culture. *J Hepatol* 1987;5:299-310.
- [200] Gressner AM, Haarmann R. Regulation of hyaluronate synthesis in rat liver fat storing cell cultures by Kupffer cells. *J Hepatol* 1988;7:310-318.
- [201] Erlinger S, Benhamou JP. Cirrhosis clinical aspects. In: Bircher J, Benhamou JP, McIntyre N, Rizzeto M, Rodés J, eds. *Oxford textbook of clinical hepatology*. Oxford: Oxford University Press, 1999;6.2:629-641.
- [202] Arroyo V, Bataller R. Historical notes on ascites in cirrhosis. In: Arroyo V, Ginès P, Rodés J, Schrier RW, eds. *Ascites and renal dysfunction in liver disease*. Malden (Mass): Blackwell Science, 1999;1:3.
- [203] Bonis PA, Friedman SL, Kaplan MM. Is liver fibrosis reversible? *N Engl J Med* 2001; 344:452-454.
- [204] Desmet VJ, Roskams T. Cirrhosis reversal: a duel between dogma and myth. *J Hepatol* 2004;40:860-867.
- [205] Poynard T, McHutchison J, Manns M, Trepo C, Lindsay K, Goodman Z, Ling MH, Albrecht J. Impact of pegylated interferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C. *Gastroenterology* 2002;122:1303-1313.

- [206] Murphy FR, Issa R, Zhou X, Ratnarajah S, Nagase H, Arthur MJ, Benyon C, Iredale JP. Inhibition of apoptosis of activated hepatic stellate cells by tissue inhibitor of metalloproteinase-1 is mediated via effects on matrix metalloproteinase inhibition: implications for reversibility of liver fibrosis. *J Biol Chem* 2002;277:11069-11076.
- [207] Rockey DC. Antifibrotic therapy in chronic liver disease. *Clin Gastroenterol Hepatol* 2005;3:95-107.
- [208] Sanderson N, Factor V, Nagy P, Kopp J, Kondaiah P, Wakefield L, Roberts AB, Sporn MB, Thorgeirsson SS. Hepatic expression of mature transforming growth factor beta 1 in transgenic mice results in multiple tissue lesions. *Proc Natl Acad Sci U S A* 1995;92:2572-2576.
- [209] Hellerbrand C, Stefanovic B, Giordano F, Burchardt ER, Brenner DA. The role of TGFbeta1 in initiating hepatic stellate cell activation in vivo. *J Hepatol* 1999;30:77-87.
- [210] George J, Roulot D, Koteliansky VE, Bissell DM. In vivo inhibition of rat stellate cell activation by soluble transforming growth factor beta type II receptor: a potential new therapy for hepatic fibrosis. *Proc Natl Acad Sci U S A* 1999;96:12719-12724.
- [211] Gressner AM, Weiskirchen R, Breitkopf K, Dooley S. Roles of TGF-beta in hepatic fibrosis. *Front Biosci* 2002;7:793-807.
- [212] Isaka Y, Brees DK, Ikegaya K, Kaneda Y, Imai E, Noble NA, Border WA. Gene therapy by skeletal muscle expression of decorin prevents fibrotic disease in rat kidney. *Nat Med* 1996;2:418-423.
- [213] Yata Y, Gotwals P, Koteliansky V, Rockey DC. Dose-dependent inhibition of hepatic fibrosis in mice by a TGF-beta soluble receptor: implications for antifibrotic therapy. *Hepatology* 2002;35:1022-1030.
- [214] Pinzani M, Milani S, Herbst H, DeFranco R, Grappone C, Gentilini A, Caligiuri A, Pellegrini G, Ngo DV, Romanelli RG, Gentilini P. Expression of platelet-derived growth factor and its receptors in normal human liver and during active hepatic fibrogenesis. *Am J Pathol* 1996;148:785-800.

