

## References

1. Sage, H.; Johnson, C.; and Bornstein, P. Characterization of a novel serum albumin-binding glycoprotein secreted by endothelial cells in culture. J Biol. Chem 259 (1984): 3993-4007.
2. Mann, K.; Deutzmann, R.; Paulsson, M.; and Timpl, R. Solubilization of protein BM-40 from a basement membrane tumor with chelating agents and evidence for its identity with osteonectin and SPARC. FEBS Lett 218 (1987): 167-172.
3. Termine, J. D.; Kleinman, H. K.; Whitson, S. W.; Conn, K. M.; McGarvey, M. L.; and Martin, G. R. Osteonectin, a bone-specific protein linking mineral to collagen. Cell 26 (1981): 99-105.
4. Maurer, P.; Hohenadl, C.; Hohenester, E.; Gohring, W.; Timpl, R.; and Engel, J. The C-terminal portion of BM-40 (SPARC/osteonectin) is an autonomously folding and crystallisable domain that binds calcium and collagen IV. J Mol. Biol. 253 (1995): 347-357.
5. Kamihagi, K.; Katayama, M.; Ouchi, R.; and Kato, I. Osteonectin/SPARC regulates cellular secretion rates of fibronectin and laminin extracellular matrix proteins. Biochem.Biophys.Res Commun. 200 (1994): 423-428.
6. Lane, T. F.; and Sage, E. H. The biology of sparc, a protein that modulates cell-matrix interactions. FASEB J. 8 (1994): 163-173.
7. Engel, J.; Taylor, W.; Paulsson, M.; Sage, H.; and Hogan, B. Calcium binding domains and calcium-induced conformational transition of SPARC/BM-40/osteonectin, an extracellular glycoprotein expressed in mineralized and nonmineralized tissues. Biochemistry 26 (1987): 6958-6965.

8. Busch, E.; Hohenester, E.; Timpl, R.; Paulsson, M.; and Maurer, P. Calcium affinity, cooperativity, and domain interactions of extracellular EF-hands present in BM-40. J Biol.Chem 275 (2000): 25508-25515.
9. Young, M. F.; Day, A. A.; Dominquez, P.; McQuillan, C. I.; Fisher, L. W.; and Termine, J. D. Structure and expression of osteonectin mRNA in human tissue. Connect.Tissue Res 24 (1990): 17-28.
10. Mason, I. J.; Taylor, A.; Williams, J. G.; Sage, H.; and Hogan, B. L. Evidence from molecular cloning that SPARC, a major product of mouse embryo parietal endoderm, is related to an endothelial cell 'culture shock' glycoprotein of Mr 43,000. EMBO J 5 (1986): 1465-1472.
11. Domenicucci, C.; Goldberg, H. A.; Hofmann, T.; Isenman, D.; Wasi, S.; and Sodek, J. Characterization of porcine osteonectin extracted from foetal calvariae. Biochem J 253 (1988): 139-151.
12. Stenner, D. D.; Tracy, R. P.; Riggs, B. L.; and Mann, K. G. Human platelets contain and secrete osteonectin, a major protein of mineralized bone. Proc.Natl.Acad.Sci.U.S.A. 83 (1986): 6892-6896.
13. Kelm, R. J., Jr; and Mann, K. G. Human platelet osteonectin: release, surface expression, and partial characterization. Blood 75 (1990): 1105-1113.
14. Malaval, L.; Darbouret, B.; Preaudat, C.; Jolu, J. P.; and Delmas, P. D. Intertissular variations in osteonectin: a monoclonal antibody directed to bone osteonectin shows reduced affinity for platelet osteonectin. J Bone Miner Res 6 (1991): 315-323.
15. Kelm, R. J., Jr; and Mann, K. G. The collagen binding specificity of bone and platelet osteonectin is related to differences in glycosylation. J Biol.Chem. 266 (1991): 9632-9639.

16. Xie, R. L.; and Long, G. L. Role of N-linked glycosylation in human osteonectin. Effect of carbohydrate removal by N-glycanase and site-directed mutagenesis on structure and binding of type V collagen. J Biol.Chem. 270 (1995): 23212-23217.
17. Mundlos, S.; Schwahn, B.; Reichert, T.; and Zabel, B. Distribution of osteonectin mRNA and protein during human embryonic and fetal development. J Histochem.Cytochem. 40 (1992): 283-291.
18. Shiba, H., *et al.* Effects of basic fibroblast growth factor on proliferation, the expression of osteonectin (SPARC) and alkaline phosphatase, and calcification in cultures of human pulp cells. Dev.Biol. 170 (1995): 457-466.
19. Maillard, C.; Malaval, L.; and Delmas, P. D. Immunological screening of SPARC/osteonectin in nonmineralized tissues. Bone 13 (1992): 257-264.
20. Porter, P. L.; Sage, E. H.; Lane, T. F.; Funk, S. E.; and Gown, A. M. Distribution of SPARC in normal and neoplastic human tissue. J Histochem.Cytochem. 43 (1995): 791-800.
21. Pichler, R. H., *et al.* SPARC is expressed by mesangial cells in experimental mesangial proliferative nephritis and inhibits platelet-derived-growth-factor-mediated mesangial cell proliferation in vitro. Am J Pathol 148 (1996): 1153-1167.
22. Wrana, J. L.; Overall, C. M.; and Sodek, J. Regulation of the expression of a secreted acidic protein rich in cysteine (SPARC) in human fibroblasts by transforming growth factor beta. Comparison of transcriptional and post-transcriptional control with fibronectin and type I collagen. Eur.J Biochem. 197 (1991): 519-528.

23. Delany, A. M.; and Canalis, E. Basic fibroblast growth factor destabilizes osteonectin mRNA in osteoblasts. Am.J Physiol. 274 (1998): C734-C740.
24. Shiba, H., *et al.* Differential effects of various growth factors and cytokines on the syntheses of DNA, type I collagen, laminin, fibronectin, osteonectin/secreted protein, acidic and rich in cysteine (SPARC), and alkaline phosphatase by human pulp cells in culture. J Cell Physiol. 174 (1998): 194-205.
25. Frizell, E.; Liu, S. L.; Abraham, A.; Ozaki, I.; Eghbali, M.; Sage, E. H.; and Zern, M. A. Expression of SPARC in normal and fibrotic livers. Hepatology 21 (1995): 847-854.
26. Pichler, R. H., *et al.* SPARC is expressed in renal interstitial fibrosis and in renal vascular injury. Kidney Int 50 (1996): 1978-1989.
27. Nakamura, S., *et al.* Enhancement of SPARC (osteonectin) synthesis in arthritic cartilage. Increased levels in synovial fluids from patients with rheumatoid arthritis and regulation by growth factors and cytokines in chondrocyte cultures. Arthritis Rheum. 39 (1996): 539-551.
28. Ledda, F.; Bravo, A. I.; Adris, S.; Bover, L.; Mordoh, J.; and Podhajcer, O. L. The expression of the secreted protein acidic and rich in cysteine (SPARC) is associated with the neoplastic progression of human melanoma. J Invest. Dermatol. 108 (1997): 210-214.
29. Le Bail, B.; Faouzi, S.; Boussarie, L.; Guirouilh, J.; Blanc, J. F.; Carles, J.; Bioulac-Sage, P.; Balabaud, C.; and Rosenbaum, J. Osteonectin/SPARC is overexpressed in human hepatocellular carcinoma. J Pathol 189 (1999): 46-52.
30. Porte, H., *et al.* Overexpression of stromelysin-3, BM-40/SPARC, and MET genes in human esophageal carcinoma: implications for prognosis. Clin.Cancer Res 4 (1998): 1375-1382.

