

References

- Abe K, Nicholson WE, Liddle GW, Orth DN, Island DP. Normal and abnormal regulation of beta-msh in man. *J Clin Invest* 1969;48(8):1580-1585.
- Abrams GM, Nilaver G, Hoffman D, Zimmerman EA, Ferin M, Krieger DT, Liotta AS. Immunocytochemical distribution of corticotropin (ACTH) in monkey brain. *Neurology* 1980;30(10):1106-1110.
- Bardin CW, Chen CL, Morris PL, Gerendai I, Boitani C, Liotta AS, Margioris A, Krieger DT. Proopiomelanocortin-derived peptides in testis, ovary, and tissues of reproduction. *Recent Prog Horm Res* 1987;43:1-28.
- Benita Y, Oosting RS, Lok MC, Wise MJ, Humphery-Smith I. Regionalized GC content of template DNA as apredictor of PCR success. *Nucl Acids Res* 2003;31(16).
- Benjannet S, Rondeau N, Day R, Chretien M, Seidah NG. PC1 and PC2 are proprotein convertases capable of cleaving proopiomelanocortin at distinct pairs of basic residues. *Proc Natl Acad Sci U S A* 1991;88(9):3564-3568.
- Benjannet S, Savaria D, Chretien M, Seidah NG. 7B2 is a specific intracellular binding protein of the prohormone convertase PC2. *J Neurochem* 1995;64(5):2303-2311.
- Bennett DL, Bailyes EM, Nielsen E, Guest PC, Rutherford NG, Arden SD, Hutton JC. Identification of the type 2 proinsulin processing endopeptidase as PC2, a member of the eukaryote subtilisin family. *J Biol Chem* 1992;267(21):15229-15236.
- Bertagna XY, Nicholson WE, Sorenson GD, Pettengill OS, Mount CD, Orth DN. Corticotropin, lipotropin, and beta-endorphin production by a human nonpituitary tumor in culture: evidence for a common precursor. *Proc Natl Acad Sci U S A* 1978;75(10):5160-5164.
- Binder W, Mousa SA, Sitte N, Kaiser M, Stein C, Schafer M. Sympathetic activation triggers endogenous opioid release and analgesia within peripheral inflamed tissue. *J Eur Neurosci* 2004;20(1):92-100.
- Brack A, Labuz D, Schiltz A, Rittner HL, Machelska H, Schafer M, Reszka R, Stein C. Tissue monocytes/macrophages in inflammation: hyperalgesia versus opioid-mediated peripheral antinociception. *Anesthesiology* 2004;101(1):204-211.
- Butcher EC, Picker LJ. Lymphocyte homing and homeostasis. *Science* 1996;272:60-66.

- Butler AA, Cone RD. Knockout studies defining different roles for melanocortin receptors in energy homeostasis. *Ann N Y Acad Sci* 2003;994:240-245.
- Buzzetti R, Ciancio A, Ciucci E, Celli V, Giovannini C. [ACTH of lymphocytic origin under normal and pathological conditions]. *Ann Ital Med Int* 1991;6(4):357-363.
- Buzzetti R, McLoughlin L, Lavender PM, Clark AJ, Rees LH. Expression of pro-opiomelanocortin gene and quantification of adrenocorticotropic hormone-like immunoreactivity in human normal peripheral mononuclear cells and lymphoid and myeloid malignancies. *J Clin Invest* 1989;83(2):733-737.
- Cabot PJ, Carter L, Gaiddon C, Zhang Q, Schafer M, Loeffler JP, Stein C. Immune cell-derived beta-endorphin. Production, release, and control of inflammatory pain in rats. *J Clin Invest* 1997;100(1):142-148.
- Castro MG, Gusovsky F, Loh YP. Transmembrane signals mediating adrenocorticotropin release from mouse anterior pituitary cells. *Mol Cell Endocrinol* 1989;65(1-2):165-173.
- Chadzinska M, Starowicz K, Scisowska-Czarnecka A, Bilecki W, Pierzchala-Koziec K, Przewlocki R, Przewlocka B, Plytycz B. Morphine-induced changes in the activity of proopiomelanocortin and prodynorphin systems in zymosan-induced peritonitis in mice. *Immunol Lett* 2005;101(2):185-192.
- Che FY, Yan L, Li H, Mzhavia N, Devi LA, Fricker LD. Identification of peptides from brain and pituitary of Cpe(fat)/Cpe(fat) mice. *Proc Natl Acad Sci U S A* 2001;98(17):9971-9976.
- Chen CL, Chang CC, Krieger DT, Bardin CW. Expression and regulation of proopiomelanocortin-like gene in the ovary and placenta: comparison with the testis. *Endocrinology* 1986;118(6):2382-2389.
- Christie DL, Batchelor DC, Palmer DJ. Identification of kex2-related proteases in chromaffin granules by partial amino acid sequence analysis. *J Biol Chem* 1991;266(24):15679-15683.
- Clark AJ, Lavender PM, Coates P, Johnson MR, Rees LH. In vitro and in vivo analysis of the processing and fate of the peptide products of the short proopiomelanocortin mRNA. *Mol Endocrinol* 1990;4(11):1737-1743.
- Cool DR, Loh YP. Identification of a sorting signal for the regulated secretory pathway at the N-terminus of pro-opiomelanocortin. *Biochimie* 1994;76(3-4):265-270.

