

4. Literaturverzeichnis

1. Libby P. Inflammation in atherosclerosis. *Nature*. 2002;420:868-874.
2. Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature*. 1993;362:801-809.
3. Springer TA. Traffic signals for lymphocyte recirculation and leukocyte emigration: the multistep paradigm. *Cell*. 1994;76:301-314.
4. Osterud B, Bjorklid E. Role of monocytes in atherogenesis. *Physiol Rev*. 2003;83:1069-1112.
5. Chapman RE, Spinale FG. Extracellular protease activation and unraveling of the myocardial interstitium: critical steps toward clinical applications. *Am J Physiol Heart Circ Physiol*. 2004;286:H1-H10.
6. Manabe I, Shindo T, Nagai R. Gene expression in fibroblasts and fibrosis: involvement in cardiac hypertrophy. *Circ Res*. 2002;91:1103-1113.
7. Steiner DF, Cunningham D, Spigelman L, Aten B. Insulin biosynthesis: evidence for a precursor. *Science*. 1967;157:697-700.
8. Chretien M, Li CH. Isolation, purification, and characterization of gammalipotropic hormone from sheep pituitary glands. *Can J Biochem*. 1967;45:1163-1174.
9. Julius D, Brake A, Blair L, Kunisawa R, Thorner J. Isolation of the putative structural gene for the lysine-arginine-cleaving endopeptidase required for processing of yeast prepro-alpha-factor. *Cell*. 1984;37:1075-1089.
10. Thomas G, Thorne BA, Thomas L, Allen RG, Hruby DE, Fuller R, Thorner J. Yeast KEX2 endopeptidase correctly cleaves a neuroendocrine prohormone in mammalian cells. *Science*. 1988;241:226-230.
11. Seidah NG, Chretien M. Proprotein and prohormone convertases: a family of subtilases generating diverse bioactive polypeptides. *Brain Res*. 1999;848:45-62.
12. Thomas G. Furin at the cutting edge: from protein traffic to embryogenesis and disease. *Nat Rev Mol Cell Biol*. 2002;3:753-766.
13. Steiner DF. The proprotein convertases. *Curr Opin Chem Biol*. 1998;2:31-39.
14. Sakai J, Rawson RB, Espenshade PJ, Cheng D, Seegmiller AC, Goldstein JL, Brown MS. Molecular identification of the sterol-regulated luminal protease that cleaves SREBPs and controls lipid composition of animal cells. *Mol Cell*. 1998;2:505-514.
15. Seidah NG, Benjannet S, Wickham L, Marcinkiewicz J, Jasmin SB, Stifani S, Basak A, Prat A, Chretien M. The secretory proprotein convertase neural apoptosis-regulated convertase 1 (NARC-1): liver regeneration and neuronal differentiation. *Proc Natl Acad Sci U S A*. 2003;100:928-933.
16. Anderson ED, VanSlyke JK, Thulin CD, Jean F, Thomas G. Activation of the furin endoprotease is a multiple-step process: requirements for acidification and internal propeptide cleavage. *Embo J*. 1997;16:1508-1518.
17. Benjannet S, Reudelhuber T, Mercure C, Rondeau N, Chretien M, Seidah NG. Proprotein conversion is determined by a multiplicity of factors including convertase processing, substrate specificity, and intracellular environment. Cell type-specific processing of human prorenin by the convertase PC1. *J Biol Chem*. 1992;267:11417-11423.
18. Duckert P, Brunak S, Blom N. Prediction of proprotein convertase cleavage sites. *Protein Eng Des Sel*. 2004;17:107-112.

19. Henrich S, Cameron A, Bourenkov GP, Kiefersauer R, Huber R, Lindberg I, Bode W, Than ME. The crystal structure of the proprotein processing proteinase furin explains its stringent specificity. *Nat Struct Biol.* 2003;10:520-526.
20. De Bie I, Marcinkiewicz M, Malide D, Lazure C, Nakayama K, Bendayan M, Seidah NG. The isoforms of proprotein convertase PC5 are sorted to different subcellular compartments. *J Cell Biol.* 1996;135:1261-1275.
21. Takahashi S, Nakagawa T, Banno T, Watanabe T, Murakami K, Nakayama K. Localization of furin to the trans-Golgi network and recycling from the cell surface involves Ser and Tyr residues within the cytoplasmic domain. *J Biol Chem.* 1995;270:28397-28401.
22. Mbikay M, Tadros H, Ishida N, Lerner CP, De Lamirande E, Chen A, El-Alfy M, Clermont Y, Seidah NG, Chretien M, Gagnon C, Simpson EM. Impaired fertility in mice deficient for the testicular germ-cell protease PC4. *Proc Natl Acad Sci U S A.* 1997;94:6842-6846.
