8. Literaturverzeichnis

1. Harbour-McMenamin D, Smith EM, Blalock JE. Bacterial lipopolysaccharide induction of leukocyte-derived corticotropin and endorphins. Infect Immun 1985; 48:813-7.
2. Stein C, Hassan AH, Przewlocki R, Gramsch C, Peter K, Herz A. Opioids from immunocytes interact with receptors on sensory nerves to inhibit nociception in inflammation. Proc Natl Acad Sci U S A 1990; 87:5935-9.
3. Przewlocki R, Hassan AH, Lason W, Epplen C, Herz A, Stein C. Gene expression and localization of opioid peptides in immune cells of inflamed tissue: functional role in antinociception. Neuroscience 1992; 48:491-500.
4. Lolait SJ, Clements JA, Markwick AJ, Cheng C, McNally M, Smith AI, Funder JW. Pro-opiomelanocortin messenger ribonucleic acid and posttranslational processing of beta endorphin in spleen macrophages. J Clin Invest 1986; 77:1776-9.
5. Kuis W, Villiger PM, Leser HG, Lotz M. Differential processing of proenkephalin-A by human peripheral blood monocytes and T lymphocytes. J Clin Invest 1991; 88:817-24.
6. Hassan AH, Pzewlocki R, Herz A, Stein C. Dynorphin, a preferential ligand for kappa-opioid receptors, is present in nerve fibers and immune cells within inflamed tissue of the rat. Neurosci Lett 1992; 140:85-8.
7. Mousa SA, Machelska H, Schäfer M, Stein C. Immunohistochemical localization of endomorphin-1 and endomorphin-2 in immune cells and spinal cord in a model of inflammatory pain. J Neuroimmunol 2002; 126:5-15.
8. Rittner HL, Brack A, Machelska H, Shaaban AM, Bauer M, Schäfer M, Stein C. Opioid peptide-expressing leukocytes: identification, recruitment, and simultaneously increasing inhibition of inflammatory pain. Anesthesiology 2001; 95:500-8.
9. Machelska H, Cabot PJ, Mousa SA, Zhang Q, Stein C. Pain control in inflammation governed by selectins. Nat Med 1998; 4:1425-8.
10. Machelska H, Mousa SA, Brack A, Schopohl JK, Rittner HL, Schäfer M, Stein C. Opioid control of inflammatory pain regulated by intercellular adhesion molecule-1. J Neurosci 2002; 22:5588-96.

11. Machelska H, Brack A, Mousa SA, Schopohl JK, Rittner HL, Schäfer M, Stein C. Selectins and integrins but not platelet-endothelial cell adhesion molecule-1 regulate opioid inhibition of inflammatory pain. Br J Pharmacol 2004; 142:772-8.
12. Cabot PJ, Carter L, Gaiddon C, Zhang Q, Schäfer M, Loeffler JP, Stein C. Immune cell-derived beta-endorphin. Production, release, and control of inflammatory pain in rats. J Clin Invest 1997; 100:142-8.
13. Cabot PJ, Carter L, Schäfer M, Stein C. Methionine-enkephalin-and Dynorphin A-release from immune cells and control of inflammatory pain. Pain 2001; 93:207-12.
14. Mousa SA, Schäfer M, Mitchell WM, Hassan AH, Stein C. Local upregulation of corticotropin-releasing hormone and interleukin-1 receptors in rats with painful hindlimb inflammation. Eur J Pharmacol 1996; 311:221-31.
15. Radulovic M, Dautzenberg FM, Sydow S, Radulovic J, Spiess J. Corticotropin-releasing factor receptor 1 in mouse spleen: expression after immune stimulation and identification of receptor-bearing cells. J Immunol 1999; 162:3013-21.
16. Schäfer M, Carter L, Stein C. Interleukin 1 beta and corticotropin-releasing factor inhibit pain by releasing opioids from immune cells in inflamed tissue. Proc Natl Acad Sci U S A 1994; 91:4219-23.
17. Bogduk ebHMaN. Classification of Chronic Pain, IASP Task Force on Taxonomy. Seattle: IASP Press, 1994:240.
18. Hassan AH, Ableitner A, Stein C, Herz A. Inflammation of the rat paw enhances axonal transport of opioid receptors in the sciatic nerve and increases their density in the inflamed tissue. Neuroscience 1993; 55:185-95.
19. Mousa SA, Zhang Q, Sitte N, Ji R, Stein C. beta-Endorphin-containing memory-cells and mu-opioid receptors undergo transport to peripheral inflamed tissue. J Neuroimmunol 2001; 115:71-8.
20. Sacerdote P, Gaspani L, Panerai AE. Role of beta-endorphin in the modulation of immune responses: perspectives in autoimmune diseases. Adv Exp Med Biol 2001; 493:137-42.
21. Zöllner C, Shaqura MA, Bopaiah CP, Mousa S, Stein C, Schäfer M. Painful inflammation-induced increase in mu-opioid receptor binding and G-protein coupling in primary afferent neurons. Mol Pharmacol 2003; 64:202-10.