31. Thomas, R.; True, L. D.; Bassuk, J. A.; Lange, P. H.; and Vessella, R. L. Differential expression of osteonectin/SPARC during human prostate cancer progression. Clin Cancer Res 6 (2000): 1140-1149.
32. Podhajcer, O. L.; Wolf, C.; Lefebvre, O.; Segain, J. P.; Rouyer, N.; Stoll, I.; Rio, M. C.; Chambon, P.; and Basset, P. Comparative expression of the SPARC and stromelysin-3 genes in mammary tumours. The Breast 5 (1996): 13-20.
33. Bellahcene, A.; and Castronovo, V. Increased expression of osteonectin and osteopontin, two bone matrix proteins, in human breast cancer. Am.J Pathol. 146 (1995): 95-100.
34. Porte, H.; Chastre, E.; Prevot, S.; Nordlinger, B.; Empeur, S.; Basset, P.; Chambon, P.; and Gespach, C. Neoplastic progression of human colorectal cancer is associated with overexpression of the stromelysin-3 and BM-40/SPARC genes. Int. J Cancer 64 (1995): 70-75.
35. Ledda, M. F.; Adris, S.; Bravo, A. I.; Kairiyama, C.; Bover, L.; Chernajovsky, Y.; Mordoh, J.; and Podhajcer, O. L. Suppression of SPARC expression by antisense RNA abrogates the tumorigenicity of human melanoma cells. Nat. Med. 3 (1997): 171-176.
36. Gilles, C.; Bassuk, J. A.; Pulyaeva, H.; Sage, E. H.; Foidart, J. M.; and Thompson, E. W. SPARC/Osteonectin induces MMP-2-activation in human breast cancer cell lines. Cancer Res. 58 (1998): 5529-5536.
37. Sage, H.; Tupper, J.; and Bramson, R. Endothelial cell injury in vitro is associated with increased secretion of an Mr 43,000 glycoprotein ligand. J Cell Physiol. 127 (1986): 373-387.
38. Yan, Q.; and Sage, E. H. SPARC, a matricellular glycoprotein with important biological functions. J Histochem Cytochem 47 (1999): 1495-1506.

39. Johnston, I. G.; Paladino, T.; Gurd, J. W.; and Brown, I. R. Molecular cloning of SC1: a putative brain extracellular matrix glycoprotein showing partial similarity to osteonectin/BM40/SPARC. Neuron 4 (1990): 165-176.
40. Girard, J. P.; and Springer, T. A. Cloning from purified high endothelial venule cells of hevin, a close relative of the antiadhesive extracellular matrix protein SPARC. Immunity 2 (1995): 113-123.
41. Guermah, M.; Crisanti, P.; Laugier, D.; Dezelee, P.; Bidou, L.; Pessac, B.; and Calothy, G. Transcription of a quail gene expressed in embryonic retinal cells is shut off sharply at hatching. Proc Natl Acad Sci U S A 88 (1991): 4503-4507.
42. Shibamura, M.; Mashimo, J.; Mita, A.; Kuroki, T.; and Nose, K. Cloning from a mouse osteoblastic cell line of a set of transforming-growth-factor-beta 1-regulated genes, one of which seems to encode a follistatin-related polypeptide. Eur J Biochem 217 (1993): 13-19.
43. Zwijsen, A.; Blockx, H.; Van Arnhem, W.; Willems, J.; Fransen, L.; Devos, K.; Raymackers, J.; Van de Voorde, A.; and Slegers, H. Characterization of a rat C6 glioma-secreted follistatin-related protein (FRP). Cloning and sequence of the human homologue. Eur J Biochem 225 (1994): 937-946.
44. Alliel, P. M.; Perin, J. P.; Jolles, P.; and Bonnet, F. J. Testican, a multidomain testicular proteoglycan resembling modulators of cell social behaviour. Eur J Biochem 214 (1993): 347-350.
45. Girard, J. P.; and Springer, T. A. Modulation of endothelial cell adhesion by hevin, an acidic protein associated with high endothelial venules. J Biol Chem 271 (1996): 4511-4517.
46. Nelson, P. S.; Plymate, S. R.; Wang, K.; True, L. D.; Ware, J. L.; Gan, L.; Liu, A. Y.; and Hood, L. Hevin, an antiadhesive extracellular matrix protein, is

- down-regulated in metastatic prostate adenocarcinoma. Cancer Res 58 (1998): 232-236.
47. Casado, F. J.; Pouponnot, C.; Jeanny, J. C.; Lecoq, O.; Calothy, G.; and Pierani, A. QRI, a retina-specific gene, encodes an extracellular matrix protein exclusively expressed during neural retina differentiation. Mech Dev 54 (1996): 237-250.
48. Maurer, P.; Mayer, U.; Bruch, M.; Jenö, P.; Mann, K.; Landwehr, R.; Engel, J.; and Timpl, R. High-affinity and low-affinity calcium binding and stability of the multidomain extracellular 40-kDa basement membrane glycoprotein (BM-40/SPARC/osteonectin). Eur.J Biochem. 205 (1992): 233-240.
49. Sage, H.; Vernon, R. B.; Funk, S. E.; Everitt, E. A.; and Angello, J. SPARC, a secreted protein associated with cellular proliferation, inhibits cell spreading in vitro and exhibits  $Ca^{2+}$ -dependent binding to the extracellular matrix. J Cell Biol. 109 (1989): 341-356.
50. Mayer, U.; Aumailley, M.; Mann, K.; Timpl, R.; and Engel, J. Calcium-dependent binding of basement membrane protein BM-40 (osteonectin, SPARC) to basement membrane collagen type IV. Eur.J Biochem. 198 (1991): 141-150.
51. Carafoli, E. Intracellular calcium homeostasis. Annu Rev Biochem 56 (1987): 395-433.
52. Pottgiesser, J.; Maurer, P.; Mayer, U.; Nischt, R.; Mann, K.; Timpl, R.; Krieg, T.; and Engel, J. Changes in calcium and collagen IV binding caused by mutations in the EF hand and other domains of extracellular matrix protein BM-40 (SPARC, osteonectin). J Mol.Biol. 238 (1994): 563-574.
53. Brekken, R. A.; and Sage, E. H. SPARC, a matricellular protein: at the crossroads of cell-matrix. Matrix Biol 19 (2000): 569-580.