- Cool DR, Normant E, Shen F, Chen HC, Pannell L, Zhang Y, Loh YP. Carboxypeptidase E is a regulated secretory pathway sorting receptor: genetic obliteration leads to endocrine disorders in Cpe(fat) mice. *Cell* 1997;88(1):73-83.
- Cowley MA, Pronchuk N, Fan W, Dinulescu DM, Colmers WF, Cone RD. Integration of NPY, AGRP, and melanocortin signals in the hypothalamic paraventricular nucleus: evidence of a cellular basis for the adipostat. *Neuron* 1999;24(1):155-163.
- Day R, Schafer MK, Watson SJ, Chretien M, Seidah NG. Distribution and regulation of the prohormone convertases PC1 and PC2 in the rat pituitary. *Mol Endocrinol* 1992;6(3):485-497.
- de Longueville F, Evrard S, Heim A. Gene expression profiling of PB and PCN. Correlation between data from DualChip rat hepato and real-time PCR. *Eppendorf Application* 2003; No. 62.
- Deakin JF, Dostrovsky JO, Smyth DG. Influence of N-terminal acetylation and C-terminal proteolysis on the analgesic activity of beta-endorphin. *Biochem J* 1980;189(3):501-506.
- DeBold CR, Menefee JK, Nicholson WE, Orth DN. Proopiomelanocortin gene is expressed in many normal human tissues and in tumors not associated with ectopic adrenocorticotropin syndrome. *Mol Endocrinol* 1988;2(9):862-870.
- DeBold CR, Nicholson WE, Orth DN. Immunoreactive proopiomelanocortin (POMC) peptides and POMC-like messenger ribonucleic acid are present in many rat nonpituitary tissues. *Endocrinology* 1988;122(6):2648-2657.
- Douglass J, Civelli O, Herbert E. Polyprotein gene expression: generation of diversity of neuroendocrine peptides. *Annu Rev Biochem* 1984;53:665-715.
- Drouin J, Chamberland M, Charron J, Jeannotte L, Nemer M. Structure of the rat proopiomelanocortin (POMC) gene. *FEBS Lett* 1985;193(1):54-58.
- Eipper BA, Mains RE. Existence of a common precursor to ACTH and endorphin in the anterior and intermediate lobes of the rat pituitary. *J Supramol Struct* 1978;8(3):247-262.
- Eipper BA, Mains RE, Guenzi D. High molecular weight forms of adrenocorticotropic hormone are glycoproteins. *J Biol Chem* 1976;251(13):4121-4126.
- Fabbri M, Bianchi E, Fumagalli L, Pardi R. Regulation of lymphocyte traffic by adhesion molecules. *Inflamm Res* 1999;48(5):239-246.