22. Shaqura MA, Zöllner C, Mousa SA, Stein C, Schäfer M. Characterization of mu opioid receptor binding and G protein coupling in rat hypothalamus, spinal cord, and primary afferent neurons during inflammatory pain. J Pharmacol Exp Ther 2004; 308:712-8.
23. Antonijevic I, Mousa SA, Schäfer M, Stein C. Perineurial defect and peripheral opioid analgesia in inflammation. J Neurosci 1995; 15:165-72.
24. Kalso E, Smith L, McQuay HJ, Andrew Moore R. No pain, no gain: clinical excellence and scientific rigour--lessons learned from IA morphine. Pain 2002; 98:269-75.
25. Stein CM, Pincus T. Placebo-controlled studies in rheumatoid arthritis: ethical issues. Lancet 1999; 353:400-3.
26. Stein C, Hassan AH, Lehrberger K, Giefing J, Yassouridis A. Local analgesic effect of endogenous opioid peptides. Lancet 1993; 342:321-4.
27. Foster PA, Wicks S, Foster M, Brain SD. Cellular pathology changes in rat skin following intradermal injection of nerve growth factor: neutrophil-dependent and -independent events. J Pathol 2002; 197:245-55.
28. van Furth R, Cohn ZA. The origin and kinetics of mononuclear phagocytes. J Exp Med 1968; 128:415-35.
29. Van Furth R, Diesselhoff-den Dulk MC, Mattie H. Quantitative study on the production and kinetics of mononuclear phagocytes during an acute inflammatory reaction. J Exp Med 1973; 138:1314-30.
30. Kuziel WA, Morgan SJ, Dawson TC, Griffin S, Smithies O, Ley K, Maeda N. Severe reduction in leukocyte adhesion and monocyte extravasation in mice deficient in CC chemokine receptor 2. Proc Natl Acad Sci U S A 1997; 94:12053-8.
31. Izikson L, Klein RS, Charo IF, Weiner HL, Luster AD. Resistance to experimental autoimmune encephalomyelitis in mice lacking the CC chemokine receptor (CCR)2. J Exp Med 2000; 192:1075-80.
32. van Rooijen N, Sanders A. Elimination, blocking, and activation of macrophages: three of a kind? J Leukoc Biol 1997; 62:702-9.
33. Van Rooijen N, Sanders A. Liposome mediated depletion of macrophages: mechanism of action, preparation of liposomes and applications. J Immunol Methods 1994; 174:83-93.