23. 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;90:4922-4926.
24. Muller L, Cameron A, Fortenberry Y, Apletalina EV, Lindberg I. Processing and sorting of the prohormone convertase 2 propeptide. *J Biol Chem.* 2000;275:39213-39222.
25. Seidah NG, Hamelin J, Mamarbachi M, Dong W, Tardos H, Mbikay M, Chretien M, Day R. cDNA structure, tissue distribution, and chromosomal localization of rat PC7, a novel mammalian proprotein convertase closest to yeast kexin-like proteinases. *Proc Natl Acad Sci U S A.* 1996;93:3388-3393.
26. Lusson J, Vleau D, Hamelin J, Day R, Chretien M, Seidah NG. cDNA structure of the mouse and rat subtilisin/kexin-like PC5: a candidate proprotein convertase expressed in endocrine and nonendocrine cells. *Proc Natl Acad Sci U S A.* 1993;90:6691-6695.
27. Roebroek AJ, Umans L, Pauli IG, Robertson EJ, van Leuven F, Van de Ven WJ, Constam DB. Failure of ventral closure and axial rotation in embryos lacking the proprotein convertase Furin. *Development.* 1998;125:4863-4876.
28. Zhu X, Zhou A, Dey A, Norrbom C, Carroll R, Zhang C, Laurent V, Lindberg I, Ugleholdt R, Holst JJ, Steiner DF. Disruption of PC1/3 expression in mice causes dwarfism and multiple neuroendocrine peptide processing defects. *Proc Natl Acad Sci U S A.* 2002;99:10293-10298.
29. Jackson RS, Creemers JW, Ohagi S, Raffin-Sanson ML, Sanders L, Montague CT, Hutton JC, O'Rahilly S. Obesity and impaired prohormone processing associated with mutations in the human prohormone convertase 1 gene. *Nat Genet.* 1997;16:303-306.
30. Jackson RS, Creemers JW, Farooqi IS, Raffin-Sanson ML, Varro A, Dockray GJ, Holst JJ, Brubaker PL, Corvol P, Polonsky KS, Ostrega D, Becker KL, Bertagna X, Hutton JC, White A, Dattani MT, Hussain K, Middleton SJ, Nicole TM, Milla PJ, Lindley KJ, O'Rahilly S. Small-intestinal dysfunction accompanies the complex endocrinopathy of human proprotein convertase 1 deficiency. *J Clin Invest.* 2003;112:1550-1560.
31. Bresnahan PA, Leduc R, Thomas L, Thorner J, Gibson HL, Brake AJ, Barr PJ, Thomas G. Human fur gene encodes a yeast KEX2-like endoprotease that cleaves pro-beta-NGF in vivo. *J Cell Biol.* 1990;111:2851-2859.

32. Dubois CM, Blanchette F, Laprise MH, Leduc R, Grondin F, Seidah NG. Evidence that furin is an authentic transforming growth factor-beta 1-converting enzyme. *Am J Pathol.* 2001;158:305-316.
33. Hallenberger S, Bosch V, Anglker H, Shaw E, Klenk HD, Garten W. Inhibition of furin-mediated cleavage activation of HIV-1 glycoprotein gp160. *Nature.* 1992;360:358-361.
34. Anderson ED, Thomas L, Hayflick JS, Thomas G. Inhibition of HIV-1 gp160-dependent membrane fusion by a furin-directed alpha 1-antitrypsin variant. *J Biol Chem.* 1993;268:24887-24891.
35. Yana I, Weiss SJ. Regulation of membrane type-1 matrix metalloproteinase activation by proprotein convertases. *Mol Biol Cell.* 2000;11:2387-2401.
36. Lissitzky JC, Luis J, Munzer JS, Benjannet S, Parat F, Chretien M, Marvaldi J, Seidah NG. Endoproteolytic processing of integrin pro-alpha subunits involves the redundant function of furin and proprotein convertase (PC) 5A, but not paired basic amino acid converting enzyme (PACE) 4, PC5B or PC7. *Biochem J.* 2000;346 Pt 1:133-138.
37. Khatib AM, Siegfried G, Chretien M, Metrakos P, Seidah NG. Proprotein convertases in tumor progression and malignancy: novel targets in cancer therapy. *Am J Pathol.* 2002;160:1921-1935.
38. Bassi DE, Mahloogi H, Lopez De Cicco R, Klein-Szanto A. Increased furin activity enhances the malignant phenotype of human head and neck cancer cells. *Am J Pathol.* 2003;162:439-447.