- Friedman TC, Loh YP, Birch NP. In vitro processing of proopiomelanocortin by recombinant PC1 (SPC3). *Endocrinology* 1994;135(3):854-862.
- Fulford AJ, Harbuz MS, Jessop DS. Antisense inhibition of pro-opiomelanocortin and proenkephalin A messenger RNA translation alters rat immune cell function in vitro. *J* 2000;106(1-2):6-13.
- Galin FS, LeBoeuf RD, Blalock JE. Corticotropin-releasing factor upregulates expression of two truncated pro-opiomelanocortin transcripts in murine lymphocytes. *J Neuroimmunol* 1991;31(1):51-58.
- Gardiner-Garden M, Frommer M. Transcripts and CpG islands associated with the pro-opiomelanocortin gene and other neurally expressed genes. *J Mol Endocrinol* 1994;12(3):365-382.
- Gee CE, Chen CL, Roberts JL, Thompson R, Watson SJ. Identification of proopiomelanocortin neurones in rat hypothalamus by in situ cDNA-mRNA hybridization. *Nature* 1983;306(5941):374-376.
- Gramsch C MT, Riethmuller G, Herz A. Binding characteristics of a monoclonal beta-endorphin antibody recognizing the N-terminus of opioid peptides. *J Neurochem* 1983;May;40(5):1220-1226.
- Grigorakis SI, Anastasiou E, Dai K, Souvatzoglou A, Alevizaki M. Three mRNA transcripts of the proopiomelanocortin gene in human placenta at term. *Eur J Endocrinol* 2000;142(5):533-536.
- Guillemin R, Vargo T, Rossier J, Minick S, Ling N, Rivier C, Vale W, Bloom F. beta-Endorphin and adrenocorticotropin are selected concomitantly by the pituitary gland. *Science* 1977;197(4311):1367-1369.
- Gumbiner B, Kelly RB. Two distinct intracellular pathways transport secretory and membrane glycoproteins to the surface of pituitary tumor cells. *Cell* 1982;28(1):51-59.
- Hall JG, Morris B. The Origin of the Cells in the Efferent Lymph from a Single Lymph Node. *J Exp Med* 1965;121:901-910.
- Harbour DV, Galin FS, Hughes TK, Smith EM, Blalock JE. Role of leukocyte-derived pro-opiomelanocortin peptides in endotoxic shock. *Circ Shock* 1991;35(3):181-191.
- Hashemi FB, Hughes TK, Smith EM. Human immunodeficiency virus induction of corticotropin in lymphoid cells. *J Clin Endocrinol Metab* 1998;83(12):4373-4381.

- Hermanussen S, Do M, Cabot PJ. Reduction of beta-endorphin-containing immune cells in inflamed paw tissue corresponds with a reduction in immune-derived antinociception: reversible by donor activated lymphocytes. *Anesth Analg* 2004;98(3):723-729.
- Hickman SP, Chan J, Salgame P. Mycobacterium tuberculosis induces differential cytokine production from dendritic cells and macrophages with divergent effects on naive T cell polarization. *J Immunol* 2002;168(9):4636-4642.
- Janeway CA, Travers P, Walport M, Shlomchik M. *Immunobiology: The immune system in health and disease* New York and London: Garland Science 2001;5th ed.
- Jeannotte L, Burbach JP, Drouin J. Unusual proopiomelanocortin ribonucleic acids in extrapituitary tissues: intronless transcripts in testes and long poly(A) tails in hypothalamus. *Mol Endocrinol* 1987;1(10):749-757.
- Jeannotte L, Burbach JPH, Drouin J. Unusual proopiomelanocortin ribonucleic acids in extrapituitary tissues: intronless transcripts in testes and long poly(A) tails in hypothalamus. *Mol Endocrinol* 1987;1(10):749-757.
- Jiao X, Lo-Man R, Guermonprez P, Fiette L, Dériaud E, Burgaud S, Gicquel B, Winter N, Leclerc C. Dendritic cells are host cells for mycobacteria in vivo that triggers innate and acquired immunity. *J Immunol* 2002;1294-1301.
- Jin WD, Boutillier AL, Glucksman MJ, Salton SR, Loeffler JP, Roberts JL. Characterization of a corticotropin-releasing hormone-responsive element in the rat proopiomelanocortin gene promoter and molecular cloning of its binding protein. *Mol Endocrinol* 1994;8(10):1377-1388.
- Katahira M, Iwasaki Y, Aoki Y, Oiso Y, Saito H. Cytokine regulation of the rat proopiomelanocortin gene expression in AtT-20 cells. *Endocrinology* 1998;139(5):2414-2422.
- Kavelaars A, Ballieux RE, Heijnen CJ. The role of IL-1 in the corticotropin-releasing factor and arginine- vasopressin-induced secretion of immunoreactive beta-endorphin by human peripheral blood mononuclear cells. *J Immunol* 1989;142(7):2338-2342.
- Kita T, Inoue A, Nakanishi S, Numa S. Purification and characterization of the messenger RNA coding for bovine corticotropin/beta-lipotropin precursor. *Eur J Biochem* 1979;93(2):213-220.