- [215] Ueki T, Kaneda Y, Tsutsui H, Nakanishi K, Sawa Y, Morishita R, Matsumoto K, Nakamura T, Takahashi H, Okamoto E, Fujimoto J. Hepatocyte growth factor gene therapy of liver cirrhosis in rats. *Nat Med* 1999;5:226-230.
- [216] Bustos M, Beraza N, Lasarte JJ, Baixeras E, Alzuguren P, Bordet T, Prieto J. Protection against liver damage by cardiotrophin-1: a hepatocyte survival factor up-regulated in the regenerating liver in rats. *Gastroenterology* 2003;125:192-201.
- [217] Rockey DC, Chung JJ. Interferon gamma inhibits lipocyte activation and extracellular matrix mRNA expression during experimental liver injury: implications for treatment of hepatic fibrosis. *J Investig Med* 1994;42:660-670.
- [218] Inagaki Y, Nemoto T, Kushida M, Sheng Y, Higashi K, Ikeda K, Kawada N, Shirasaki F, Takehara K, Sugiyama K, Fujii M, Yamauchi H, Nakao A, de Crombrugghe B, Watanabe T, Okazaki I. Interferon alfa down-regulates collagen gene transcription and suppresses experimental hepatic fibrosis in mice. *Hepatology* 2003;38:890-899.
- [219] Kawada N, Kristensen DB, Asahina K, Nakatani K, Minamiyama Y, Seki S, Yoshizato K. Characterization of a stellate cell activation-associated protein (STAP) with peroxidase activity found in rat hepatic stellate cells. *J Biol Chem* 2001;276:25318-25323.
- [220] Kamada Y, Tamura S, Kiso S, Matsumoto H, Saji Y, Yoshida Y, Fukui K, Maeda N, Nishizawa H, Nagaretani H, Okamoto Y, Kihara S, Miyagawa J, Shinomura Y, Funahashi T, Matsuzawa Y. Enhanced carbon tetrachloride-induced liver fibrosis in mice lacking adiponectin. *Gastroenterology* 2003;125:1796-1807.
- [221] Weng HL, Cai WM, Liu RH. Animal experiment and clinical study of effect of gamma-interferon on hepatic fibrosis. *World J Gastroenterol* 2001;7:42-48.
- [222] Czaja MJ, Weiner FR, Eghbali M, Giambrone MA, Eghbali M, Zern MA. Differential effects of gamma-interferon on collagen and fibronectin gene expression. *J Biol Chem* 1987;262:13348-13351.
- [223] Rockey DC, Maher JJ, Jarnagin WR, Gabbiani G, Friedman SL. Inhibition of rat hepatic lipocyte activation in culture by interferon-gamma. *Hepatology* 1992;16:776-784.

- [224] Toyonaga T, Hino O, Sugai S, Wakasugi S, Abe K, Shichiri M, Yamamura K. Chronic active hepatitis in transgenic mice expressing interferon-gamma in the liver. *Proc Natl Acad Sci U S A* 1994;91:614-618.
- [225] Muir A, Rockey DC. Treatment of acute hepatitis C with interferon alfa-2b. *N Engl J Med* 2002;346:1091-1092.
- [226] Akriviadis E, Botla R, Briggs W, Han S, Reynolds T, Shakil O. Pentoxifylline improves short-term survival in severe acute alcoholic hepatitis: a double-blind, placebo-controlled trial. *Gastroenterology* 2000;119:1637-1648.
- [227] Spahr L, Rubbia-Brandt L, Frossard JL, Giostra E, Rougemont AL, Pugin J, Fischer M, Egger H, Hadengue A. Combination of steroids with infliximab or placebo in severe alcoholic hepatitis: a randomized controlled pilot study. *J Hepatol* 2002;37:448-455.
- [228] Tilg H, Jalan R, Kaser A, Davies NA, Offner FA, Hodges SJ, Ludwiczek O, Shawcross D, Zoller H, Alisa A, Mookerjee RP, Graziadei I, Datz C, Trauner M, Schuppan D, Obrist P, Vogel W, Williams R. Anti-tumor necrosis factor-alpha monoclonal antibody therapy in severe alcoholic hepatitis. *J Hepatol* 2003;38:419-425.
- [229] Menon KV, Stadheim L, Kamath PS, Wiesner RH, Gores GJ, Peine CJ, Shah V. A pilot study of the safety and tolerability of etanercept in patients with alcoholic hepatitis. *Am J Gastroenterol* 2004;99:255-260.
- [230] Naveau S, Chollet-Martin S, Dharancy S, Mathurin P, Jouet P, Piquet MA, Davion T, Oberti F, Broet P, Emilie D. A double-blind randomized controlled trial of infliximab associated with prednisolone in acute alcoholic hepatitis. *Hepatology* 2004;39:1390-1397.
- [231] Tsukamoto H. Is interleukin-10 antifibrogenic in chronic liver injury? *Hepatology* 1998;28:1707-1709.
- [232] Nelson DR, Tu Z, Soldevila-Pico C, Abdelmalek M, Zhu H, Xu YL, Cabrera R, Liu C, Davis GL. Long-term interleukin 10 therapy in chronic hepatitis C patients has a proviral and anti-inflammatory effect. *Hepatology* 2003;38:859-868.