39. Bassi DE, Lopez De Cicco R, Mahloogi H, Zucker S, Thomas G, Klein-Szanto AJ. Furin inhibition results in absent or decreased invasiveness and tumorigenicity of human cancer cells. *Proc Natl Acad Sci U S A.* 2001;98:10326-10331.
40. Negishi M, Lu D, Zhang YQ, Sawada Y, Sasaki T, Kayo T, Ando J, Izumi T, Kurabayashi M, Kojima I, Masuda H, Takeuchi T. Upregulatory expression of furin and transforming growth factor-beta by fluid shear stress in vascular endothelial cells. *Arterioscler Thromb Vasc Biol.* 2001;21:785-790.
41. Denault JB, D'Orleans-Juste P, Masaki T, Leduc R. Inhibition of convertase-related processing of proendothelin-1. *J Cardiovasc Pharmacol.* 1995;26 Suppl 3:S47-50.
42. Mercure C, Jutras I, Day R, Seidah NG, Reudelhuber TL. Prohormone convertase PC5 is a candidate processing enzyme for prorenin in the human adrenal cortex. *Hypertension.* 1996;28:840-846.
43. Sawada Y, Inoue M, Kanda T, Sakamaki T, Tanaka S, Minamino N, Nagai R, Takeuchi T. Co-elevation of brain natriuretic peptide and proprotein-processing endoprotease furin after myocardial infarction in rats. *FEBS Lett.* 1997;400:177-182.
44. Sawada Y, Suda M, Yokoyama H, Kanda T, Sakamaki T, Tanaka S, Nagai R, Abe S, Takeuchi T. Stretch-induced hypertrophic growth of cardiocytes and processing of brain-type natriuretic peptide are controlled by proprotein-processing endoprotease furin. *J Biol Chem.* 1997;272:20545-20554.
45. Owens GK. Regulation of differentiation of vascular smooth muscle cells. *Physiol Rev.* 1995;75:487-517.
46. Stawowy P, Marcinkiewicz J, Graf K, Seidah N, Chretien M, Fleck E, Marcinkiewicz M. Selective expression of the proprotein convertases furin, PC5, and PC7 in proliferating vascular smooth muscle cells of the rat aorta in vitro. *J Histochem Cytochem.* 2001;49:323-332.

47. Hao H, Hirota S, Tsukamoto Y, Imaoka M, Ishibashi-Ueda H, Yutani C. Alterations of bone matrix protein mRNA expression in rat aorta in vitro. *Arterioscler Thromb Vasc Biol.* 1995;15:1474-1480.
48. Takasaki I, Chobanian AV, Brecher P. Biosynthesis of fibronectin by rabbit aorta. *J Biol Chem.* 1991;266:17686-17694.
49. Creedon D, Tuttle JB. Nerve growth factor synthesis in vascular smooth muscle. *Hypertension.* 1991;18:730-741.
50. Stawowy P, Blaschke F, Kilimnik A, Goetze S, Kallisch H, Chretien M, Marcinkiewicz M, Fleck E, Graf K. Proprotein convertase PC5 regulation by PDGF-BB involves PI3-kinase/p70(s6)-kinase activation in vascular smooth muscle cells. *Hypertension.* 2002;39:399-404.
51. Wood SA, Park JE, Brown WJ. Brefeldin A causes a microtubule-mediated fusion of the trans-Golgi network and early endosomes. *Cell.* 1991;67:591-600.
52. Chege NW, Pfeffer SR. Compartmentation of the Golgi complex: brefeldin-A distinguishes trans-Golgi cisternae from the trans-Golgi network. *J Cell Biol.* 1990;111:893-899.
53. Xiang Y, Molloy SS, Thomas L, Thomas G. The PC6B cytoplasmic domain contains two acidic clusters that direct sorting to distinct trans-Golgi network/endosomal compartments. *Mol Biol Cell.* 2000;11:1257-1273.
54. Pullen N, Thomas G. The modular phosphorylation and activation of p70s6k. *FEBS Lett.* 1997;410:78-82.
55. Waltenberger J. Modulation of growth factor action: implications for the treatment of cardiovascular diseases. *Circulation.* 1997;96:4083-4094.
56. Berk BC, Vekshtein V, Gordon HM, Tsuda T. Angiotensin II-stimulated protein synthesis in cultured vascular smooth muscle cells. *Hypertension.* 1989;13:305-314.
57. Davies SP, Reddy H, Caivano M, Cohen P. Specificity and mechanism of action of some commonly used protein kinase inhibitors. *Biochem J.* 2000;351:95-105.