54. Bradshaw, A. D.; and Sage, E. H. SPARC, a matricellular protein that functions in cellular differentiation and tissue response to injury. J Clin Invest 107 (2001): 1049-1054.
55. Iruela-Arispe, M. L.; Vernon, R. B.; Wu, H.; Jaenisch, R.; and Sage, E. H. Type I collagen-deficient Mov-13 mice do not retain SPARC in the extracellular matrix: implications for fibroblast function. Dev.Dyn. 207 (1996): 171-183.
56. Sasaki, T.; Gohring, W ; Mann, K.; Maurer, P.; Hohenester, E.; Knauper, V.; Murphy, G.; and Timpl, R. Limited cleavage of extracellular matrix protein BM-40 by matrix metalloproteinases increases its affinity for collagens. J Biol.Chem. 272 (1997): 9237-9243.
57. Francki, A.; Bradshaw, A. D.; Bassuk, J. A.; Howe, C. C.; Couser, W. G.; and Sage, E. H. SPARC regulates the expression of collagen type I and transforming growth factor-beta1 in mesangial cells. J Biol Chem 274 (1999): 32145-32152.
58. Tremble, P. M.; Lane, T. F.; Sage, E. H.; and Werb, Z. Sparc, a secreted protein associated with morphogenesis and tissue remodeling, induces expression of metalloproteinases in fibroblasts through a novel extracellular matrix-dependent pathway. J.Cell Biol. 121 (1993): 1433-1444.
59. Shankavaram, U. T.; DeWitt, D. L.; Funk, S. E.; Sage, E. H.; and Wahl, L. M. Regulation of human monocyte matrix metalloproteinases by SPARC. J Cell Physiol. 173 (1997): 327-334.
60. Lane, T. F.; Iruela-Arispe, M. L.; and Sage, E. H. Regulation of gene expression by SPARC during angiogenesis in vitro. Changes in fibronectin, thrombospondin-1, and plasminogen activator inhibitor-1. J Biol.Chem. 267 (1992): 16736-16745.



61. Strandjord, T. P.; Sage, E. H.; and Clark, J. G. SPARC participates in the branching morphogenesis of developing fetal rat lung. Am.J.Respir.Cell Mol.Biol. 13 (1995): 279-287.
62. Fitzgerald, M. C.; and Schwarzbauer, J. E. Importance of the basement membrane protein SPARC for viability and fertility in *Caenorhabditis elegans*. Curr Biol 8 (1998): 1285-1288.
63. Schwarzbauer, J. E.; and Spencer, C. S. The *Caenorhabditis elegans* homologue of the extracellular calcium binding protein SPARC/osteonectin affects nematode body morphology and mobility. Mol Biol Cell 4 (1993): 941-952.
64. Purcell, L.; Gruia-Gray, J.; Scanga, S.; and Ringuette, M. Developmental anomalies of *Xenopus* embryos following microinjection of SPARC antibodies. J Exp Zool 265 (1993): 153-164.
65. Damjanovski, S.; Karp, X.; Funk, S.; Sage, E. H.; and Ringuette, M. J. Ectopic expression of SPARC in *Xenopus* embryos interferes with tissue morphogenesis: identification of a bioactive sequence in the C-terminal EF hand. J Histochem Cytochem 45 (1997): 643-655.
66. Gilmour, D. T.; Lyon, G. J.; Carlton, M. B.; Sanes, J. R.; Cunningham, J. M.; Anderson, J. R.; Hogan, B. L.; Evans, M. J.; and Colledge, W. H. Mice deficient for the secreted glycoprotein SPARC/osteonectin/BM40 develop normally but show severe age-onset cataract formation and disruption of the lens. EMBO J 17 (1998): 1860-1870.
67. Norose, K.; Lo, W. K.; Clark, J. I.; Sage, E. H.; and Howe, C. C. Lenses of SPARC-null mice exhibit an abnormal cell surface-basement membrane interface. Exp Eye Res 71 (2000): 295-307.

68. Delany, A. M.; Amling, M.; Priemel, M.; Howe, C.; Baron, R.; and Canalis, E. Osteopenia and decreased bone formation in osteonectin-deficient mice. J Clin Invest 105 (2000): 915-923.
69. Romberg, R. W.; Werness, P. G.; Lollar, P.; Riggs, B. L.; and Mann, K. G. Isolation and characterization of native adult osteonectin. J Biol.Chem. 260 (1985): 2728-2736.
70. Sage, E. H.; and Bornstein, P. Extracellular proteins that modulate cell-matrix interactions. SPARC, tenascin, and thrombospondin. J Biol.Chem. 266 (1991): 14831-14834.
71. Lane, T. F.; and Sage, E. H. Functional mapping of SPARC: peptides from two distinct  $Ca^{2+}$ -binding sites modulate cell shape. J Cell Biol. 111 (1990): 3065-3076.
72. Nischt, R.; Pottgiesser, J.; Krieg, T.; Mayer, U.; Aumailley, M.; and Timpl, R. Recombinant expression and properties of the human calcium-binding extracellular matrix protein BM-40. Eur J Biochem 200 (1991): 529-536.
73. Jacob, K.; Webber, M.; Benayahu, D.; and Kleinman, H. K. Osteonectin promotes prostate cancer cell migration and invasion: a possible mechanism for metastasis to bone. Cancer Res 59 (1999): 4453-4457.
74. Funk, S. E.; and Sage, E. H. The  $Ca^{2+}$ -binding glycoprotein SPARC modulates cell cycle progression in bovine aortic endothelial cells. Proc Natl Acad Sci U S A. 88 (1991): 2648-2652.
75. Mok, S. C.; Chan, W. Y.; Wong, K. K.; Muto, M. G.; and Berkowitz, R. S. SPARC, an extracellular matrix protein with tumor-suppressing activity in human ovarian epithelial cells. Oncogene 12 (1996): 1895-1901.

76. Bradshaw, A. D.; Francki, A.; Motamed, K.; Howe, C.; and Sage, E. H. Primary mesenchymal cells isolated from SPARC-null mice exhibit altered morphology and rates of proliferation. Mol Biol Cell 10 (1999): 1569-1579.
77. Kupprion, C.; Motamed, K.; and Sage, E. H. SPARC (BM-40, osteonectin) inhibits the mitogenic effect of vascular endothelial growth factor on microvascular endothelial cells. J Biol. Chem 273 (1998): 29635-29640.
78. Raines, E. W.; Lane, T. F.; Iruela-Arispe, M. L.; Ross, R.; and Sage, E. H. The extracellular glycoprotein SPARC interacts with platelet-derived growth factor (PDGF)-AB and -BB and inhibits the binding of PDGF to its receptors. Proc.Natl.Acad.Sci.U.S.A. 89 (1992): 1281-1285.
79. Hasselaar, P.; and Sage, E. H. SPARC antagonizes the effect of basic fibroblast growth factor on the migration of bovine aortic endothelial cells. J Cell Biochem. 49 (1992): 272-283.
80. Funk, S. E.; and Sage, E. H. Differential effects of SPARC and cationic SPARC peptides on DNA synthesis by endothelial cells and fibroblasts. J Cell Physiol 154 (1993): 53-63.
81. Rempel, S. A.; Ge, S.; and Gutierrez, J. A. SPARC: a potential diagnostic marker of invasive meningiomas. Clin Cancer Res 5 (1999): 237-241.
82. Rempel, S. A.; Golembieski, W. A.; Ge, S.; Lemke, N.; Elisevich, K.; Mikkelsen, T.; and Gutierrez, J. A. SPARC: a signal of astrocytic neoplastic transformation and reactive response in human primary and xenograft gliomas. J Neuropathol Exp Neurol 57 (1998): 1112-1121.
83. Graham, J. D.; Balleine, R. L.; Milliken, J. S.; Bilous, A. M.; and Clarke, C. L. Expression of osteonectin mRNA in human breast tumours is inversely correlated with oestrogen receptor content. Eur.J Cancer 33 (1997): 1654-1660.