Bibliografia

- [233] Zheng WD, Zhang LJ, Shi MN, Chen ZX, Chen YX, Huang YH, Wang XZ. Expression of matrix metalloproteinase-2 and tissue inhibitor of metalloproteinase-1 in hepatic stellate cells during rat hepatic fibrosis and its intervention by IL-10. *World J Gastroenterol* 2005;11:1753-1758.
- [234] Thompson K, Maltby J, Fallowfield J, McAulay M, Millward-Sadler H, Sheron N. Interleukin-10 expression and function in experimental murine liver inflammation and fibrosis. *Hepatology* 1998;28:1597-1606.
- [235] Balkwill F. Cancer and the chemokine network. *Nat Rev Cancer* 2004;4:540-550.
- [236] Bataller R, Schwabe RF, Choi YH, Yang L, Paik YH, Lindquist J, Qian T, Schoonhoven R, Hagedorn CH, Lemasters JJ, Brenner DA. NADPH oxidase signal transduces angiotensin II in hepatic stellate cells and is critical in hepatic fibrosis. *J Clin Invest* 2003;112:1383-1394.
- [237] Rockey DC, Chung JJ. Endothelin antagonism in experimental hepatic fibrosis. Implications for endothelin in the pathogenesis of wound healing. *J Clin Invest* 1996;98:1381-1388.
- [238] Rockey DC. Vascular mediators in the injured liver. *Hepatology* 2003;37:4-12.
- [239] Cho JJ, Hocher B, Herbst H, Jia JD, Ruehl M, Hahn EG, Riecken EO, Schuppan D. An oral endothelin-A receptor antagonist blocks collagen synthesis and deposition in advanced rat liver fibrosis. *Gastroenterology* 2000;118:1169-1178.
- [240] Jonsson JR, Clouston AD, Ando Y, Kelemen LI, Horn MJ, Adamson MD, Purdie DM, Powell EE. Angiotensin-converting enzyme inhibition attenuates the progression of rat hepatic fibrosis. *Gastroenterology* 2001;121:148-155.
- [241] Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S; RENAAL Study Investigators. *N Engl J Med* 2001;345:861-869.
- [242] Dubuisson L, Desmouliere A, Decourt B, Evade L, Bedin C, Boussarie L, Barrier L, Vidaud M, Rosenbaum J. Inhibition of rat liver fibrogenesis through noradrenergic antagonism. *Hepatology* 2002;35:325-331.

- [243] Oben JA, Roskams T, Yang S, Lin H, Sinelli N, Torbenson M, Smedh U, Moran TH, Li Z, Huang J, Thomas SA, Diehl AM. Hepatic fibrogenesis requires sympathetic neurotransmitters. *Gut* 2004;53:438-445.
- [244] Czaja AJ, Carpenter HA. Decreased fibrosis during corticosteroid therapy of autoimmune hepatitis. *J Hepatol* 2004;40:646-652.
- [245] Cheng J, Imanishi H, Iijima H, Shimomura S, Yamamoto T, Amuro Y, Kubota A, Hada T. Expression of cyclooxygenase 2 and cytosolic phospholipase A(2) in the liver tissue of patients with chronic hepatitis and liver cirrhosis. *Hepatol Res* 2002;23:185-195.
- [246] Mohammed NA, Abd El-Aleem SA, El-Hafiz HA, McMahon RF. Distribution of constitutive (COX-1) and inducible (COX-2) cyclooxygenase in postviral human liver cirrhosis: a possible role for COX-2 in the pathogenesis of liver cirrhosis. *J Clin Pathol* 2004;57:350-354.
- [247] Núñez O, Fernández-Martínez A, Majano PL, Apolinario A, Gómez-Gonzalo M, Benedicto I, López-Cabrera M, Boscá L, Clemente G, García-Monzón C, Martín-Sanz P. Increased intrahepatic cyclooxygenase 2, matrix metalloproteinase 2, and matrix metalloproteinase 9 expression is associated with progressive liver disease in chronic hepatitis C virus infection: role of viral core and NS5A proteins. *Gut* 2004;53:1665-1672.
- [248] Nanji AA, Zakim D, Rahemtulla A, Daly T, Miao L, Zhao S, Khwaja S, Tahan SR, Dannenberg AJ. Dietary saturated fatty acids down-regulate cyclooxygenase-2 and tumor necrosis factor alfa and reverse fibrosis in alcohol-induced liver disease in the rat. *Hepatology* 1997;26:1538-1545.
- [249] Nanji AA, Miao L, Thomas P, Rahemtulla A, Khwaja S, Zhao S, Peters D, Tahan SR, Dannenberg AJ. Enhanced cyclooxygenase-2 gene expression in alcoholic liver disease in the rat. *Gastroenterology* 1997;112:943-951.
- [250] Yamamoto H, Kondo M, Shoji N, Nagano H, Wakasa KI, Sugita Y, Chang-De J, Kobayashi S, Damdinsuren B, Dono K, Umehita K, Sekimoto M, Sakon M, Matsuura N, Monden M. JTE-522, a cyclooxygenase-2 inhibitor, is an effective chemopreventive agent against rat experimental liver fibrosis. *Gastroenterology* 2003;125:556-571.