- Korner J, Chun J, O'Bryan L, Axel R. Prohormone processing in *Xenopus* oocytes: characterization of cleavage signals and cleavage enzymes. *Proc Natl Acad Sci U S A* 1991;88(24):11393-11397.
- Krude H, Biebermann H, Luck W, Horn R, Brabant G, Gruters A. Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans. *Nat Genet* 1998;19(2):155-157.
- Krude H, Biebermann H, Schnabel D, Tansek MZ, Theunissen P, Mullis PE, Gruters A. Obesity due to proopiomelanocortin deficiency: three new cases and treatment trials with thyroid hormone and ACTH4-10. *J Clin Endocrinol Metab* 2003;88(10):4633-4640.
- Lacaze-Masmonteil T, de Keyzer Y, Luton JP, Kahn A, Bertagna X. Characterization of proopiomelanocortin transcripts in human nonpituitary tissues. *Proc Natl Acad Sci U S A* 1987;84(20):7261-7265.
- Lamango NS, Zhu X, Lindberg I. Purification and enzymatic characterization of recombinant prohormone convertase 2: stabilization of activity by 21 kDa 7B2. *Arch Biochem Biophys* 1996;330(2):238-250.
- Lamolet B, Pulichino AM, Lamonerie T, Gauthier Y, Brue T, Enjalbert A, Drouin J. A pituitary cell-restricted T box factor, Tpit, activates POMC transcription in cooperation with Pitx homeoproteins. *Cell* 2001;104(6):849-859.
- Lamonerie T, Tremblay JJ, Lanctot C, Therrien M, Gauthier Y, Drouin J. Ptx1, a bicoid-related homeo box transcription factor involved in transcription of the pro-opiomelanocortin gene. *Genes Dev* 1996;10(10):1284-1295.
- Lansac G, Dong W, Dubois CM, Benlarbi N, Afonso C, Fournier I, Salzet M, Day R. Lipopolysaccharide mediated regulation of neuroendocrine associated proprotein convertases and neuropeptide precursor processing in the rat spleen. *J Neuroimmunol* 2006;171(1-2):57-71.
- Li CH, Chung D. Isolation and structure of an untriakontapeptide with opiate activity from camel pituitary glands. *Proc Natl Acad Sci U S A* 1976;73(4):1145-1148.
- Li CH, Chung D, Doneen BA. Isolation, characterization and opiate activity of beta-endorphin from human pituitary glands. *Biochem Biophys Res Commun* 1976;72(4):1542-1547.
- Lodish H, Berk A, Zipursky SL, Matsudaira P, Baltimore D, Darnell JE. Molekulare Zellbiology: Prozessierung von mRNA bei Eukaryoten. Spectrum Akademischer Verlag GmbH Heidelberg - Berlin 2001;4th ed:447-459.

- Loh HH, Tseng LF, Wei E, Li CH. beta-endorphin is a potent analgesic agent. *Proc Natl Acad Sci U S A* 1976;73(8):2895-2898.
- Loh YP, Maldonado A, Zhang C, Tam WH, Cawley N. Mechanism of sorting proopiomelanocortin and proenkephalin to the regulated secretory pathway of neuroendocrine cells. *Ann N Y Acad Sci* 2002;971:416-425.
- 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(6):1776-1779.
- Lolait SJ, Lim AT, Toh BH, Funder JW. Immunoreactive beta-endorphin in a subpopulation of mouse spleen macrophages. *J Clin Invest* 1984;73(1):277-280.
- Lyons PD, Blalock JE. The kinetics of ACTH expression in rat leukocyte subpopulations. *J Neuroimmunol* 1995;63(2):103-112.
- Lyons PD, Blalock JE. Pro-opiomelanocortin gene expression and protein processing in rat mononuclear leukocytes. *J Neuroimmunol* 1997;78(1-2):47-56.
- Machelska H, Brack A, Mousa SA, Schopohl JK, Rittner HL, Schafer 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(4):772-780.
- Machelska H, Cabot PJ, Mousa SA, Zhang Q, Stein C. Pain control in inflammation governed by selectins. *Nat Med* 1998;4(12):1425-1428.
- Machelska H, Mousa SA, Brack A, Schopohl JK, Rittner HL, Schafer M, Stein C. Opioid control of inflammatory pain regulated by intercellular adhesion molecule-1. *J Neurosci* 2002;22(13):5588-5596.
- Machelska H, Schopohl JK, Mousa SA, Labuz D, Schafer M, Stein C. Different mechanisms of intrinsic pain inhibition in early and late inflammation. *J Neuroimmunol* 2003;141(1-2):30-39.
- Mackay CR, Marston W, Dudler L. Altered patterns of T cell migration through lymph nodes and skin following antigen challenge. *Eur J Immunol* 1992;22(9):2205-2210.
- Maier CC, Blalock JE. PCR-based cloning, sequencing, and exon mapping of lymphocyte-derived neuroendocrine peptides. *Immunomethods* 1994;5(1):3-7.

