REFERENCES

1. Chen EI, Yates JR. Maspin and tumor metastasis. IUBMB Life. 2006 Jan;58(1):25-9.

2. Shi HY, Zhang W, Liang R, Abraham S, Kittrell FS, Medina D, et al. Blocking tumor growth, invasion, and metastasis by maspin in a syngeneic breast cancer model. Cancer Res. 2001 Sep 15;61(18):6945-51.

3. Sheng S, Carey J, Seftor EA, Dias L, Hendrix MJ, Sager R. Maspin acts at the cell membrane to inhibit invasion and motility of mammary and prostatic cancer cells. Proc Natl Acad Sci U S A. 1996 Oct 15;93(21):11669-74.

4. Dinarello CA. The paradox of pro-inflammatory cytokines in cancer. Cancer Metastasis Rev. 2006 Sep;25(3):307-13.

5. Karin M, Greten FR. NF-kappaB: linking inflammation and immunity to cancer development and progression. Nat Rev Immunol. 2005 Oct;5(10):749-59.

6. Cox R. Human cancer predisposition and the implications for radiological protection. Int J Radiat Biol. 1994 Nov;66(5):643-7.

7. Allan JM, Travis LB. Mechanisms of therapy-related carcinogenesis. Nat Rev Cancer. 2005 Dec;5(12):943-55.

8. Upton AC. Evolving perspectives on the biology and mechanisms of carcinogenesis. Leuk Res. 1986;10(7):727-34.

9. Hartwell L, Weinert T, Kadyk L, Garvik B. Cell cycle checkpoints, genomic integrity, and cancer. Cold Spring Harb Symp Quant Biol. 1994;59:259-63.

10. Fishel R, Kolodner RD. Identification of mismatch repair genes and their role in the development of cancer. Curr Opin Genet Dev. 1995 Jun;5(3):382-95.

11. Chaffer CL, Weinberg RA. A perspective on cancer cell metastasis. Science. Mar 25;331(6024):1559-64.

12. Liu FT, Rabinovich GA. Galectins as modulators of tumour progression. Nat Rev Cancer. 2005 Jan;5(1):29-41.

13. Hanahan D, Weinberg RA. The hallmarks of cancer. Cell. 2000 Jan 7;100(1):57-70.

13. Hanahan D, Weinberg RA. The hallmarks of cancer. Cell. 2000 Jan 7;100(1):57-70.

14. Mantovani A. Cancer: Inflaming metastasis. Nature. 2009 Jan 1;457(7225):36-7.

15. Zou Z, Anisowicz A, Hendrix MJ, Thor A, Neveu M, Sheng S, et al. Maspin, a serpin with tumor-suppressing activity in human mammary epithelial cells. Science. 1994 Jan 28;263(5146):526-9.

16. Silverman GA, Bird PI, Carrell RW, Church FC, Coughlin PB, Gettins PG, et al. The serpins are an expanding superfamily of structurally similar but funtionally diverse proteins: Evolution, mechanism of inhibition, novel functions, and a revised nomenclature. J Biol Chem. 2001;276:33293-6.

17. Fitzpatrick PA, Wong DT, Barr PJ, Pemberton PA. Functional implications of the modeled structure of maspin. Protein Eng. 1996 Jul;9(7):585-9.

18. Shi HY, Zhang W, Liang R, Kittrell F, Templeton NS, Medina D, et al. Modeling human breast cancer metastasis in mice: maspin as a paradigm. Histol Histopathol. 2003 Jan;18(1):201-6.

19. Bailey CM, Khalkhali-Ellis Z, Seftor EA, Hendrix MJ. Biological functions of maspin. J Cell Physiol. 2006 Dec;209(3):617-24.

20. Sheng S. A role of novel serpin maspin in tumor progression: the divergence revealed through efforts to converge. J Cell Physiol. 2006 Dec;209(3):631-5.

21. Seftor RE, Seftor EA, Sheng S, Pemberton PA, Sager R, Hendrix MJ. maspin suppresses the invasive phenotype of human breast carcinoma. Cancer Res. 1998 Dec 15;58(24):5681-5.

22. Odero-Marah VA, Khalkhali-Ellis Z, Chunthapong J, Amir S, Seftor RE, Seftor EA, et al. Maspin regulates different signaling pathways for motility and adhesion in aggressive breast cancer cells. Cancer Biol Ther. 2003 Jul-Aug;2(4):398-403.

23. Biliran H, Jr., Sheng S. Pleiotrophic inhibition of pericellular urokinase-type plasminogen activator system by endogenous tumor suppressive maspin. Cancer Res. 2001 Dec 15;61(24):8676-82.

24. Yin S, Lockett J, Meng Y, Biliran H, Jr., Blouse GE, Li X, et al. Maspin retards cell detachment via a novel interaction with the urokinase-type plasminogen activator/urokinase-type plasminogen activator receptor system. Cancer Res. 2006 Apr 15;66(8):4173-81.

25. Li X, Yin S, Meng Y, Sakr W, Sheng S. Endogenous inhibition of histone deacetylase 1 by tumor-suppressive maspin. Cancer Res. 2006 Sep 15;66(18):9323-9.

26. Bailey CM, Khalkhali-Ellis Z, Kondo S, Margaryan NV, Seftor RE, Wheaton WW, et al. Mammary serine protease inhibitor (Maspin) binds directly to interferon regulatory factor 6: identification of a novel serpin partnership. J Biol Chem. 2005 Oct 7;280(40):34210-7.