58. Reiske HR, Kao SC, Cary LA, Guan JL, Lai JF, Chen HC. Requirement of phosphatidylinositol 3-kinase in focal adhesion kinase-promoted cell migration. *J Biol Chem.* 1999;274:12361-12366.
59. Stawowy P, Graf K, Goetze S, Roser M, Chretien M, Seidah NG, Fleck E, Marcinkiewicz M. Coordinated regulation and colocalization of alpha v integrin and its activating enzyme proprotein convertase PC5 in vivo. *Histochem Cell Biol.* 2003;239-245.
60. Schwartz SM, Stemerman MB, Benditt EP. The aortic intima. II. Repair of the aortic lining after mechanical denudation. *Am J Pathol.* 1975;81:15-42.
61. Wei GL, Krasinski K, Kearney M, Isner JM, Walsh K, Andres V. Temporally and spatially coordinated expression of cell cycle regulatory factors after angioplasty. *Circ Res.* 1997;80:418-426.
62. Hynes RO. Integrins: versatility, modulation, and signaling in cell adhesion. *Cell.* 1992;69:11-25.
63. Coppolino MG, Dedhar S. Bi-directional signal transduction by integrin receptors. *Int J Biochem Cell Biol.* 2000;32:171-188.
64. Ingber DE. Mechanical signaling and the cellular response to extracellular matrix in angiogenesis and cardiovascular physiology. *Circ Res.* 2002;91:877-887.
65. Schaller MD, Hildebrand JD, Shannon JD, Fox JW, Vines RR, Parsons JT. Autophosphorylation of the focal adhesion kinase, pp125FAK, directs SH2-dependent binding of pp60src. *Mol Cell Biol.* 1994;14:1680-1688.

66. Slepian MJ, Massia SP, Dehdashti B, Fritz A, Whitesell L. Beta 3-integrins rather than beta 1-integrins dominate integrin-matrix interactions involved in postinjury smooth muscle cell migration. *Circulation*. 1998;97:1818-1827.
67. Dufourcq P, Couffignal T, Alzieu P, Daret D, Moreau C, Duplaa C, Bonnet J. Vitronectin is up-regulated after vascular injury and vitronectin blockade prevents neointima formation. *Cardiovasc Res*. 2002;53:952-962.
68. Dufourcq P, Louis H, Moreau C, Daret D, Boisseau MR, Lamaziere JM, Bonnet J. Vitronectin expression and interaction with receptors in smooth muscle cells from human atheromatous plaque. *Arterioscler Thromb Vasc Biol*. 1998;18:168-176.
69. Hoshiga M, Alpers CE, Smith LL, Giachelli CM, Schwartz SM. Alpha-v beta-3 integrin expression in normal and atherosclerotic artery. *Circ Res*. 1995;77:1129-1135.
70. Liaw L, Skinner MP, Raines EW, Ross R, Cheresh DA, Schwartz SM, Giachelli CM. The adhesive and migratory effects of osteopontin are mediated via distinct cell surface integrins. Role of alpha v beta 3 in smooth muscle cell migration to osteopontin in vitro. *J Clin Invest*. 1995;95:713-724.
71. Coleman KR, Braden GA, Willingham MC, Sane DC. Vitaxin, a humanized monoclonal antibody to the vitronectin receptor (alpha v beta 3), reduces neointimal hyperplasia and total vessel area after balloon injury in hypercholesterolemic rabbits. *Circ Res*. 1999;84:1268-1276.
72. Suzuki S, Argraves WS, Pytela R, Arai H, Krusius T, Pierschbacher MD, Ruoslahti E. cDNA and amino acid sequences of the cell adhesion protein receptor recognizing vitronectin reveal a transmembrane domain and homologies with other adhesion protein receptors. *Proc Natl Acad Sci U S A*. 1986;83:8614-8618.
73. Rigot V, Andre F, Lehmann M, Lissitzky JC, Marvaldi J, Luis J. Biogenesis of alpha6beta4 integrin in a human colonic adenocarcinoma cell line involvement of calnexin. *Eur J Biochem*. 1999;261:659-666.
74. Delwel GO, Hogervorst F, Sonnenberg A. Cleavage of the alpha6A subunit is essential for activation of the alpha 6A beta 1 integrin by phorbol 12-myristate 13-acetate. *J Biol Chem*. 1996;271:7293-7296.
75. Stawowy P, Kallisch H, Veinot JP, Kilimnik A, Prichett W, Goetze S, Seidah NG, Chretien M, Fleck E, Graf K. Endoproteolytic activation of alpha (v) integrin by proprotein convertase PC5 is required for vascular smooth muscle cell adhesion to vitronectin and integrin-dependent signaling. *Circulation*. 2004;109:770-776.