Bibliografia

- [251] Miyajima A, Ito K, Asano T, Seta K, Ueda A, Hayakawa M. Does cyclooxygenase-2 inhibitor prevent renal tissue damage in unilateral ureteral obstruction? *J Urol* 2001;166:1124-1129.
- [252] Frungieri MB, Weidinger S, Meineke V, Kohn FM, Mayerhofer A. Proliferative action of mast-cell tryptase is mediated by PAR2, COX2, prostaglandins, and PPARgamma: Possible relevance to human fibrotic disorders. *Proc Natl Acad Sci U S A* 2002;99:15072-15077.
- [253] Tsai CH, Hsieh YS, Yang SF, Chou MY, Chang YC. Matrix metalloproteinase 2 and matrix metalloproteinase 9 expression in human oral squamous cell carcinoma and the effect of protein kinase C inhibitors: preliminary observations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:710-716.
- [254] Marra F, Efsen E, Romanelli RG, Caligiuri A, Pastacaldi S, Bagnani G, Bonacchi A, Caporale R, Laffi G, Pinzani M, Gentilini P. Ligands of peroxisome proliferator-activated receptor gamma modulate profibrogenic and proinflammatory actions in hepatic stellate cells. *Gastroenterology* 2000;119:466-478.
- [255] Wright MC, Issa R, Smart DE, Trim N, Murray GI, Primrose JN, Arthur MJ, Iredale JP, Mann DA. Gliotoxin stimulates the apoptosis of human and rat hepatic stellate cells and enhances the resolution of liver fibrosis in rats. *Gastroenterology* 2001;121:685-698.
- [256] Evans RM. The steroid and thyroid hormone receptor superfamily. *Science*. 1988;240:889-895.
- [257] Bishop-Bailey D, Warner TD. PPARgamma ligands induce prostaglandin production in vascular smooth muscle cells: indomethacin acts as a peroxisome proliferator-activated receptor-gamma antagonist. *FASEB J*. 2003;17:1925-1927.
- [258] Mangelsdorf DJ, Thummel C, Beato M, Herrlich P, Schutz G, Umesono K, Blumberg B, Kastner P, Mark M, Chambon P, Evans RM. The nuclear receptor superfamily: the second decade. *Cell* 1995;83:835-839.
- [259] Kersten S, Desvergne B, Wahli W. Roles of PPARs in health and disease. *Nature* 2000;405:421-424.

- [260] Kersten S, Seydoux J, Peters JM, González FJ, Desvergne B, Wahli W. Peroxisome proliferator-activated receptor alpha mediates the adaptive response to fasting. *J Clin Invest* 1999;103:1489-1498.
- [261] Desvergne B, Wahli W. Peroxisome proliferator-activated receptors: nuclear control of metabolism. *Endocr Rev* 1999;20:649-688.
- [262] Moya-Camarena SY, Vanden Heuvel JP, Blanchard SG, Leesnitzer LA, Belury MA. Conjugated linoleic acid is a potent naturally occurring ligand and activator of PPARalpha. *J Lipid Res* 1999;40:1426-1433.
- [263] Forman BM, Tontonoz P, Chen J, Brun RP, Spiegelman BM, Evans RM. 15-Deoxy-delta 12, 14-prostaglandin J2 is a ligand for the adipocyte determination factor PPAR gamma. *Cell* 1995;83:803-812.
- [264] Negishi M, Katoh H. Cyclopentenone prostaglandin receptors. *Prostaglandins Other Lipid Mediat* 2002;68-69:611-617.
- [265] Ricote M, Li AC, Willson TM, Kelly CJ, Glass CK. The peroxisome proliferator-activated receptor-gamma is a negative regulator of macrophage activation. *Nature* 1998;391:79-82.
- [266] Jiang C, Ting AT, Seed B. PPAR-gamma agonists inhibit production of monocyte inflammatory cytokines. *Nature* 1998;391:82-86.
- [267] Miyahara T, Schrum L, Rippe R, Xiong S, Yee HF Jr, Motomura K, Anania FA, Willson TM, Tsukamoto H. Peroxisome proliferator-activated receptors and hepatic stellate cell activation. *J Biol Chem* 2000;275:35715-35722.
- [268] Hazra S, Xiong S, Wang J, Rippe RA, Krishna V, Chatterjee K, Tsukamoto H. Peroxisome proliferator-activated receptor gamma induces a phenotypic switch from activated to quiescent hepatic stellate cells. *J Biol Chem* 2004;279:11392-11401.
- [269] Galli A, Crabb DW, Ceni E, Salzano R, Mello T, Svegliati-Baroni G, Ridolfi F, Trozzi L, Surrenti C, Casini A. Antidiabetic thiazolidinediones inhibit collagen synthesis and hepatic stellate cell activation in vivo and in vitro. *Gastroenterology* 2002;122:1924-1940.