- Mains RE, Eipper BA. Biosynthesis of adrenocorticotrophic hormone in mouse pituitary tumor cells. *J Biol Chem* 1976;251(13):4115-4120.
- Mains RE, Eipper BA. Synthesis and secretion of corticotropins, melanotropins, and endorphins by rat intermediate pituitary cells. *J Biol Chem* 1979;254(16):7885-7894.
- Mains RE, Eipper BA, Ling N. Common precursor to corticotropins and endorphins. *Proc Natl Acad Sci U S A* 1977;74(7):3014-3018.
- Marcinkiewicz M, Day R, Seidah NG, Chretien M. Ontogeny of the prohormone convertases PC1 and PC2 in the mouse hypophysis and their colocalization with corticotropin and alpha-melanotropin. *Proc Natl Acad Sci U S A* 1993;90(11):4922-4926.
- Max N, Wolf K, Thiel E, Keilholz U. Quantitative nested real-time RT-PCR specific for tyrosinase transcripts to quantitate minimal residual disease. *Clin Chim Acta* 2002;317(1-2):39-46.
- Mbikay M, Seidah NG, Chretien M. Neuroendocrine secretory protein 7B2: structure, expression and functions. *Biochem J* 2001;357(Pt 2):329-342.
- Mechanick JI, Levin N, Roberts JL, Autelitano DJ. Proopiomelanocortin gene expression in a distinct population of rat spleen and lung leukocytes. *Endocrinology* 1992;131(1):518-525.
- Mertvetsov NP, Karginov VA, Golovin S, Bondar AA, Morozov IV, Zelenin SM, Blinov VM. Nucleotide sequence of cDNA coding for mink proopiomelanocortin (POMC) and its comparative analysis with POMC mRNA primary structures from pituitaries of other animal species and man. *Biomed Biochim Acta* 1991;50(9):1057-1064.
- Mizuno TM, Kleopoulos SP, Bergen HT, Roberts JL, Priest CA, Mobbs CV. Hypothalamic pro-opiomelanocortin mRNA is reduced by fasting and in ob/ob and db/db mice, but is stimulated by leptin. *Diabetes* 1998;47:294-297.
- Mousa SA, Machelska H, Schafer M, Stein C. Co-expression of beta-endorphin with adhesion molecules in a model of inflammatory pain. *J Neuroimmunol* 2000;108(1-2):160-170.
- Mousa SA, Schafer 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(2-3):221-231.

- Mousa SA, Shakibaei M, Sitte N, Schafer M, Stein C. Subcellular pathways of beta-endorphin synthesis, processing, and release from immunocytes in inflammatory pain. *Endocrinology* 2004;145(3):1331-1341.
- 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(1-2):71-78.
- Muller L, Lindberg I. The cell biology of the prohormone convertases PC1 and PC2. *Prog Nucleic Acid Res Mol Biol* 1999;63:69-108.
- Nakanishi S, Inoue A, Kita T, Nakamura M, Chang AC, Cohen SN, Numa S. Nucleotide sequence of cloned cDNA for bovine corticotropin-beta-lipotropin precursor. *Nature* 1979;278(5703):423-427.
- Newell-Price J. Proopiomelanocortin gene expression and DNA methylation: implications for Cushing's syndrome and beyond. *J Endocrinol* 2003;177(3):365-372.
- Newell-Price J, King P, Clark AJ. The CpG island promoter of the human proopiomelanocortin gene is methylated in nonexpressing normal tissue and tumors and represses expression. *Mol Endocrinol* 2001;15(2):338-348.
- Oates E, Herbert E. 5' sequence of porcine and rat pro-opiomelanocortin mRNA. One porcine and two rat forms. *J Biol Chem* 1984;259(12):7421-7425.
- Oates EL, Allaway GP, Armstrong GR, Boyajian RA, Kehrl JH, Prabhakar BS. Human lymphocytes produce pro-opiomelanocortin gene-related transcripts. Effects of lymphotropic viruses. *J Biol Chem* 1988;263(21):10041-10044.
- Ohta K, Shichiri M, Kameya T, Matsubara O, Imai T, Marumo F, Hirata Y. Thymic hyperplasia as a source of ectopic ACTH production. *Endocr J* 2000;47(4):487-492.
- Olszewski WL, Pazdur J, Kubasiewicz E, Zaleska M, Cooke CJ, Miller NE. Lymph draining from foot joints in rheumatoid arthritis provides insight into local cytokine and chemokine production and transport to lymph nodes. *Arthritis Rheum* 2001;44(3):541-549.
- Orth DN, Nicholson WE, Mitchell WM, Island DP, Shapiro M, Byyny RL. ACTH and MSH production by a single cloned mouse pituitary tumor cell line. *Endocrinology* 1973;92(2):385-393.
- Panerai AE, Manfredi B, Granucci F, Sacerdote P. The beta-endorphin inhibition of mitogen-induced splenocytes proliferation is mediated by central and