76. Deryugina EI, Ratnikov BI, Postnova TI, Rozanov DV, Strongin AY. Processing of integrin alpha(v) subunit by membrane type 1 matrix metalloproteinase stimulates migration of breast carcinoma cells on vitronectin and enhances tyrosine phosphorylation of focal adhesion kinase. *J Biol Chem*. 2002;277:9749-9756.
77. Berthet V, Rigot V, Champion S, Secchi J, Fouchier F, Marvaldi J, Luis J. Role of endoproteolytic processing in the adhesive and signaling functions of alpha v beta 5 integrin. *J Biol Chem*. 2000;275:33308-33313.
78. Benjannet S, Savaria D, Laslop A, Munzer JS, Chretien M, Marcinkiewicz M, Seidah NG. Alpha 1-antitrypsin Portland inhibits processing of precursors mediated by proprotein convertases primarily within the constitutive secretory pathway. *J Biol Chem*. 1997;272:26210-26218.
79. Cary LA, Chang JF, Guan JL. Stimulation of cell migration by overexpression of focal adhesion kinase and its association with Src and Fyn. *J Cell Sci*. 1996;109 (Pt 7):1787-1794.

80. Chen HC, Guan JL. Association of focal adhesion kinase with its potential substrate phosphatidylinositol 3-kinase. *Proc Natl Acad Sci U S A.* 1994;91:10148-10152.
81. Lin TH, Aplin AE, Shen Y, Chen Q, Schaller M, Romer L, Aukhil I, Juliano RL. Integrin-mediated activation of MAP kinase is independent of FAK: evidence for dual integrin signaling pathways in fibroblasts. *J Cell Biol.* 1997;136:1385-1395.
82. Wilcox JN, Nelken NA, Coughlin SR, Gordon D, Schall TJ. Local expression of inflammatory cytokines in human atherosclerotic plaques. *J Atheroscler Thromb.* 1994;1:S10-13.
83. Weerasinghe D, McHugh KP, Ross FP, Brown EJ, Gisler RH, Imhof BA. A role for the alpha v beta 3 integrin in the transmigration of monocytes. *J Cell Biol.* 1998;142:595-607.
84. Bishop GG, McPherson JA, Sanders JM, Hesselbacher SE, Feldman MJ, McNamara CA, Gimple LW, Powers ER, Mousa SA, Sarembock IJ. Selective alpha (v) beta (3)-receptor blockade reduces macrophage infiltration and restenosis after balloon angioplasty in the atherosclerotic rabbit. *Circulation.* 2001;103:1906-1911.
85. Patel SS, Thiagarajan R, Willerson JT, Yeh ET. Inhibition of alpha4 integrin and ICAM-1 markedly attenuate macrophage homing to atherosclerotic plaques in ApoE-deficient mice. *Circulation.* 1998;97:75-81.
86. Stawowy P, Kallisch H, Borges Pereira Stawowy N, Stibenz D, Veinot JP, Grafe M, Seidah NG, Chretien M, Fleck E, Graf K. Immunohistochemical localization of subtilisin/kexin-like proprotein convertases in human atherosclerosis. *Virchows Arch.* 2005;446:351-359.
87. Auwerx J. The human leukemia cell line, THP-1: a multifaceted model for the study of monocyte-macrophage differentiation. *Experientia.* 1991;47:22-31.
88. Moreno PR, Falk E, Palacios IF, Newell JB, Fuster V, Fallon JT. Macrophage infiltration in acute coronary syndromes. Implications for plaque rupture. *Circulation.* 1994;90:775-778.
89. Visse R, Nagase H. Matrix metalloproteinases and tissue inhibitors of metalloproteinases: structure, function, and biochemistry. *Circ Res.* 2003;92:827-839.
90. Newby AC. Dual role of matrix metalloproteinases (matrixins) in intimal thickening and atherosclerotic plaque rupture. *Physiol Rev.* 2005;85:1-31.
91. English WR, Puente XS, Freije JM, Knauper V, Amour A, Merryweather A, Lopez-Otin C, Murphy G. Membrane type 4 matrix metalloproteinase (MMP17) has tumor necrosis factor-alpha convertase activity but does not activate pro-MMP2. *J Biol Chem.* 2000;275:14046-14055.
92. McQuibban GA, Gong JH, Tam EM, McCulloch CA, Clark-Lewis I, Overall CM. Inflammation dampened by gelatinase A cleavage of monocyte chemoattractant protein-3. *Science.* 2000;289:1202-1206.
93. Yu Q, Stamenkovic I. Cell surface-localized matrix metalloproteinase-9 proteolytically activates TGF-beta and promotes tumor invasion and angiogenesis. *Genes Dev.* 2000;14:163-176.