34. Zimmermann M. Ethical guidelines for investigations of experimental pain in conscious animals. Pain 1983; 16:109-10.
35. Baatz H, Puchta J, Reszka R, Pleyer U. Macrophage depletion prevents leukocyte adhesion and disease induction in experimental melanin-protein induced uveitis. Exp Eye Res 2001; 73:101-9.
36. Ormerod MGH. Flow cytometry a practical approach. The practical approach series. Oxford: Oxford Univ. Press, 2000.
37. Sunderland CA, McMaster WR, Williams AF. Purification with monoclonal antibody of a predominant leukocyte-common antigen and glycoprotein from rat thymocytes. Eur J Immunol 1979; 9:155-9.
38. Gotoh S, Itoh M, Fujii Y, Arai S, Sendo F. Enhancement of the expression of a rat neutrophil-specific cell surface antigen by activation with phorbol myristate acetate and concanavalin A. J Immunol 1986; 137:643-50.
39. 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; 54:589-99.
40. Damoiseaux JG, Dopp EA, Calame W, Chao D, MacPherson GG, Dijkstra CD. Rat macrophage lysosomal membrane antigen recognized by monoclonal antibody ED1. Immunology 1994; 83:140-7.
41. Scriba A, Schneider M, Grau V, van der Meide PH, Steiniger B. Rat monocytes up-regulate NKR-P1A and down-modulate CD4 and CD43 during activation in vivo: monocyte subpopulations in normal and IFN-gamma-treated rats. J Leukoc Biol 1997; 62:741-52.
42. Morris DL, Komocsar WJ. Immunophenotyping analysis of peripheral blood, splenic, and thymic lymphocytes in male and female rats. J Pharmacol Toxicol Methods 1997; 37:37-46.
43. Gramsch C, Meo T, Riethmuller G, Herz A. Binding characteristics of a monoclonal beta-endorphin antibody recognizing the N-terminus of opioid peptides. J Neurochem 1983; 40:1220-6.
44. Stein C, Gramsch C, Herz A. Intrinsic mechanisms of antinociception in inflammation: local opioid receptors and beta-endorphin. J Neurosci 1990; 10:1292-8.

45. Frith JC, Mönkkönen J, Auriola S, Mönkkönen H, Rogers MJ. The molecular mechanism of action of the antiresorptive and antiinflammatory drug clodronate: evidence for the formation in vivo of a metabolite that inhibits bone resorption and causes osteoclast and macrophage apoptosis. Arthritis Rheum 2001; 44:2201-10.

46. Heiskanen KM, Bhat MB, Wang HW, Ma J, Nieminen AL. Mitochondrial depolarization accompanies cytochrome c release during apoptosis in PC6 cells. J Biol Chem 1999; 274:5654-8.

47. Lehenkari PP, Kellinsalmi M, Napankangas JP, Ylitalo KV, Mönkönen J, Rogers MJ, Azhayev A, Väänänen HK, Hassinen IE. Further insight into mechanism of action of clodronate: inhibition of mitochondrial ADP/ATP translocase by a nonhydrolyzable, adenine-containing metabolite. Mol Pharmacol 2002; 61:1255-62.

48. Mönkkönen H, Rogers MJ, Makkonen N, Niva S, Auriola S, Mönkkönen J. The cellular uptake and metabolism of clodronate in RAW 264 macrophages. Pharm Res 2001; 18:1550-5.

49. Stein C, Millan MJ, Herz A. Unilateral inflammation of the hindpaw in rats as a model of prolonged noxious stimulation: alterations in behavior and nociceptive thresholds. Pharmacol Biochem Behav. 1988 Oct;31(2):455-51.

50. Stein C, Pfluger M, Yassouridis A, Hoelzl J, Lehrberger K, Welte C, Hassan AHS. No tolerance to peripheral morphine analgesia in presence of opioid expression in inflamed synovia. J Clin Invest 1996; 98:793-9.

51. Abbadie C, Lindia JA, Cumiskey AM, Peterson LB, Mudgett JS, Bayne EK, DeMartino JA, MacIntyre DE, Forrest MJ. Impaired neuropathic pain responses in mice lacking the chemokine receptor CCR2. Proc Natl Acad Sci U S A 2003; 100:7947-52.

52. Radhakrishnan R, Moore SA, Sluka KA. Unilateral carrageenan injection into muscle or joint induces chronic bilateral hyperalgesia in rats. Pain 2003; 104:567-77.

53. Galin FS, LeBoeuf RD, Blalock JE. Corticotropin-releasing factor upregulates expression of two truncated pro-opiomelanocortin transcripts in murine lymphocytes. J Neuroimmunol 1991; 31:51-8.