84. Golembieski, W. A.; Ge, S.; Nelson, K.; Mikkelsen, T.; and Rempel, S. A. Increased SPARC expression promotes U87 glioblastoma invasion in vitro. Int J Dev Neurosci 17 (1999): 463-472.
85. Sage, E. H. Terms of attachment: SPARC and tumorigenesis. Nat Med 3 (1997): 144-146.
86. Kato, Y., *et al.* Stimulation of motility of human renal cell carcinoma by SPARC/Osteonectin/BM-40 associated with type IV collagen. Invasion Metastasis 18 (1998): 105-114.
87. Vial, E.; and Castellazzi, M. Down-regulation of the extracellular matrix protein SPARC in vSrc- and vJun-transformed chick embryo fibroblasts contributes to tumor formation in vivo. Oncogene 19 (2000): 1772-1782.
88. Sternlicht, M. D.; and Bergers, G. Matrix metalloproteinases as emerging targets in anticancer therapy: status and prospects. Emerging Therapeutic Targets 4 (2000): 609 - 633.
89. Velasco, G.; Cal, S.; Merlos-Suarez, A.; Ferrando, A. A.; Alvarez, S.; Nakano, A.; Arribas, J.; and Lopez-Otin, C. Human MT6-matrix metalloproteinase: identification, progelatinase A activation, and expression in brain tumors. Cancer Res 60 (2000): 877-882.
90. Sato, H.; Takino, T.; Okada, Y.; Cao, J.; Shinagawa, A.; Yamamoto, E.; and Seiki, M. A matrix metalloproteinase expressed on the surface of invasive tumour cells. Nature 370 (1994): 61-65.
91. Takino, T.; Sato, H.; Shinagawa, A.; and Seiki, M. Identification of the second membrane-type matrix metalloproteinase (MT-MMP-2) gene from a human placenta cDNA library. MT-MMPs form a unique membrane-type subclass in the MMP family. J Biol. Chem 270 (1995): 23013-23020.

92. Will, H.; and Hinzmann, B. cDNA sequence and mRNA tissue distribution of a novel human matrix metalloproteinase with a potential transmembrane segment. Eur J Biochem 231 (1995): 602-608.
93. Puente, X. S.; Pendas, A. M.; Llano, E.; Velasco, G.; and Lopez-Otin, C. Molecular cloning of a novel membrane-type matrix metalloproteinase from a human breast carcinoma. Cancer Res 56 (1996): 944-949.
94. Pei, D. Identification and characterization of the fifth membrane-type matrix metalloproteinase MT5-MMP. J Biol. Chem 274 (1999): 8925-8932.
95. Belaaouaj, A.; Shipley, J. M.; Kobayashi, D. K.; Zimonjic, D. B.; Popescu, N.; Silverman, G. A.; and Shapiro, S. D. Human macrophage metalloelastase. Genomic organization, chromosomal location, gene linkage, and tissue-specific expression. J Biol Chem 270 (1995): 14568-14575.
96. Murphy, G.; Segain, J. P.; O'Shea, M.; Cockett, M.; Ioannou, C.; Lefebvre, O.; Chambon, P.; and Basset, P. The 28-kDa N-terminal domain of mouse stromelysin-3 has the general properties of a weak metalloproteinase. J Biol. Chem 268 (1993): 15435-15441.
97. Overall, C. M., *et al.* Identification of the TIMP-2 binding site on the gelatinase A hemopexin C-domain by site-directed mutagenesis and the yeast two-hybrid system. Ann N Y Acad Sci 878 (1999): 747-753.
98. Murphy, G.; Willenbrock, F.; Ward, R. V.; Cockett, M. I.; Eaton, D.; and Docherty, A. J. The C-terminal domain of 72 kDa gelatinase A is not required for catalysis, but is essential for membrane activation and modulates interactions with tissue inhibitors of metalloproteinases [published erratum appears in Biochem J 1992 Jun 15;284(Pt 3):935]. Biochem J 283 (1992): 637-641.

99. Strongin, A. Y.; Collier, I.; Bannikov, G.; Marmar, B. L.; Grant, G. A.; and Goldberg, G. I. Mechanism of cell surface activation of 72-kda type IV collagenase. Isolation of the activated form of the membrane metalloprotease. J Biol.Chem 270 (1995): 5331-5338.
100. Benaud, C.; Dickson, R. B.; and Thompson, E. W. Roles of the matrix metalloproteinases in mammary gland development and cancer. Breast Cancer Res. Treat. 50 (1998): 97-116.
101. Polette, M.; and Birembaut, P. Matrix metalloproteinases in breast cancer. The Breast J. 2 (1996): 209-220.
102. Werb, Z.; Tremble, P. M.; Behrendtsen, O.; Crowley, E.; and Damsky, C. H. Signal transduction through the fibronectin receptor induces collagenase and stromelysin gene expression. J Cell Biol 109 (1989): 877-889.
103. Van Wart, H. E.; and Birkedal-Hansen, H. The cysteine switch: a principle of regulation of metalloproteinase activity with potential applicability to the entire matrix metalloproteinase gene family. Proc Natl Acad Sci U S A 87 (1990): 5578-5582.
104. Woessner, J. F., Jr. Matrix metalloproteinases and their inhibitors in connective tissue remodeling. FASEB J 5 (1991): 2145-2154.
105. Birkedal-Hansen, H.; Moore, W. G.; Bodden, M. K.; Windsor, L. J.; Birkedal-Hansen, B.; De Carlo, A.; and Engler, J. A. Matrix metalloproteinases: A review. Crit.Rev.Oral Biol.Med. 4 (1993): 197-250.
106. Chambers, A. F.; and Matrisian, L. M. Changing views of the role of matrix metalloproteinases in metastasis. J Natl.Cancer Inst. 89 (1997): 1260-1270.

107. Deryugina, E. I.; Luo, G. X.; Reisfeld, R. A.; Bourdon, M. A.; and Strongin, A. Tumor cell invasion through matrigel is regulated by activated matrix metalloproteinase-2. Anticancer Res 17 (1997): 3201-3210.
108. Atkinson, S. J.; Ward, R. V.; Reynolds, J. J.; and Murphy, G. Cell-mediated degradation of type IV collagen and gelatin films is dependent on the activation of matrix metalloproteinases. Biochem.J 288 (1992): 605-611.
109. Sasaguri, Y.; Komiya, S.; Sugama, K.; Suzuki, K.; Inoue, A.; Morimatsu, M.; and Nagase, H. Production of matrix metalloproteinases 2 and 3 (stromelysin) by stromal cells of giant cell tumor of bone. Am J Pathol 141 (1992): 611-621.
110. MacDougall, J. R.; and Matrisian, L. M. Contributions of tumor and stromal matrix metalloproteinases to tumor progression, invasion and metastasis. Cancer Metastasis Rev 14 (1995): 351-362.
111. Poulson, R.; Pignatelli, M.; Stetler-Stevenson, W. G.; Liotta, L. A.; Wright, P. A.; Jeffery, R. E.; Longcroft, J. M.; Rogers, L.; and Stamp, G. W. Stromal expression of 72 kda type IV collagenase (MMP-2) and TIMP-2 mRNAs in colorectal neoplasia. Am.J Pathol. 141 (1992): 389-396.
112. Pyke, C.; Ralfkiaer, E.; Huhtala, P.; Hurskainen, T.; Dano, K.; and Tryggvason, K. Localization of messenger RNA for mw 72,000 and 92,000 type IV collagenases in human skin cancers by in situ hybridization. Cancer Res. 52 (1992): 1336-1341.
113. Koshiba, T.; Hosotani, R.; Wada, M.; Miyamoto, Y.; Fujimoto, K.; Lee, J. U.; Doi, R.; Arii, S.; and Imamura, M. Involvement of matrix metalloproteinase-2 activity in invasion and metastasis of pancreatic carcinoma. Cancer 82 (1998): 642-650.