Bibliografia

- [270] Tomita K, Azuma T, Kitamura N, Nishida J, Tamiya G, Oka A, Inokuchi S, Nishimura T, Suematsu M, Ishii H. Pioglitazone prevents alcohol-induced fatty liver in rats through up-regulation of c-Met. *Gastroenterology* 2004;126:873-885.
- [271] Neuschwander-Tetri BA, Brunt EM, Wehmeier KR, Oliver D, Bacon BR. Improved nonalcoholic steatohepatitis after 48 weeks of treatment with the PPAR-gamma ligand rosiglitazone. *Hepatology* 2003;38:1008-1017.
- [272] Arthur MJ. Fibrogenesis II. Metalloproteinases and their inhibitors in liver fibrosis. *Am J Physiol Gastrointest Liver Physiol* 2000;279:G245-G249.
- [273] Benyon RC, Arthur MJP. Extracellular matrix degradation and the role of Hepatic stellate cells. *Seminars in Liver Disease* 2001;21:373-384.
- [274] Springman EB, Angleton EL, Birkedal-Hansen H, Van Wart HE. Multiple modes of activation of latent human fibroblast collagenase: evidence for the role of a Cys73 active-site zinc complex in latency and a "cysteine switch" mechanism for activation. *Proc Natl Acad Sci U S A* 1990;87:364-368.
- [275] Takahara T, Furui K, Funaki J, Nakayama Y, Itoh H, Miyabayashi C, Sato H, Seiki M, Ooshima A, Watanabe A. Increased expression of matrix metalloproteinase-II in experimental liver fibrosis in rats. *Hepatology* 1995;21:787-795.
- [276] Benyon RC, Iredale JP, Goddard S, Winwood PJ, Arthur MJ. Expression of tissue inhibitor of metalloproteinases 1 and 2 is increased in fibrotic human liver. *Gastroenterology* 1996;110:821-831.
- [277] Preaux AM, Mallat A, Van Nhieu JT, D'Ortho MP, Hembry RM, Mavie P. Matrix metalloproteinase-2 activation in human hepatic fibrosis regulation by cell-matrix interactions. *Hepatology* 1999;30:944-950.
- [278] Kossakowska AE, Edwards DR, Lee SS, Urbanski LS, Stabbler AL, Zhang CL, Phillips BW, Zhang Y, Urbanski SJ. Altered balance between matrix metalloproteinases and their inhibitors in experimental biliary fibrosis. *Am J Pathol* 1998;153:1895-1902.

- [279] García-Bañuelos J, Siller-López F, Miranda A, Aguilar LK, Aguilar-Córdova E, Armendariz-Borunda J. Cirrhotic rat livers with extensive fibrosis can be safely transduced with clinical-grade adenoviral vectors. Evidence of cirrhosis reversion. *Gene Ther* 2002;9:127-134.
- [280] Rodríguez L, Carbon-Ambriz J, Muñoz ML. Effects of colchicine and colchicine in a biochemical model of liver injury and fibrosis. *Arch Med Res* 1998;29:109-116.
- [281] Kaplan MM, Alling DW, Zimmerman HJ, Wolfe HJ, Sepersky RA, Hirsch GS, Elta GH, Glick KA, Eagen KA. A prospective trial of colchicine for primary biliary cirrhosis. *N Engl J Med* 1986;315:1448-1454.
- [282] Kershenobich D, Vargas F, Garcia-Tsao G, Perez Tamayo R, Gent M, Rojkind M. Colchicine in the treatment of cirrhosis of the liver. *N Engl J Med* 1988;318:1709-1713.
- [283] Rambaldi A, Gluud C. Colchicine for alcoholic and non-alcoholic liver fibrosis or cirrhosis. *Liver* 2001;21:129-136.
- [284] Morgan TR, Weiss DG, Nemchausky B, Schiff ER, Anand B, Simon F, Kidao J, Cecil B, Mendenhall CL, Nelson D, Lieber C, Pedrosa M, Jeffers L, Bloor J, Lumeng L, Marsano L, McClain C, Mishra G, Myers B, Leo M, Ponomarenko Y, Taylor D, Chedid A, French S, Kanel G, Murray N, Pinto P, Fong TL, Sather MR. Colchicine treatment of alcoholic cirrhosis: a randomized, placebo-controlled clinical trial of patient survival. *Gastroenterology* 2005;128:882-890.
- [285] Tome S, Lucey MR. Review article: current management of alcoholic liver disease. *Aliment Pharmacol Ther* 2004;19:707-714.
- [286] Lieber CS. Role of oxidative stress and antioxidant therapy in alcoholic and nonalcoholic liver diseases. *Adv Pharmacol* 1997;38:601-628.
- [287] Harrison SA, Torgerson S, Hayashi P, Ward J, Schenker S. Vitamin E and vitamin C treatment improves fibrosis in patients with nonalcoholic steatohepatitis. *Am J Gastroenterol* 2003;98:2485-2490.