54. Maier CC, Blalock JE. PCR-based cloning, sequencing, and exon mapping of lymphocyte-derived neuroendocrine peptides. Immunomethods 1994; 5:3-7.

55. Mechanick JI, Levin N, Roberts JL, Autelitano DJ. Proopiomelanocortin gene expression in a distinct population of rat spleen and lung leukocytes. Endocrinology 1992; 131:518-25.

56. Lyons PD, Blalock JE. Pro-opiomelanocortin gene expression and protein processing in rat mononuclear leukocytes. J Neuroimmunol 1997; 78:47-56.

57. van Woudenberg AD, Metzelaar MJ, van der Kleij AA, de Wied D, Burbach JP, Wiegant VM. Analysis of proopiomelanocortin (POMC) messenger ribonucleic acid and POMC-derived peptides in human peripheral blood mononuclear cells: no evidence for a lymphocyte-derived POMC system. Endocrinology 1993; 133:1922-33.

58. Mousa SA, Shakibaei M, Sitte N, Schäfer M, Stein C. Subcellular pathways of beta-endorphin synthesis, processing, and release from immunocytes in inflammatory pain. Endocrinology 2004; 145:1331-41.

59. Danenberg HD, Fishbein I, Gao J, Mönkkönen J, Reich R, Gati I, Moerman E, Golomb G. Macrophage depletion by clodronate-containing liposomes reduces neointimal formation after balloon injury in rats and rabbits. Circulation 2002; 106:599-605.

60. van Rooijen N, Kors N, Kraal G. Macrophage subset repopulation in the spleen: differential kinetics after liposome-mediated elimination. J Leukoc Biol 1989; 45:97-104.

61. Kinne RW, Schmidt-Weber CB, Hoppe R, Buchner E, Palombo-Kinne E, Nurnberg E, Emmrich F. Long-term amelioration of rat adjuvant arthritis following systemic elimination of macrophages by clodronate-containing liposomes. Arthritis Rheum 1995; 38:1777-90.

62. Barrera P, Blom A, van Lent PL, van Bloois L, Beijnen JH, van Rooijen N, de Waal Malefijt MC, van de Putte LB, Storm G, van den Berg WB. Synovial macrophage depletion with clodronate-containing liposomes in rheumatoid arthritis. Arthritis Rheum 2000; 43:1951-9.

63. Bergh A, Damber JE, van Rooijen N. Liposome-mediated macrophage depletion: an experimental approach to study the role of testicular macrophages in the rat. J Endocrinol 1993; 136:407-13.

64. Cheung DO, Halsey K, Speert DP. Role of pulmonary alveolar macrophages in defense of the lung against Pseudomonas aeruginosa. Infect Immun 2000; 68:4585-92.

65. Koay MA, Gao X, Washington MK, Parman KS, Sadikot RT, Blackwell TS, Christman JW. Macrophages are necessary for maximal nuclear factor-kappa B activation in response to endotoxin. Am J Respir Cell Mol Biol 2002; 26:572-8.

66. Slegers TP, van Rooijen N, van Rij G, van der Gaag R. Delayed graft rejection in pre-vascularised corneas after subconjunctival injection of clodronate liposomes. Curr Eye Res 2000; 20:322-4.

67. Schmidt-Weber CB, Rittig M, Buchner E, Hauser I, Schmidt I, Palombo-Kinne E, Emmrich F, Kinne RW. Apoptotic cell death in activated monocytes following incorporation of clodronate-liposomes. J Leukoc Biol 1996; 60:230-44.

68. Mutsaers SE, Whitaker D, Papadimitriou JM. Stimulation of mesothelial cell proliferation by exudate macrophages enhances serosal wound healing in a murine model. Am J Pathol 2002; 160:681-92.

69. Mönkkönen H, Tormalehto S, Asunmaa K, Niemi R, Auriola S, Vepsalainen J, Mönkkönen J. Cellular uptake and metabolism of clodronate and its derivatives in Caco-2 cells: a possible correlation with bisphosphonate-induced gastrointestinal side-effects. Eur J Pharm Sci 2003; 19:23-9.