114. Pacheco, M. M.; Mourao, M.; Mantovani, E. B.; Nishimoto, I. N.; and Brentani, M. M. Expression of gelatinases A and B, stromelysin-3 and matrilysin genes in breast carcinomas: clinico-pathological correlations. Clin Exp Metastasis 16 (1998): 577-585.
115. Nomura, H.; Fujimoto, N.; Seiki, M.; Mai, M.; and Okada, Y. Enhanced production of matrix metalloproteinases and activation of matrix metalloproteinase 2 (gelatinase A) in human gastric carcinomas. Int J Cancer 69 (1996): 9-16.
116. Tokuraku, M.; Sato, H.; Murakami, S.; Okada, Y.; Watanabe, Y.; and Seiki, M. Activation of the precursor of gelatinase A/72 kDa type IV collagenase/MMP-2 in lung carcinomas correlates with the expression of membrane-type matrix metalloproteinase (MT-MMP) and with lymph node metastasis. Int J Cancer 64 (1995): 355-359.
117. Davies, B.; Miles, D. W.; Happerfield, L. C.; Naylor, M. S.; Bobrow, L. G.; Rubens, R. D.; and Balkwill, F. R. Activity of type IV collagenases in benign and malignant breast disease. Br J Cancer 67 (1993): 1126-1131.
118. Ueno, H.; Nakamura, H.; Inoue, M.; Imai, K.; Noguchi, M.; Sato, H.; Seiki, M.; and Okada, Y. Expression and tissue localization of membrane-types 1, 2, and 3 matrix metalloproteinases in human invasive breast carcinomas. Cancer Res 57 (1997): 2055-2060.
119. Nakamura, H., *et al.* Enhanced production and activation of progelatinase A mediated by membrane-type 1 matrix metalloproteinase in human papillary thyroid carcinomas. Cancer Res 59 (1999): 467-473.
120. Ikebe, T.; Shinohara, M.; Takeuchi, H.; Beppu, M.; Kurahara, S.; Nakamura, S.; and Shirasuna, K. Gelatinolytic activity of matrix metalloproteinase in tumor



- tissues correlates with the invasiveness of oral cancer. Clin Exp Metastasis 17 (1999): 315-323.
121. Itoh, T.; Tanioka, M.; Yoshida, H.; Yoshioka, T.; Nishimoto, H.; and Itoharu, S. Reduced angiogenesis and tumor progression in gelatinase A-deficient mice. Cancer Res 58 (1998): 1048-1051.
122. Okada, Y.; Morodomi, T.; Enghild, J. J.; Suzuki, K.; Yasui, A.; Nakanishi, I.; Salvesen, G.; and Nagase, H. Matrix metalloproteinase 2 from human rheumatoid synovial fibroblasts. Purification and activation of the precursor and enzymic properties. Eur J Biochem 194 (1990): 721-730.
123. Butler, G. S., *et al.* The TIMP2 membrane type 1 metalloproteinase "receptor" regulates the concentration and efficient activation of progelatinase A. A kinetic study. J Biol.Chem. 273 (1998): 871-880.
124. Atkinson, S. J.; Crabbe, T.; Cowell, S.; Ward, R. V.; Butler, M. J.; Sato, H.; Seiki, M.; Reynolds, J. J.; and Murphy, G. Intermolecular autolytic cleavage can contribute to the activation of progelatinase A by cell membranes. J Biol.Chem. 270 (1995): 30479-30485.
125. Deryugina, E. I.; Ratnikov, B.; Monosov, E.; Postnova, T. I.; DiScipio, R.; Smith, J. W.; and Strongin, A. Y. MT1-MMP initiates activation of pro-MMP-2 and integrin  $\alpha$ v $\beta$ 3 promotes maturation of MMP-2 in breast carcinoma cells. Exp Cell Res 263 (2001): 209-223.
126. Yu, M.; Sato, H.; Seiki, M.; and Thompson, E. W. Complex regulation of membrane-type matrix metalloproteinase expression and matrix metalloproteinase-2 activation by concanavalin A in MDA-MB-231 human breast cancer cells. Cancer Res. 55 (1995): 3272-3277.

127. Brown, P. D.; Levy, A. T.; Margulies, I. M.; Liotta, L. A.; and Stetler-Stevenson, W. G. Independent expression and cellular processing of Mr 72,000 type IV collagenase and interstitial collagenase in human tumorigenic cell lines. Cancer Res 50 (1990): 6184-6191.
128. Brown, P. D.; Kleiner, D. E.; Unsworth, E. J.; and Stetler-Stevenson, W. G. Cellular activation of the 72 kDa type IV procollagenase/TIMP-2 complex. Kidney Int 43 (1993): 163-170.
129. Strongin, A. Y.; Marmor, B. L.; Grant, G. A.; and Goldberg, G. I. Plasma membrane-dependent activation of the 72-kDa type IV collagenase is prevented by complex formation with TIMP-2. J Biol Chem 268 (1993): 14033-14039.
130. Maiti, S. N.; Yu, M.; Bueno, J.; Tirgari, R. H.; Palao-Marco, F. L.; Pulyaeva, H.; and Thompson, E. W. Differential regulation of matrix metalloproteinase-2 activation in human breast cancer cell lines. Ann.N.Y.Acad.Sci. 732 (1994): 456-458.
131. Ailenberg, M.; and Silverman, M. Cellular activation of mesangial gelatinase A by cytochalasin D is accompanied by enhanced mRNA expression of both gelatinase A and its membrane-associated gelatinase A activator (MT-MMP). Biochem J 313 (1996): 879-884.
132. Azzam, H. S.; and Thompson, E. W. Collagen-induced activation of the Mr 72,000 type IV collagenase in normal and malignant human fibroblastoid cells. Cancer Res. 52 (1992): 4540-4544.
133. Azzam, H. S.; Arand, G.; Lippman, M. E.; and Thompson, E. W. Association of MMP-2 activation potential with metastatic progression in human breast cancer cell lines independent of MMP- 2 production. J.Natl.Cancer Inst. 85 (1993): 1758-1764.