Bibliografia

- [288] Brown KE, Poulos JE, Li L, Soweid AM, Ramm GA, O'Neill R, Britton RS, Bacon BR. Effect of vitamin E supplementation on hepatic fibrogenesis in chronic dietary iron overload. *Am J Physiol* 1997;272:G116-G123.
- [289] Hougum K, Venkataramani A, Lyche K, Chojkier M. A pilot study of the effects of d-alpha-tocopherol on hepatic stellate cell activation in chronic hepatitis C. *Gastroenterology* 1997;113:1069-1073.
- [290] Hasegawa T, Yoneda M, Nakamura K, Makino I, Terano A. Plasma transforming growth factor-beta1 level and efficacy of alpha-tocopherol in patients with non-alcoholic steatohepatitis: a pilot study. *Aliment Pharmacol Ther* 2001;15:1667-1672.
- [291] Mezey E, Potter J, Rennie-Tankersley L, Caballeria J, Pares A. A randomized placebo controlled trial of vitamin E in alcoholic hepatitis. *Hepatology* 2003;38:264A.
- [292] Stewart S, Prince M, Bassendine M, Hudson M, James O, Jone D, Record C, Day C. A trial of antioxidant therapy alone or with corticosteroids in acute alcoholic hepatitis. *J Hepatol* 2002;36:16.
- [293] Lu SC, Tsukamoto H, Mato JM. Role of abnormal methionine metabolism in alcoholic liver injury. *Alcohol* 2002;27:155-162.
- [294] Mato JM, Camara J, Fernández de Paz J, Caballeria L, Coll S, Caballero A, García-Buey L, Beltrán J, Benita V, Caballeria J, Sola R, Moreno-Otero R, Barrao F, Martín-Duce A, Correa JA, Parés A, Barrao E, García-Magaz I, Puerta JL, Moreno J, Boissard G, Ortiz P, Rodés J. S-adenosylmethionine in alcoholic liver cirrhosis: a randomized, placebo-controlled, double-blind, multicenter clinical trial. *J Hepatol* 1999;30:1081-1089.
- [295] Aleynik SI, Leo MA, Ma X, Aleynik MK, Lieber CS. Polyenylphosphatidylcholine prevents carbon tetrachloride-induced lipid peroxidation while it attenuates liver fibrosis. *J Hepatol* 1997;27:554-561.
- [296] Lieber CS, Weiss DG, Groszmann R, Paronetto F, Schenker S II. Veterans Affairs Cooperative Study of Polyenylphosphatidylcholine in Alcoholic Liver Disease. *Alcohol Clin Exp Res* 2003;27:1765-1772.

- [297] Boigk G, Stroedter L, Herbst H, Waldschmidt J, Riecken EO, Schuppan D. Silymarin retards collagen accumulation in early and advanced biliary fibrosis secondary to complete bile duct obliteration in rats. *Hepatology* 1997;26:643-649.
- [298] Jia JD, Bauer M, Cho JJ, Ruehl M, Milani S, Boigk G, Riecken EO, Schuppan D. Antifibrotic effect of silymarin in rat secondary biliary fibrosis is mediated by downregulation of procollagen alpha1(I) and TIMP-1. *J Hepatol* 2001;35:392-398.
- [299] Lieber CS, Leo MA, Cao Q, Ren C, DeCarli LM. Silymarin retards the progression of alcohol-induced hepatic fibrosis in baboons. *J Clin Gastroenterol* 2003;37:336-339.
- [300] Ferenci P, Dragosics B, Dittrich H, Frank H, Benda L, Lochs H, Meryn S, Base W, Schneider B. Randomized controlled trial of silymarin treatment in patients with cirrhosis of the liver *J Hepatol* 1989;9:105-113.
- [301] Parés A, Planas R, Torres M, Caballeria J, Viver JM, Acero D, Panés J, Rigau J, Santos J, Rodés J. Effects of silymarin in alcoholic patients with cirrhosis of the liver: results of a controlled, double-blind, randomized and multicenter trial. *J Hepatol* 1998;28:615-621.
- [302] Shimizu I. Sho-saiko-to: Japanese herbal medicine for protection against hepatic fibrosis and carcinoma. *J Gastroenterol Hepatol* 2000;15 Suppl:D84-90.
- [303] Wang BE. Treatment of chronic liver diseases with traditional Chinese medicine. *J Gastroenterol Hepatol* 2000;15 Suppl:E67-70.
- [304] Stedman C. Herbal hepatotoxicity. *Semin Liver Dis* 2002;22:195-206.
- [305] Bataller R, Brenner DA. Hepatic stellate cells as a target for the treatment of liver fibrosis. *Semin Liver Dis* 2001;21:437-451.
- [306] Rockey DC, Boyles JK, Gabbiani G, Friedman SL. Rat hepatic lipocytes express smooth muscle actin upon activation in vivo and in culture. *J Submicrosc Cytol Pathol* 1992;24:193-203.
- [307] Xu G, Rockey DC. Regulation of smooth muscle myosin heavy chain isoforms in hepatic myofibroblasts during liver injury (abstr). *Hepatology* 1999;30:492A.