70. Ceponis A, Waris E, Mönkkönen J, Laasonen L, Hyttinen M, Solovieva SA, Hanemaaijer R, Bitsch A, Konttinen YT. Effects of low-dose, noncytotoxic, intraarticular liposomal clodronate on development of erosions and proteoglycan loss in established antigen-induced arthritis in rabbits. Arthritis Rheum 2001; 44:1908-16.

71. Richards PJ, Williams AS, Goodfellow RM, Williams BD. Liposomal clodronate eliminates synovial macrophages, reduces inflammation and ameliorates joint destruction in antigen-induced arthritis. Rheumatology (Oxford) 1999; 38:818-25.

72. Liu T, van Rooijen N, Tracey DJ. Depletion of macrophages reduces axonal degeneration and hyperalgesia following nerve injury. Pain 2000; 86:25-32.

73. Bruck W, Huitinga I, Dijkstra CD. Liposome-mediated monocyte depletion during wallerian degeneration defines the role of hematogenous phagocytes in myelin removal. J Neurosci Res 1996; 46:477-84.

74. Laverman P, Carstens MG, Boerman OC, Dams ET, Oyen WJ, van Rooijen N, Corstens FH, Storm G. Factors affecting the accelerated blood clearance of polyethylene glycol-liposomes upon repeated injection. J Pharmacol Exp Ther 2001; 298:607-12.

75. Nishikawa K, Arai H, Inoue K. Scavenger receptor-mediated uptake and metabolism of lipid vesicles containing acidic phospholipids by mouse peritoneal macrophages. J Biol Chem 1990; 265:5226-31.

76. Fadok VA, Voelker DR, Campbell PA, Cohen JJ, Bratton DL, Henson PM. Exposure of phosphatidylserine on the surface of apoptotic lymphocytes triggers specific recognition and removal by macrophages. J Immunol 1992; 148:2207-16.

77. Schäfer M, Imai Y, Uhl GR, Stein C. Inflammation enhances peripheral mu-opioid receptor-mediated analgesia, but not mu-opioid receptor transcription in dorsal root ganglia. Eur J Pharmacol 1995; 279:165-9.

78. Puehler W, Zollner C, Brack A, Shaqura MA, Krause H, Schäfer M, Stein C. Rapid upregulation of mu opioid receptor mRNA in dorsal root ganglia in response to peripheral inflammation depends on neuronal conduction. Neuroscience 2004; 129:473-9.

79. Brack A, Rittner HL, Machelska H, Leder K, Mousa SA, Schäfer M, Stein C. Control of inflammatory pain by chemokine-mediated recruitment of opioid-containing polymorphonuclear cells. Pain 2004; 112:229-38.

80. Khodorova A, Navarro B, Jouaville LS, Murphy JE, Rice FL, Mazurkiewicz JE, Long-Woodward D, Stoffel M, Strichartz GR, Yukhananov R, Davar G. Endothelin-B receptor activation triggers an endogenous analgesic cascade at sites of peripheral injury. Nat Med 2003; 9:1055-61.

81. Stein C, Comisel K, Haimerl E, Yassouridis A, Lehrberger K, Herz A, Peter K. Analgesic effect of intraarticular morphine after arthroscopic knee surgery. N Engl J Med 1991; 325:1123-6.

82. Lu CY, Chou AK, Wu CL, Yang CH, Chen JT, Wu PC, Lin SH, Muhammad R, Yang LC. Gene-gun particle with pro-opiomelanocortin cDNA produces analgesia against formalin-induced pain in rats. Gene Ther 2002; 9:1008-14.

83. Xu Y, Gu Y, Xu GY, Wu P, Li GW, Huang LY. Adeno-associated viral transfer of opioid receptor gene to primary sensory neurons: a strategy to increase opioid antinociception. Proc Natl Acad Sci U S A 2003; 100:6204-9.

84. Brack A, Rittner HL, Machelska H, Shaqura M, Mousa SA, Labuz D, Zollner C, Schäfer M, Stein C. Endogenous peripheral antinociception in early inflammation is

not limited by the number of opioid-containing leukocytes but by opioid receptor expression. Pain 2004; 108:67-75.