134. Thompson, E. W., *et al.* Collagen induced MMP-2 activation in human breast cancer. Breast Cancer Res.Treat. 31 (1994): 357-370.
135. Gilles, C.; Polette, M.; Seiki, M.; Birembaut, P.; and Thompson, E. W. Implication of collagen type I-induced membrane-type 1-matrix metalloproteinase expression and matrix metalloproteinase-2 activation in the metastatic progression of breast carcinoma. Lab.Invest. 76 (1997): 651-660.
136. Ruangpanit, N.; Chan, D.; Holmbeck, K.; Birkedal-Hansen, H.; Polarek, J.; Yang, C.; Bateman, J. F.; and Thompson, E. W. Gelatinase A (MMP-2) activation by skin fibroblasts: dependence on MT1-MMP expression and fibrillar collagen form. Matrix Biol 20 (2001): 193-203.
137. Haas, T. L.; Davis, S. J.; and Madri, J. A. Three-dimensional type I collagen lattices induce coordinate expression of matrix metalloproteinases MT1-MMP and MMP-2 in microvascular endothelial cells. J Biol. Chem 273 (1998): 3604-3610.
138. Haas, T. L.; Stitelman, D.; Davis, S. J.; Apte, S. S.; and Madri, J. A. Egr-1 mediates extracellular matrix-driven transcription of membrane type 1 matrix metalloproteinase in endothelium. J Biol. Chem 274 (1999): 22679-22685.
139. Kurschat, P.; Zigrino, P.; Nischt, R.; Breitkopf, K.; Steurer, P.; Klein, C. E.; Krieg, T.; and Mauch, C. Tissue inhibitor of matrix metalloproteinase-2 regulates matrix metalloproteinase-2 activation by modulation of membrane-type 1 matrix metalloproteinase activity in high and low invasive melanoma cell lines. J Biol. Chem 274 (1999): 21056-21062.
140. Stetler-Stevenson, W. G.; Brown, P. D.; Onisto, M.; Levy, A. T.; and Liotta, L. A. Tissue inhibitor of metalloproteinases-2 (TIMP-2) mRNA expression in

- tumor cell lines and human tumor tissues. J Biol. Chem 265 (1990): 13933-13938.
141. Miyake, H.; Hara, I.; Gohji, K.; Yamanaka, K.; Hara, S.; Arakawa, S.; Nakajima, M.; and Kamidono, S. Relative expression of matrix metalloproteinase-2 and tissue inhibitor of metalloproteinase-2 in mouse renal cell carcinoma cells regulates their metastatic potential. Clin Cancer Res 5 (1999): 2824-2829.
142. Remacle, A.; McCarthy, K.; Noel, A.; Maguire, T.; McDermott, E.; O'Higgins, N.; Foidart, J. M.; and Duffy, M. J. High levels of TIMP-2 correlate with adverse prognosis in breast cancer. Int J Cancer 89 (2000): 118-121.
143. Caterina, J. J.; Yamada, S.; Caterina, N. C.; Longenecker, G.; Holmback, K.; Shi, J.; Yermovsky, A. E.; Engler, J. A.; and Birkedal-Hansen, H. Inactivating mutation of the mouse tissue inhibitor of metalloproteinases-2(Timp-2) gene alters proMMP-2 activation. J Biol. Chem 275 (2000): 26416-26422.
144. Wang, Z.; Juttermann, R.; and Soloway, P. D. TIMP-2 is required for efficient activation of proMMP-2 in vivo. J Biol. Chem 275 (2000): 26411-26415.
145. Itoh, Y.; Kajita, M.; Kinoh, H.; Mori, H.; Okada, A.; and Seiki, M. Membrane type 4 matrix metalloproteinase (MT4-MMP, MMP-17) is a glycosylphosphatidylinositol-anchored proteinase. J Biol. Chem 274 (1999): 34260-34266.
146. Basset, P., *et al.* A novel metalloproteinase gene specifically expressed in stromal cells of breast carcinomas. Nature 348 (1990): 699-704.
147. Sato, H.; Kinoshita, T.; Takino, T.; Nakayama, K.; and Seiki, M. Activation of a recombinant membrane type 1-matrix metalloproteinase (MT1-MMP) by furin

- and its interaction with tissue inhibitor of metalloproteinases (TIMP)-2. FEBS Lett 393 (1996): 101-104.
148. Okumura, Y.; Sato, H.; Seiki, M.; and Kido, H. Proteolytic activation of the precursor of membrane type 1 matrix metalloproteinase by human plasmin. A possible cell surface activator. FEBS Lett 402 (1997): 181-184.
149. Cao, J.; Hymowitz, M.; Conner, C.; Bahou, W. F.; and Zucker, S. The propeptide domain of membrane type 1-matrix metalloproteinase acts as an intramolecular chaperone when expressed in trans with the mature sequence in COS-1 cells. J Biol. Chem 275 (2000): 29648-29653.
150. Cao, J.; Rehemtulla, A.; Bahou, W.; and Zucker, S. Membrane type matrix metalloproteinase 1 activates pro-gelatinase A without furin cleavage of the N-terminal domain. J Biol. Chem 271 (1996): 30174-30180.
151. Pei, D.; and Weiss, S. J. Transmembrane-deletion mutants of the membrane-type matrix metalloproteinase-1 process progelatinase A and express intrinsic matrix-degrading activity. J Biol. Chem 271 (1996): 9135-9140.
152. Maquoi, E.; Noel, A.; Frankenre, F.; Angliker, H.; Murphy, G.; and Foidart, J. M. Inhibition of matrix metalloproteinase 2 maturation and HT1080 invasiveness by a synthetic furin inhibitor. FEBS Lett 424 (1998): 262-266.
153. Cao, J.; Drews, M.; Lee, H. M.; Conner, C.; Bahou, W. F.; and Zucker, S. The propeptide domain of membrane type 1 matrix metalloproteinase is required for binding of tissue inhibitor of metalloproteinases and for activation of pro-gelatinase A. J Biol. Chem 273 (1998): 34745-34752.
154. Cao, J.; Sato, H.; Takino, T.; and Seiki, M. The C-terminal region of membrane type matrix metalloproteinase is a functional transmembrane domain required for pro-gelatinase A activation. J Biol. Chem 270 (1995): 801-805.

155. Nomura, H.; Sato, H.; Seiki, M.; Mai, M.; and Okada, Y. Expression of membrane-type matrix metalloproteinase in human gastric carcinomas. Cancer Res. 55 (1995): 3263-3266.
156. Okada, A.; Bellocq, J. P.; Rouyer, N.; Chenard, M. P.; Rio, M. C.; Chambon, P.; and Basset, P. Membrane-type matrix metalloproteinase (MT-MMP) gene is expressed in stromal cells of human colon, breast, and head and neck carcinomas. Proc.Natl.Acad.Sci.U.S.A. 92 (1995): 2730-2734.
157. Hofmann, U. B.; Westphal, J. R.; Zendman, A. J.; Becker, J. C.; Ruiter, D. J.; and van Muijen, G. N. Expression and activation of matrix metalloproteinase-2 (MMP-2) and its co-localization with membrane-type 1 matrix metalloproteinase (MT1-MMP) correlate with melanoma progression. J Pathol 191 (2000): 245-256.
158. Pulyaeva, H.; Washington, D.; Bueno, J.; Sato, H.; Seiki, M.; Azumi, N.; and Thompson, E. W. MT1-MMP correlates with MMP-2 activation potential seen after epithelial to mesenchymal transition in human breast carcinoma cells. Clin.Exp.Metastasis 15 (1997): 111-120.
159. Pei, D.; and Weiss, S. J. Transmembrane-deletion mutants of the membrane-type matrix metalloproteinase-1 process progelatinase A and express intrinsic matrix-degrading activity. J Biol. Chem 271 (1996): 9135-9140.
160. Ohuchi, E.; Imai, K.; Fujii, Y.; Sato, H.; Seiki, M.; and Okada, Y. Membrane type 1 matrix metalloproteinase digests interstitial collagens and other extracellular matrix macromolecules. J Biol. Chem 272 (1997): 2446-2451.
161. Fidler, I. J.; and Hart, I. R. Biological diversity in metastatic neoplasms: origins and implications. Science 217 (1982): 998-1003.