- peripheral paracrine/autocrine effects of the opioid. *J Neuroimmunol* 1995;58(1):71-76.
- Panerai AE, Sacerdote P. Beta-endorphin in the immune system: a role at last? *Immunol Today* 1997;18(7):317-319.
- Parsons CG, Czlonkowski A, Stein C, Herz A. Peripheral opioid receptors mediating antinociception in inflammation. Activation by endogenous opioids and role of the pituitary-adrenal axis. *Pain* 1990;41(1):81-93.
- Phifer RF, Orth DN, Spicer SS. Specific demonstration of the human hypophyseal adrenocortico-melanotropic (ACTH-MSH) cell. *J Clin Endocrinol Metab* 1974;39(4):684-692.
- 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(2):491-500.
- Puehler W, Zollner C, Brack A, Shaqura MA, Krause H, Schafer 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(2):473-479.
- Raffin-Sanson ML, de Keyzer Y, Bertagna X. Proopiomelanocortin, a polypeptide precursor with multiple functions: from physiology to pathological conditions. *Eur J Endocrinol* 2003;149(2):79-90.
- Rees LH, Burke CW, Chard T, Evans SW, Letchworth AT. Possible placental origin of ACTH in normal human pregnancy. *Nature* 1975;254(5501):620-622.
- Ringholm A, Klovins J, Rudzish R, Phillips S, Rees JL, Schioth HB. Pharmacological characterization of loss of function mutations of the human melanocortin 1 receptor that are associated with red hair. *J Invest Dermatol* 2004;123(5):917-923.
- Rittner HL, Brack A, Machelska H, Mousa SA, Bauer M, Schafer M, Stein C. Opioid peptide-expressing leukocytes: identification, recruitment, and simultaneously increasing inhibition of inflammatory pain. *Anesthesiology* 2001;95(2):500-508.
- Rittner HL, Labuz D, Schaefer M, Mousa SA, Schulz S, Schafer M, Stein C, Brack A. Pain control by CXCR2 ligands through Ca²⁺-regulated release of opioid peptides from polymorphonuclear cells. *Faseb J* 2006;20(14):2627-2629.
- Roberts JL, Herbert E. Characterization of a common precursor to corticotropin and beta-lipotropin: cell-free synthesis of the precursor and identification of

- corticotropin peptides in the molecule. Proc Natl Acad Sci U S A 1977;74(11):4826-4830.
- Roberts JL, Herbert E. Characterization of a common precursor to corticotropin and beta-lipotropin: identification of beta-lipotropin peptides and their arrangement relative to corticotropin in the precursor synthesized in a cell-free system. Proc Natl Acad Sci U S A 1977;74(12):5300-5304.
- Rodriguez-Palmero M, Pelegri C, Ferri MJ, Castell M, Franch A, Castellote C. Alterations of lymphocyte populations in lymph nodes but not in spleen during the latency period of adjuvant arthritis. Inflammation 1999;23(2):153-165.
- Rogers J, Wall R. A mechanism for RNA splicing. Proc Natl Acad Sci U S A 1980;77(4):1877-1879.
- Rubinstein M, Mogil JS, Japon M, Chan EC, Allen RG, Low MJ. Absence of opioid stress-induced analgesia in mice lacking beta-endorphin by site-directed mutagenesis. Proc Natl Acad Sci U S A 1996;93(9):3995-4000.
- Rubinstein M, Stein S, Udenfriend S. Characterization of pro-opiocortin, a precursor to opioid peptides and corticotropin. Proc Natl Acad Sci U S A 1978;75(2):669-671.
- 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(10):4219-4223.
- Schäfer M, Mousa SA, Zhang Q, Carter L, Stein C. Expression of corticotropin-releasing factor in inflamed tissue is required for intrinsic peripheral opioid analgesia. Proc Natl Acad Sci U S A 1996;93(12):6096-6100.
- Schauer E, Trautinger F, Kock A, Schwarz A, Bhardwaj R, Simon M, Ansel JC, Schwarz T, Luger TA. Proopiomelanocortin-derived peptides are synthesized and released by human keratinocytes. J Clin Invest 1994;93(5):2258-2262.
- Schiebler TH, Schmidt W. Anatomie: Zentralnervensystem – Hypophyse. Springer-Heidelberg 1999; 8. Auflage:750-753.
- Schiott HB, Phillips SR, Rudzish R, Birch-Machin MA, Wikberg JE, Rees JL. Loss of function mutations of the human melanocortin 1 receptor are common and are associated with red hair. Biochem Biophys Res Commun 1999;260(2):488-491.