94. Miranda L, Wolf J, Pichuantes S, Duke R, Franzusoff A. Isolation of the human PC6 gene encoding the putative host protease for HIV-1 gp160 processing in CD4+ T lymphocytes. *Proc Natl Acad Sci U S A.* 1996;93:7695-7700.
95. Munzer JS, Basak A, Zhong M, Mamarbachi A, Hamelin J, Savaria D, Lazure C, Hendy GN, Benjannet S, Chretien M, Seidah NG. In vitro characterization of the novel proprotein convertase PC7. *J Biol Chem.* 1997;272:19672-19681.

96. Galis ZS, Muszynski M, Sukhova GK, Simon-Morrissey E, Unemori EN, Lark MW, Amento E, Libby P. Cytokine-stimulated human vascular smooth muscle cells synthesize a complement of enzymes required for extracellular matrix digestion. *Circ Res.* 1994;75:181-189.
97. Rajavashisth TB, Xu XP, Jovinge S, Meisel S, Xu XO, Chai NN, Fishbein MC, Kaul S, Cercek B, Sharifi B, Shah PK. Membrane type 1 matrix metalloproteinase expression in human atherosclerotic plaques: evidence for activation by proinflammatory mediators. *Circulation.* 1999;99:3103-3109.
98. Uzui H, Harpf A, Liu M, Doherty TM, Shukla A, Chai NN, Tripathi PV, Jovinge S, Wilkin DJ, Asotra K, Shah PK, Rajavashisth TB. Increased expression of membrane type 3-matrix metalloproteinase in human atherosclerotic plaque: role of activated macrophages and inflammatory cytokines. *Circulation.* 2002;106:3024-3030.
99. Stawowy P, Meyborg H, Stibenz D, Borges Pereira Stawowy N, Roser M, Thanabalasingam U, Veinot JP, Chretien M, Seidah NG, Fleck E, Graf K. Furin-like proprotein convertases are central regulators of the membrane type matrix metalloproteinase-pro-matrix metalloproteinase - 2 proteolytic cascade in atherosclerosis. *Circulation.* 2005;111:2820-2827.
100. Welgus HG, Campbell EJ, Cury JD, Eisen AZ, Senior RM, Wilhelm SM, Goldberg GI. Neutral metalloproteinases produced by human mononuclear phagocytes. Enzyme profile, regulation, and expression during cellular development. *J Clin Invest.* 1990;86:1496-1502.
101. Welgus HG, Senior RM, Parks WC, Kahn AJ, Ley TJ, Shapiro SD, Campbell EJ. Neutral proteinase expression by human mononuclear phagocytes: a prominent role of cellular differentiation. *Matrix Suppl.* 1992;1:363-367.
102. Wesley RB, 2nd, Meng X, Godin D, Galis ZS. Extracellular matrix modulates macrophage functions characteristic to atheroma: collagen type I enhances acquisition of resident macrophage traits by human peripheral blood monocytes in vitro. *Arterioscler Thromb Vasc Biol.* 1998;18:432-440.
103. Worley JR, Baugh MD, Hughes DA, Edwards DR, Hogan A, Sampson MJ, Gavrilovic J. Metalloproteinase expression in PMA-stimulated THP-1 cells. Effects of peroxisome proliferator-activated receptor-gamma (PPAR gamma) agonists and 9-cis-retinoic acid. *J Biol Chem.* 2003;278:51340-51346.
104. Chase AJ, Bond M, Crook MF, Newby AC. Role of nuclear factor-kappa B activation in metalloproteinase-1, -3, and -9 secretion by human macrophages in vitro and rabbit foam cells produced in vivo. *Arterioscler Thromb Vasc Biol.* 2002;22:765-771.
105. Strongin AY, Collier I, Bannikov G, Marmer BL, Grant GA, Goldberg GI. Mechanism of cell surface activation of 72-kDa type IV collagenase. Isolation of the activated form of the membrane metalloprotease. *J Biol Chem.* 1995;270:5331-5338.
106. Will H, Atkinson SJ, Butler GS, Smith B, Murphy G. The soluble catalytic domain of membrane type 1 matrix metalloproteinase cleaves the propeptide of progelatinase A and initiates autoproteolytic activation. Regulation by TIMP-2 and TIMP-3. *J Biol Chem.* 1996;271:17119-17123.
107. Butler GS, Butler MJ, Atkinson SJ, Will H, Tamura T, van Westrum SS, Crabbe T, Clements J, d'Ortho MP, Murphy G. The TIMP2 membrane type 1 metalloproteinase "receptor" regulates the concentration and efficient activation of progelatinase A. A kinetic study. *J Biol Chem.* 1998;273:871-880.