Bibliografia

- [308] Fang B, Shi M, Liao L, Yang S, Liu Y, Zhao RC. Systemic infusion of FLK1(+) mesenchymal stem cells ameliorate carbon tetrachloride-induced liver fibrosis in mice. *Transplantation* 2004;78:83-88.
- [309] Kollet O, Shivtiel S, Chen YQ, Suriawinata J, Thung SN, Dabeva MD, Kahn J, Spiegel A, Dar A, Samira S, Goichberg P, Kalinkovich A, Arenzana-Seisdedos F, Nagler A, Hardan I, Revel M, Shafritz DA, Lapidot T. HGF, SDF-1, and MMP-9 are involved in stress-induced human CD34+ stem cell recruitment to the liver. *J Clin Invest* 2003;112:160-169.
- [310] Berry MN, Friend DS. High-yield preparation of isolated rat liver parenchymal cells: a biochemical and fine structural study. *J Cell Biol* 1969;43:506-520.
- [311] Seglen PO. Preparation of rat liver cells. I. Effect of Ca²⁺ on enzymatic dispersion of isolated, perfused liver. *Exp Cell Res* 1972;74:450-454.
- [312] Patrono C. Aspirin: new cardiovascular uses for an old drug. *Am J Med* 2001;110(1A):62S-65S.
- [313] Thun MJ, Henley SJ, Patrono C. Nonsteroidal anti-inflammatory drugs as anticancer agents: mechanistic, pharmacologic, and clinical issues. *J Natl Cancer Inst* 2002;94:252-266.
- [314] Bochner F, Williams DB, Morris, PM, Siebert DM i Lloyd JV. Pharmacokinetics of low-dose oral modified release, soluble and intravenous aspirin in man and effects on platelet functions. *Eur J Clin Pharmacol* 1988;35:287-294.
- [315] Ali B, Kaur S. Mammalian tissue acetylsalicylic acid esterase(s): identification, distribution and discrimination from other esterases. *J Pharmacol Exp Ther* 1983;226:589-594.
- [316] Kim D, Yang HYS, Jakoby WB. Aspirin hydrolyzing esterases from rat liver cytosol. *Biochem Pharmacol* 1990;40:481-487.
- [317] Livio M, Benigni A, Zoja C, Begnis R, Morelli C, Rossini M, Garattini S, Remuzzi G. Differential inhibition by aspirin of platelet thromboxane and renal prostaglandins in the rat. *J Pharmacol Exp Ther* 1989;248:334-341.
- [318] Levy BD. Lipid mediator class switching during acute inflammation: signals in resolution. *Nat Immunol* 2001;2:612-619.