162. Stetler-Stevenson, W. G.; Liotta, L. A.; and Kleiner, D. E., Jr. Extracellular matrix 6: role of matrix metalloproteinases in tumor invasion and metastasis. FASEB J 7 (1993): 1434-1441.
163. Sung, V.; Cattell, D. A.; Bueno, J. M.; Murray, A.; Zwiebel, J. A.; Aaron, A. D.; and Thompson, E. W. Human breast cancer cell metastasis to long bone and soft organs of nude mice: a quantitative assay. Clin Exp Metastasis 15 (1997): 173-183.
164. Thompson, E. W.; Martin, M. B.; Saceda, M.; Clarke, R.; Brunner, N.; Lippman, M. E.; and Dickson, R. B. Regulation of breast cancer cells by hormones and growth factors: effects on proliferation and basement membrane invasiveness. Horm Res 32 (1989): 242-249.
165. Leonessa, F.; Boulay, V.; Wright, A.; Thompson, E. W.; Brunner, N.; and Clarke, R. The biology of breast tumor progression. Acquisition of hormone independence and resistance to cytotoxic drugs. Acta Oncol 31 (1992): 115-123.
166. Raymond, W. A.; and Leong, A. S. Vimentin--a new prognostic parameter in breast carcinoma? J Pathol 158 (1989): 107-114.
167. Cattoretti, G.; Andreola, S.; Clemente, C.; D'Amato, L.; and Rilke, F. Vimentin and p53 expression on epidermal growth factor receptor-positive, oestrogen receptor-negative breast carcinomas. Br J Cancer 57 (1988): 353-357.
168. Raymond, W. A.; and Leong, A. S. Co-expression of cytokeratin and vimentin intermediate filament proteins in benign and neoplastic breast epithelium. J Pathol 157 (1989): 299-306.
169. Thompson, E. W., *et al.* Association of increased basement membrane invasiveness with absence of estrogen receptor and expression of vimentin in human breast cancer cell lines. J Cell Physiol 150 (1992): 534-544.

170. Cailleau, R.; Young, R.; Olive, M.; and Reeves, W. J., Jr. Breast tumor cell lines from pleural effusions. J Natl Cancer Inst 53 (1974): 661-674.
171. Price, J. E.; Polyzos, A.; Zhang, R. D.; and Daniels, L. M. Tumorigenicity and metastasis of human breast carcinoma cell lines in nude mice. Cancer Res 50 (1990): 717-721.
172. Brunner, N.; Thompson, E. W.; Spang-Thomsen, M.; Rygaard, J.; Dano, K.; and Zwiebel, J.A. LacZ transduced human breast cancer xenografts as an in vivo model for the study of invasion and metastasis. Eur.J.Cancer 28A (1992): 1989-1995.
173. Nangia-Makker, P.; Thompson, E. W.; Hogan, C.; Ochieng, J.; and Raz, A. Induction of tumorigenicity by galectin-3 in a non-tumorigenic human breast carcinoma cell line. Int.J.Oncology 7 (1995): 1079-1087.
174. Kleinman, H. K.; McGarvey, M. L.; Hassell, J. R.; Star, V. L.; Cannon, F. B.; Laurie, G. W.; and Martin, G. R. Basement membrane complexes with biological activity. Biochemistry 25 (1986): 312-318.
175. Albini, A.; Iwamoto, Y.; Kleinman, H. K.; Martin, G. R.; Aaronson, S. A.; Kozlowski, J. M.; and McEwan, R. N. A rapid in vitro assay for quantitating the invasive potential of tumor cells. Cancer Res 47 (1987): 3239-3245.
176. Kramer, R. H.; Bensch, K. G.; and Wong, J. Invasion of reconstituted basement membrane matrix by metastatic human tumor cells. Cancer Res 46 (1986): 1980-1989.
177. Bae, S. N.; Arand, G.; Azzam, H.; Pavasant, P.; Torri, J.; Frandsen, T. L.; and Thompson, E. W. Molecular and cellular analysis of basement membrane invasion by human breast cancer cells in matrigel-based in vitro assays. Breast Cancer Res.Treat. 24 (1993): 241-255.



178. Terranova, V. P.; Hujanen, E. S.; and Martin, G. R. Basement membrane and the invasive activity of metastatic tumor cells. J Natl Cancer Inst 77 (1986): 311-316.
179. Poulson, R.; Hanby, A. M.; Pignatelli, M.; Jeffery, R. E.; Longcroft, J. M.; Rogers, L.; and Stamp, G. W. Expression of gelatinase a and timp-2 mrnas in desmoplastic fibroblasts in both mammary carcinomas and basal cell carcinomas of the skin. J.Clin.Pathol. 46 (1993): 429-436.
180. Polette, M.; Gilbert, N.; Stas, I.; Nawrocki, B.; Noel, A.; Remacle, A.; Stetler-Stevenson, W. G.; Birembaut, P.; and Foidart, M. Gelatinase A expression and localization in human breast cancers. An in situ hybridization study and immunohistochemical detection using confocal microscopy. Virchows Arch 424 (1994): 641-645.
181. Polette, M.; Clavel, C.; Cockett, M.; Girod de Bentzmann, S.; Murphy, G.; and Birembaut, P. Detection and localization of mRNAs encoding matrix metalloproteinases and their tissue inhibitor in human breast pathology. Invasion Metastasis 13 (1993): 31-37.
182. Iwata, H.; Kobayashi, S.; Iwase, H.; Masaoka, A.; Fujimoto, N.; and Okada, Y. Production of matrix metalloproteinases and tissue inhibitors of metalloproteinases in human breast carcinomas. Jpn J Cancer Res 87 (1996): 602-611.
183. Soini, Y.; Paakko, P.; and Autio-Harmanen, H. Genes of laminin B1 chain, alpha 1 (IV) chain of type IV collagen, and 72-kd type IV collagenase are mainly expressed by the stromal cells of lung carcinomas. Am J Pathol 142 (1993): 1622-1630.

184. Soini, Y.; Hurskainen, T.; Hoyhtya, M.; Oikarinen, A.; and Autio-Harmainen, H. 72 KD and 92 KD type IV collagenase, type IV collagen, and laminin mRNAs in breast cancer: a study by in situ hybridization. J Histochem Cytochem 42 (1994): 945-951.
185. Shimada, T.; Nakamura, H.; Yamashita, K.; Kawata, R.; Murakami, Y.; Fujimoto, N.; Sato, H.; Seiki, M.; and Okada, Y. Enhanced production and activation of progelatinase A mediated by membrane-type 1 matrix metalloproteinase in human oral squamous cell carcinomas: implications for lymph node metastasis. Clin Exp Metastasis 18 (2000): 179-188.
186. Davies, B., *et al.* Levels of matrix metalloproteases in bladder cancer correlate with tumor grade and invasion. Cancer Res 53 (1993): 5365-5369.
187. Gomez, D. E.; Alonso, D. F.; Yoshiji, H.; and Thorgeirsson, U. P. Tissue inhibitors of metalloproteinases: structure, regulation and biological functions. Eur J Cell Biol 74 (1997): 111-122.
188. Sato, H.; and Seiki, M. Membrane-type matrix metalloproteinases (MT-MMPs) in tumor metastasis. J Biochem (Tokyo) 119 (1996): 209-215.
189. Liotta, L. A.; Steeg, P. S.; and Stetler-Stevenson, W. G. Cancer metastasis and angiogenesis: An imbalance of positive and negative regulation. Cell 64 (1991): 327-336.
190. Stanton, H.; Gavrilovic, J.; Atkinson, S. J.; d'Ortho, M. P.; Yamada, K. M.; Zardi, L.; and Murphy, G. The activation of ProMMP-2 (gelatinase A) by HT1080 fibrosarcoma cells is promoted by culture on a fibronectin substrate and is concomitant with an increase in processing of MT1-MMP (MMP-14) to a 45 kDa form. J Cell Sci 111 (1998): 2789-2798.