108. Stawowy P, Kallisch H, Kilimnik A, Margeta C, Seidah NG, Chretien M, Fleck E, Graf K. Proprotein convertases regulate insulin-like growth factor 1-induced

- membrane-type 1 matrix metalloproteinase in VSMCs via endoproteolytic activation of the insulin-like growth factor-1 receptor. *Biochem Biophys Res Commun.* 2004;321:531-538.
109. Overall CM, Sodek J. Concanavalin A produces a matrix-degradative phenotype in human fibroblasts. Induction and endogenous activation of collagenase, 72-kDa gelatinase, and Pump-1 is accompanied by the suppression of the tissue inhibitor of matrix metalloproteinases. *J Biol Chem.* 1990;265:21141-21151.
110. Sato T, Kondo T, Fujisawa T, Seiki M, Ito A. Furin-independent pathway of membrane type 1-matrix metalloproteinase activation in rabbit dermal fibroblasts. *J Biol Chem.* 1999;274:37280-37284.
111. Rozanov DV, Strongin AY. Membrane type-1 matrix metalloproteinase functions as a proprotein self-convertase. Expression of the latent zymogen in *Pichia pastoris*, autolytic activation, and the peptide sequence of the cleavage forms. *J Biol Chem.* 2003;278:8257-8260.
112. Zahradka P, Harding G, Litchie B, Thomas S, Werner JP, Wilson DP, Yurkova N. Activation of MMP-2 in response to vascular injury is mediated by phosphatidylinositol 3-kinase-dependent expression of MT1-MMP. *Am J Physiol Heart Circ Physiol.* 2004;287:H2861-2870.
113. Shofuda KI, Hasenstab D, Kenagy RD, Shofuda T, Li ZY, Lieber A, Clowes AW. Membrane-type matrix metalloproteinase-1 and -3 activity in primate smooth muscle cells. *Faseb J.* 2001;15:2010-2012.
114. Zhang D, Brodt P. Type 1 insulin-like growth factor regulates MT1-MMP synthesis and tumor invasion via PI 3-kinase/Akt signaling. *Oncogene.* 2003;22:974-982.
115. Delafontaine P, Lou H, Alexander RW. Regulation of insulin-like growth factor I messenger RNA levels in vascular smooth muscle cells. *Hypertension.* 1991;18:742-747.
116. Duan C, Bauchat JR, Hsieh T. Phosphatidylinositol 3-kinase is required for insulin-like growth factor-I-induced vascular smooth muscle cell proliferation and migration. *Circ Res.* 2000;86:15-23.
117. LeRoith D, Werner H, Beitner-Johnson D, Roberts CT, Jr. Molecular and cellular aspects of the insulin-like growth factor I receptor. *Endocr Rev.* 1995;16:143-163.
118. Lehmann M, Andre F, Bellan C, Remacle-Bonnet M, Garrouste F, Parat F, Lissitsky JC, Marvaldi J, Pommier G. Deficient processing and activity of type I insulin-like growth factor receptor in the furin-deficient LoVo-C5 cells. *Endocrinology.* 1998;139:3763-3771.
119. Khatib AM, Siegfried G, Prat A, Luis J, Chretien M, Metrakos P, Seidah NG. Inhibition of proprotein convertases is associated with loss of growth and tumorigenicity of HT-29 human colon carcinoma cells: importance of insulin-like growth factor-1 (IGF-1) receptor processing in IGF-1-mediated functions. *J Biol Chem.* 2001;276:30686-30693.
120. Spinale FG, Coker ML, Bond BR, Zellner JL. Myocardial matrix degradation and metalloproteinase activation in the failing heart: a potential therapeutic target. *Cardiovasc Res.* 2000;46:225-238.
121. Hayashidani S, Tsutsui H, Ikeuchi M, Shiomi T, Matsusaka H, Kubota T, Imanaka-Yoshida K, Itoh T, Takeshita A. Targeted deletion of MMP-2 attenuates early LV rupture and late remodeling after experimental myocardial infarction. *Am J Physiol.* 2003;285:H1229-1235.
122. Swynghedauw B. Molecular mechanisms of myocardial remodeling. *Physiol Rev.* 1999;79:215-262.

123. Yuan W, Varga J. Transforming growth factor-beta repression of matrix metalloproteinase-1 in dermal fibroblasts involves Smad 3. *J Biol Chem.* 2001;276:38502-38510.
124. Overall CM, Wrana JL, Sodek J. Transcriptional and post-transcriptional regulation of 72-kDa gelatinase/type IV collagenase by transforming growth factor-beta 1 in human fibroblasts. Comparisons with collagenase and tissue inhibitor of matrix metalloproteinase gene expression. *J Biol Chem.* 1991;266:14064-14071.