- Schmitt TK, Mousa SA, Brack A, Schmidt DK, Rittner HL, Welte M, Schafer M, Stein C. Modulation of peripheral endogenous opioid analgesia by central afferent blockade. *Anesthesiology* 2003;98(1):195-202.
- Scholzen TE, Kalden DH, Brzoska T, Fisbeck T, Fastrich M, Schiller M, Bohm M, Schwarz T, Armstrong CA, Ansel JC, Luger TA. Expression of proopiomelanocortin peptides in human dermal microvascular endothelial cells: evidence for a regulation by ultraviolet light and interleukin-1. *J* 2000;115(6):1021-1028.
- Seidah NG, Benjannet S, Hamelin J, Mamarbachi AM, Basak A, Marcinkiewicz J, Mbikay M, Chretien M, Marcinkiewicz M. The subtilisin/kexin family of precursor convertases. Emphasis on PC1, PC2/7B2, POMC and the novel enzyme SKI-1. *Ann N Y Acad Sci* 1999;885:57-74.
- Seidah NG, Marcinkiewicz M, Benjannet S, Gaspar L, Beaubien G, Mattei MG, Lazure C, Mbikay M, Chretien M. Cloning and primary sequence of a mouse candidate prohormone convertase PC1 homologous to PC2, Furin, and Kex2: distinct chromosomal localization and messenger RNA distribution in brain and pituitary compared to PC2. *Mol Endocrinol* 1991;5(1):111-122.
- Sibinga NE, Goldstein A. Opioid peptides and opioid receptors in cells of the immune system. *Annu Rev Immunol* 1988;6:219-249.
- Sitte N, Busch M, Mousa SA, Labuz D, Rittner H, Gore C, Krause H, Stein C, Schafer M. Lymphocytes upregulate signal sequence-encoding proopiomelanocortin mRNA and beta-endorphin during painful inflammation in vivo. *J Neuroimmunol* 2007;183(1-2):133-145.
- Smeekens SP, Steiner DF. Identification of a human insulinoma cDNA encoding a novel mammalian protein structurally related to the yeast dibasic processing protease Kex2. *J Biol Chem* 1990;265(6):2997-3000.
- Smith AI, Funder JW. Proopiomelanocortin processing in the pituitary, central nervous system, and peripheral tissues. *Endocr Rev* 1988;9(1):159-179.
- Smith EM, Blalock JE. Human lymphocyte production of corticotropin and endorphin-like substances: association with leukocyte interferon. *Proc Natl Acad Sci U S A* 1981;78(12):7530-7534.
- Smith EM, Galin FS, LeBoeuf RD, Coppenhaver DH, Harbour DV, Blalock JE. Nucleotide and amino acid sequence of lymphocyte-derived corticotropin:

- endotoxin induction of a truncated peptide. Proc Natl Acad Sci U S A 1990;87(3):1057-1060.
- Smith EM, Morrill AC, Meyer WJr, Blalock JE. Corticotropin releasing factor induction of leukocyte-derived immunoreactive ACTH and endorphins. Nature 1986;321(6073):881-882.
- Smyth DG, Massey DE, Zakarian S, Finnie MD. Endorphins are stored in biologically active and inactive forms: isolation of alpha-N-acetyl peptides. Nature 1979;279(5710):252-254.
- Stein C, Gramsch C, Herz A. Intrinsic mechanisms of antinociception in inflammation: local opioid receptors and beta-endorphin. J Neurosci 1990;10(4):1292-1298.
- Stein C, Hassan AH, Lehrberger K, Giebing J, Yassouridis A. Local analgesic effect of endogenous opioid peptides. Lancet 1993;342(8867):321-324.
- 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(15):5935-5939.
- 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;31(2):455-451.
- Stein C, Pfluger M, Yassouridis A, Hoelzl J, Lehrberger K, Welte C, Hassan AH. No tolerance to peripheral morphine analgesia in presence of opioid expression in inflamed synovia. J Clin Invest 1996;98(3):793-799.
- Stein C, Schafer M, Machelska H. Attacking pain at its source: new perspectives on opioids. Nat Med 2003;9(8):1003-1008.
- Stephanou A, Fitzharris P, Knight RA, Lightman SL. Characteristics and kinetics of proopiomelanocortin mRNA expression by human leucocytes. Brain Behav Immun 1991;5(4):319-327.
- Stephanou A, Sarlis NJ, Knight RA, Chowdrey HS, Lightman SL. Response of pituitary and spleen pro-opiomelanocortin mRNA, and spleen and thymus interleukin-1 beta mRNA to adjuvant arthritis in the rat. J Neuroimmunol 1992;37(1-2):59-63.
- Takahashi H, Hakamata Y, Watanabe Y, Kikuno R, Miyata T, Numa S. Complete nucleotide sequence of the human corticotropin-beta-lipotropin precursor gene. Nucleic Acids Res 1983;11(19):6847-6858.

- Tanaka S. Comparative aspects of intracellular proteolytic processing of peptide hormone precursors: studies of proopiomelanocortin processing. *Zoolog Sci* 2003;20(10):1183-1198.
- Tanaka S, Kurosumi K. A certain step of proteolytic processing of proopiomelanocortin occurs during the transition between two distinct stages of secretory granule maturation in rat anterior pituitary corticotrophs. *Endocrinology* 1992;131(2):779-786.
- Tanaka S, Nomizu M, Kurosumi K. Intracellular sites of proteolytic processing of proopiomelanocortin in melanotrophs and corticotrophs in rat pituitary. *J Histochem Cytochem* 1991;39(6):809-821.
- Tanaka T, Ebisuno Y, Kanemitsu N, Umemoto E, Yang BG, Jang MH, Miyasaka M. Molecular determinants controlling homeostatic recirculation and tissue-specific trafficking of lymphocytes. *Int Arch Allergy Immunol* 2004;134(2):120-134.
- Tietz W, Hamann A. The migratory behavior of murine CD4+ cells of memory phenotype. *Eur J Immunol* 1997;27(9):2225-2232.
- van Epps DE, Saland L. Beta-endorphin and met-enkephalin stimulate human peripheral blood mononuclear cell chemotaxis. *J Immunol* 1984;132(6):3046-3053.
- 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(5):1922-1933.
- Verma-Gandhu M, Bercik P, Motomura Y, Verdu EF, Khan WI, Blennerhassett PA, Wang L, El-Sharkawy RT, Collins SM. CD4(+) T-Cell Modulation of Visceral Nociception in Mice. *Gastroenterology* 2006;130(6):1721-1728.
- Vindrola O, Mayer AM, Citera G, Spitzer JA, Espinoza LR. Prohormone convertases PC2 and PC3 in rat neutrophils and macrophages. Parallel changes with proenkephalin-derived peptides induced by LPS in vivo. *Neuropeptides* 1994;27(4):235-244.
- Westly HJ, Kleiss AJ, Kelley KW, Wong PK, Yuen PH. Newcastle disease virus-infected splenocytes express the proopiomelanocortin gene. *J Exp Med* 1986;163(6):1589-1594.

- Wintzen M, Yaar M, Burbach JP, Gilchrest BA. Proopiomelanocortin gene product regulation in keratinocytes. *J Invest Dermatol* 1996;106(4):673-678.
- Wollemann M, Benyhe S. Non-opioid actions of opioid peptides. *Life Sci* 2004;75(3):257-270.
- Yaswen L, Diehl N, Brennan MB, Hochgeschwender U. Obesity in the mouse model of pro-opiomelanocortin deficiency responds to peripheral melanocortin. *Nat Med* 1999;5(9):1066-1070.
- Zhou A, Bloomquist BT, Mains RE. The prohormone convertases PC1 and PC2 mediate distinct endoproteolytic cleavages in a strict temporal order during proopiomelanocortin biosynthetic processing. *J Biol Chem* 1993;268(3):1763-1769.
- Zhou Y, Lindberg I. Purification and characterization of the prohormone convertase PC1(PC3). *J Biol Chem* 1993;268(8):5615-5623.
- Zimmermann M. Ethical guidelines for investigations of experimental pain in conscious animals. *Pain* 1983;16(2):109-110.