- [319] Castrillo A, Tontonoz P. Nuclear receptors in macrophage biology: at the crossroads of lipid metabolism and inflammation. *Annu Rev Cell Dev Biol* 2004;20:455-480.
- [320] Boyer TD, Zia P, Reynolds TB. Effect of indomethacin and prostaglandin A1 on renal function and plasma renin activity in alcoholic liver disease. *Gastroenterology* 1979;77:215-222.
- [321] Zipser RD, Hoefs JC, Speckart PF, Zia PK, Horton R. Prostaglandins: modulators of renal function and pressor resistance in chronic liver disease. *J Clin Endocrinol Metab* 1979;48:895-900.
- [322] Arroyo V, Planas R, Gaya J, Deulofeu R, Rimola A, Pérez-Ayuso RM, Rivera F, Rodés J. Sympathetic nervous activity, renin-angiotensin system and renal excretion of prostaglandin E2 in cirrhosis. Relationship to functional renal failure and sodium and water excretion. *Eur J Clin Invest* 1983;13:271-278.
- [323] Mirouze D, Zipser RD, Reynolds TB. Effect of inhibitors of prostaglandin synthesis on induced diuresis in cirrhosis. *Hepatology* 1983;3:50-55.
- [324] Quintero E, Ginès P, Arroyo V, Rimola A, Camps J, Gaya J, Guevara A, Rodamilans M, Rodés J. Sulindac reduces the urinary excretion of prostaglandins and impairs renal function in cirrhosis with ascites. *Nephron* 1986;42:298-303.
- [325] Uaamnuichai M, Day RB, Brater DC. Bayesian and least-squares methods for vancomycin dosing. *Am J Med Sci* 1987;294:100-104.
- [326] Arroyo V, Ginès P, Rimola A, Gaya J. Renal function abnormalities, prostaglandins, and effects of nonsteroidal anti-inflammatory drugs in cirrhosis with ascites. An overview with emphasis on pathogenesis. *Am J Med* 1986;81:104-122.
- [327] Clària J, Arroyo V. Prostaglandins and other cyclooxygenase-dependent arachidonic acid metabolites and the kidney in liver disease. *Prostaglandins Other Lipid Mediat* 2003;72:19-33.
- [328] Souto EO, Miyoshi H, Dubois RN, Gores GJ. Kupffer cell-derived cyclooxygenase-2 regulates hepatocyte Bcl-2 expression in choledocho-venous fistula rats. *Am J Physiol Gastrointest Liver Physiol* 2001;280:G805-811.

Bibliografia

- [329] Seibert K, Zhang Y, Leahy K, Hauser S, Masferrer J, Perkins W, Lee L, Isakson P. Pharmacological and biochemical demonstration of the role of cyclooxygenase 2 in inflammation and pain. *Proc Natl Acad Sci U S A* 1994;91:12013-12017.
- [330] Bosch-Marcé M, Clària J, Titos E, Masferrer JL, Altuna R, Poo JL, Jiménez W, Arroyo V, Rivera F, Rodés J. Selective inhibition of cyclooxygenase 2 spares renal function and prostaglandin synthesis in cirrhotic rats with ascites. *Gastroenterology* 1999;116:1167-1175.
- [331] López-Parra M, Clària J, Planagumà A, Titos E, Masferrer JL, Woerner BM, Koki AT, Jiménez W, Altuna R, Arroyo V, Rivera F, Rodés J. Cyclooxygenase-1 derived prostaglandins are involved in the maintenance of renal function in rats with cirrhosis and ascites. *Br J Pharmacol* 2002;135:891-900.
- [332] Clària J, Kent JD, López-Parra M, Escolar G, Ruiz-Del-Arbol L, Ginès P, Jiménez W, Vucelic B, Arroyo V. Effects of celecoxib and naproxen on renal function in nonazotemic patients with cirrhosis and ascites. *Hepatology* 2005;41:579-587.
- [333] Jiang XH, Lam SK, Lin MC, Jiang SH, Kung HF, Slosberg, ED, Soh JW, Weinstein IB, Wong BC. Novel target for induction of apoptosis by cyclooxygenase-2 inhibitor SC-236 through a protein kinase C-beta(1)-dependent pathway. *Oncogene* 2002;21:6113-6122.
- [334] Badawi AF, Eldeen MB, Liu Y, Ross EA, Badr MZ. Inhibition of rat mammary gland carcinogenesis by simultaneous targeting of cyclooxygenase-2 and peroxisome proliferator-activated receptor gamma. *Cancer Res* 2004; 64:1181-1189.
- [335] Wong, BC, Jiang XH, Lin MC, Tu SP, Cui JT, Jiang SH, Wong WM, Yuen MF, Lam SK, Kung HF. Cyclooxygenase-2 inhibitor (SC-236) suppresses activator protein-1 through c-Jun NH₂-terminal kinase. *Gastroenterology* 2004;126:136-147.
- [336] Leng J, Han C, Demetris AJ, Michalopoulos GK, Wu T. Cyclooxygenase-2 promotes hepatocellular carcinoma cell growth through Akt activation: evidence for Akt inhibition in celecoxib-induced apoptosis. *Hepatology* 2003;38:756-768.

- [337] López-Parra M, Clària J, Titos E, Planagumà A, Párrizas M, Masferrer JL, Jiménez W, Arroyo V, Rivera F, Rodés J. The selective cyclooxygenase-2 inhibitor celecoxib modulates the formation of vasoconstrictor eicosanoids and activates PPARgamma. Influence of albumin. *J Hepatol* 2005;42:75-81.