125. Stawowy P, Margeta C, Kallisch H, Seidah NG, Chretien M, Fleck E, Graf K. Regulation of matrix metalloproteinase MT1-MMP/MMP-2 in cardiac fibroblasts by TGF-beta1 involves furin-convertase. *Cardiovasc Res.* 2004;63:87-97.
126. Gentry LE, Lioubin MN, Purchio AF, Marquardt H. Molecular events in the processing of recombinant type 1 pre-pro-transforming growth factor beta to the mature polypeptide. *Mol Cell Biol.* 1988;8:4162-4168.
127. Oklu R, Hesketh R. The latent transforming growth factor beta binding protein (LTBP) family. *Biochem J.* 2000;352 Pt 3:601-610.
128. Campbell SE, Katwa LC. Angiotensin II stimulated expression of transforming growth factor-beta1 in cardiac fibroblasts and myofibroblasts. *J Mol Cell Cardiol.* 1997;29:1947-1958.
129. Flanders KC, Holder MG, Winokur TS. Autoinduction of mRNA and protein expression for transforming growth factor-beta S in cultured cardiac cells. *J Mol Cell Cardiol.* 1995;27:805-812.
130. Orlandi A, Ehrlich HP, Ropraz P, Spagnoli LG, Gabbiani G. Rat aortic smooth muscle cells isolated from different layers and at different times after endothelial denudation show distinct biological features in vitro. *Arterioscler Thromb.* 1994;14:982-989.
131. Berton G, Lowell CA. Integrin signalling in neutrophils and macrophages. *Cell Signal.* 1999;11:621-635.
132. Wouters S, Leruth M, Decroly E, Vandenbranden M, Creemers JW, van de Loo JW, Ruysschaert JM, Courtoy PJ. Furin and proprotein convertase 7 (PC7)/lymphoma PC endogenously expressed in rat liver can be resolved into distinct post-Golgi compartments. *Biochem J.* 1998;336:311-316.
133. Brooks PC, Stromblad S, Sanders LC, von Schalscha TL, Aimes RT, Stetler-Stevenson WG, Quigley JP, Cheresh DA. Localization of matrix metalloproteinase MMP-2 to the surface of invasive cells by interaction with integrin alpha v beta 3. *Cell.* 1996;85:683-693.
134. Kanda S, Kuzuya M, Ramos MA, Koike T, Yoshino K, Ikeda S, Iguchi A. Matrix metalloproteinase and alphavbeta3 integrin-dependent vascular smooth muscle cell invasion through a type I collagen lattice. *Arterioscler Thromb Vasc Biol.* 2000;20:998-1005.
135. Giannelli G, Falk-Marzillier J, Schiraldi O, Stetler-Stevenson WG, Quaranta V. Induction of cell migration by matrix metalloprotease-2 cleavage of laminin-5. *Science.* 1997;277:225-228.
136. Galis ZS, Sukhova GK, Lark MW, Libby P. Increased expression of matrix metalloproteinases and matrix degrading activity in vulnerable regions of human atherosclerotic plaques. *J Clin Invest.* 1994;94:2493-2503.
137. Hein S, Arnon E, Kostin S, Schonburg M, Elsasser A, Polyakova V, Bauer EP, Kloekorn WP, Schaper J. Progression from compensated hypertrophy to failure in the pressure-overloaded human heart: structural deterioration and compensatory mechanisms. *Circulation.* 2003;107:984-991.

138. Klappacher G, Franzen P, Haab D, Mehrabi M, Binder M, Plesch K, Pacher R, Grimm M, Pribill I, Eichler HG, et al. Measuring extracellular matrix turnover in the serum of patients with idiopathic or ischemic dilated cardiomyopathy and impact on diagnosis and prognosis. *Am J Cardiol.* 1995;75:913-918.
139. Spinale FG, Coker ML, Heung LJ, Bond BR, Gunasinghe HR, Etoh T, Goldberg AT, Zellner JL, Crumbley AJ. A matrix metalloproteinase induction/activation system exists in the human left ventricular myocardium and is upregulated in heart failure. *Circulation.* 2000;102:1944-1949.
140. Cameron A, Appel J, Houghten RA, Lindberg I. Polyarginines are potent furin inhibitors. *J Biol Chem.* 2000;275:36741-36749.
141. Sarac MS, Peinado JR, Leppla SH, Lindberg I. Protection against anthrax toxemia by hexa-D-arginine in vitro and in vivo. *Infect Immun.* 2004;72:602-605.