191. Bassuk, J. A.; Baneyx, F.; Vernon, R. B.; Funk, S. E.; and Sage, E. H. Expression of biologically active human sparc in *escherichia coli*. Arch.Biochem.Biophys. 325 (1996): 8-19.
192. Fridman, R., *et al.* Expression of human recombinant 72 kDa gelatinase and tissue inhibitor of metalloproteinase-2 (TIMP-2): characterization of complex and free enzyme. Biochem J 289 (1993): 411-416.
193. Overall, C. M.; Tam, E.; McQuibban, G. A.; Morrison, C.; Wallon, U. M.; Bigg, H. F.; King, A. E.; and Roberts, C. R. Domain interactions in the gelatinase A.TIMP-2.MT1-MMP activation complex. The ectodomain of the 44-kDa form of membrane type-1 matrix metalloproteinase does not modulate gelatinase A activation. J Biol. Chem 275 (2000): 39497-39506.
194. Maurer, P.; Gohring, W.; Sasaki, T.; Mann, K.; Timpl, R.; and Nischt, R. Recombinant and tissue-derived mouse BM-40 bind to several collagen types and have increased affinities after proteolytic activation. Cell Mol.Life Sci. 53 (1997): 478-484.
195. Itoh, Y.; Ito, A.; Iwata, K.; Tanzawa, K.; Mori, Y.; and Nagase, H. Plasma membrane-bound tissue inhibitor of metalloproteinases (TIMP)-2 specifically inhibits matrix metalloproteinase 2 (gelatinase A) activated on the cell surface. J Biol. Chem 273 (1998): 24360-24367.
196. Wang, T.; and Brown, M. J. mRNA quantification by real time TaqMan polymerase chain reaction: validation and comparison with RNase protection. Anal Biochem 269 (1999): 198-201.
197. Lockey, C.; Otto, E.; and Long, Z. Real-time fluorescence detection of a single DNA molecule. Biotechniques 24 (1998): 744-746.

198. Zucker, S.; Drews, M.; Conner, C.; Foda, H. D.; DeClerck, Y. A.; Langley, K. E.; Bahou, W. F.; Docherty, A. J.; and Cao, J. Tissue inhibitor of metalloproteinase-2 (TIMP-2) binds to the catalytic domain of the cell surface receptor, membrane type 1-matrix metalloproteinase 1 (MT1-MMP). J Biol. Chem 273 (1998): 1216-1222.
199. Maquoi, E.; Frankenre, F.; Baramova, E.; Munaut, C.; Sounni, N. E.; Remacle, A.; Noel, A.; Murphy, G.; and Foidart, J. M. Membrane type 1 matrix metalloproteinase-associated degradation of tissue inhibitor of metalloproteinase 2 in human tumor cell lines. J Biol. Chem 275 (2000): 11368-11378.
200. Reed, M. J.; Puolakkainen, P.; Lane, T. F.; Dickerson, D.; Bornstein, P.; and Sage, E. H. Differential expression of SPARC and thrombospondin 1 in wound repair: immunolocalization and in situ hybridization. J Histochem Cytochem 41 (1993): 1467-1477.
201. Cho, W. J.; Kim, E. J.; Lee, S. J.; Kim, H. D.; Shin, H. J.; and Lim, W. K. Involvement of SPARC in in vitro differentiation of skeletal myoblasts. Biochem Biophys Res Commun 271 (2000): 630-634.
202. Gilles, C.; and Thompson, E. W. The epithelial to mesenchymal transition and metastatic progression in carcinoma. The Breast J. 2 (1996): 83-96.
203. Gossen, M.; Freundlieb, S.; Bender, G.; Muller, G.; Hillen, W.; and Bujard, H. Transcriptional activation by tetracyclines in mammalian cells. Science 268 (1995): 1766-1769.
204. Resnitzky, D.; Gossen, M.; Bujard, H.; and Reed, S. I. Acceleration of the G1/S phase transition by expression of cyclins D1 and E with an inducible system. Mol Cell Biol 14 (1994): 1669-1679.

205. Miller, D. L.; el-Ashry, D.; Cheville, A. L.; Liu, Y.; McLeskey, S. W.; and Kern, F. G. Emergence of MCF-7 cells overexpressing a transfected epidermal growth factor receptor (EGFR) under estrogen-depleted conditions: Evidence for a role of EGFR in breast cancer growth and progression. Cell Growth Differ. 5 (1994): 1263-1274.
206. Price, J. T.; Tiganis, T.; Agarwal, A.; Djakiew, D.; and Thompson, E. W. Epidermal growth factor promotes MDA-MB-231 breast cancer cell migration through a phosphatidylinositol 3'-kinase and phospholipase C-dependent mechanism. Cancer Res 59 (1999): 5475-5478.
207. Price, J. T.; and Thompson, E. W. Models for studying cellular invasion of basement membranes. Methods Mol Biol 129 (1999): 231-249.
208. Sommers, C. L.; Byers, S. W.; Thompson, E. W.; Torri, J. A.; and Gelmann, E. P. Differentiation state and invasiveness of human breast cancer cell lines. Breast Cancer Res. Treat. 31 (1994): 325-335.
- Pichler, R. H., *et al.* SPARC is expressed in renal interstitial fibrosis and in renal vascular injury. Kidney Int. 50 (1996): 1978-1989.
210. Meng, Q.; Xu, J.; Goldberg, I. D.; Rosen, E. M.; Greenwald, R. A.; and Fan, S. Influence of chemically modified tetracyclines on proliferation, invasion and migration properties of MDA-MB-468 human breast cancer cells. Clin Exp Metastasis 18 (2000): 139-146.
211. Scherf, U., *et al.* A gene expression database for the molecular pharmacology of cancer. Nat Genet 24 (2000): 236-244.
212. Ross, D. T., *et al.* Systematic variation in gene expression patterns in human cancer cell lines. Nat Genet 24 (2000): 227-235.

213. Stetler-Stevenson, W. G.; Brown, P. D.; Onisto, M.; Levy, A. T.; and Liotta, L. A. Tissue inhibitor of metalloproteinases-2 (timp-2) mRNA expression in tumor cell lines and human tumor tissues. J Biol.Chem 265 (1990): 13933-13938.
214. Gossen, M.; and Bujard, H. Tight control of gene expression in mammalian cells by tetracycline- responsive promoters. Proc.Natl.Acad.Sci.U.S.A. 89 (1992): 5547-5551.
215. Lee, J.; Weber, M.; Mejia, S.; Bone, E.; Watson, P.; and Orr, W. A matrix metalloproteinase inhibitor, batimastat, retards the development of osteolytic bone metastases by MDA-MB-231 human breast cancer cells in Balb C nu/nu mice. Eur J Cancer 37 (2001): 106-113.
216. Tester, A.; Sharp, J.; Dhanesuan, N.; Waltham, M. and Thompson, E. Correlation between extent of osteolytic damage and metastatic burden of human breast cancer metastasis in nude mice: real-time PCR quantitation. In press

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