27. Yin S, Li X, Meng Y, Finley RL, Jr., Sakr W, Yang H, et al. Tumor-suppressive maspin regulates cell response to oxidative stress by direct interaction with glutathione S-transferase. J Biol Chem. 2005 Oct 14;280(41):34985-96.

28. Ngamkitidechakul C, Burke JM, O'Brien WJ, Twining SS. Maspin: synthesis by human cornea and regulation of in vitro stromal cell adhesion to extracellular matrix. Invest Ophthalmol Vis Sci. 2001 Dec;42(13):3135-41.

29. Reis-Filho JS, Milanezi F, Schmitt FC. Maspin is expressed in the nuclei of breast myoepithelial cells. J Pathol. 2002 Jun;197(2):272-3; author reply 3-4.

30. Pemberton PA, Tipton AR, Pavloff N, Smith J, Erickson JR, Mouchabeck ZM, et al. Maspin is an intracellular serpin that partitions into secretory vesicles and is present at the cell surface. J Histochem Cytochem. 1997 Dec;45(12):1697-706.

31. Sood AK, Fletcher MS, Gruman LM, Coffin JE, Jabbari S, Khalkhali-Ellis Z, et al. The paradoxical expression of maspin in ovarian carcinoma. Clin Cancer Res. 2002 Sep;8(9):2924-32.

32. Lonardo F, Li X, Siddiq F, Singh R, Al-Abbadi M, Pass HI, et al. Maspin nuclear localization is linked to favorable morphological features in pulmonary adenocarcinoma. Lung Cancer. 2006 Jan;51(1):31-9.

33. Nicolai ML, Martin Z, Koike H, Pierre R. Maspin locates to the nucleus in certain cell types. J Pathol. 2002;197:274-5.

34. Rose SL, Fitzgerald MP, White NO, Hitchler MJ, Futscher BW, De Geest K, et al. Epigenetic regulation of maspin expression in human ovarian carcinoma cells. Gynecol Oncol. 2006 Aug;102(2):319-24.

35. Reis-Filho JS, Torio B, Albergaria A, Schmitt FC. Maspin expression in normal skin and usual cutaneous carcinomas. Virchows Arch. 2002 Dec;441(6):551-8.

36. Katz AB, Taichman LB. A partial catalog of proteins secreted by epidermal keratinocytes in culture. J Invest Dermatol. 1999 May;112(5):818-21.

37. Fitzgerald M, Oshiro M, Holtan N, Krager K, Cullen JJ, Futscher BW, et al. Human pancreatic carcinoma cells activate maspin expression through loss of epigenetic control. Neoplasia. 2003 Sep-Oct;5(5):427-36.

38. Sato N, Fukushima N, Matsubayashi H, Goggins M. Identification of maspin and S100P as novel hypomethylation targets in pancreatic cancer using global gene expression profiling. Oncogene. 2004 Feb 26;23(8):1531-8.

39. Yatabe Y, Mitsudomi T, Takahashi T. Maspin expression in normal lung and non-small-cell lung cancers: cellular property-associated expression under the control of promoter DNA methylation. Oncogene. 2004 May 20;23(23):4041-9.

40. Marioni G, Blandamura S, Giacomelli L, Calgaro N, Segato P, Leo G, et al. Nuclear expression of maspin is associated with a lower recurrence rate and a longer disease-free interval after surgery for squamous cell carcinoma of the larynx. Histopathology. 2005 May;46(5):576-82.

41. Bettstetter M, Woenckhaus M, Wild PJ, Rummele P, Blaszyk H, Hartmann A, et al. Elevated nuclear maspin expression is associated with microsatellite instability and high tumour grade in colorectal cancer. J Pathol. 2005 Apr;205(5):606-14.

42. Zhang M, Sheng S, Maass N, Sager R. mMaspin: the mouse homolog of a human tumor suppressor gene inhibits mammary tumor invasion and motility. Mol Med. 1997 Jan;3(1):49-59.

43. Dokras A, Gardner LM, Kirschmann DA, Seftor EA, Hendrix MJ. The tumour suppressor gene maspin is differentially regulated in cytotrophoblasts during human placental development. Placenta. 2002 Apr;23(4):274-80.

44. Zhang M, Magit D, Sager R. Expression of maspin in prostate cells is regulated by a positive ets element and a negative hormonal responsive element site recognized by androgen receptor. Proc Natl Acad Sci U S A. 1997 May 27;94(11):5673-8.

45. Zou Z, Zhang W, Young D, Gleave MG, Rennie P, Connell T, et al. Maspin expression profile in human prostate cancer (CaP) and in vitro induction of Maspin expression by androgen ablation. Clin Cancer Res. 2002 May;8(5):1172-7.

46. Khalkhali-Ellis Z, Christian AL, Kirschmann DA, Edwards EM, Rezaie-Thompson M, Vasef MA, et al. Regulating the tumor suppressor gene maspin in breast cancer cells: a potential mechanism for the anticancer properties of tamoxifen. Clin Cancer Res. 2004 Jan 15;10(2):449-54.

47. Zou Z, Gao C, Nagaich AK, Connell T, Saito S, Moul JW, et al. p53 regulates the expression of the tumor suppressor gene maspin. J Biol Chem. 2000 Mar 3;275(9):6051-4.

48. Oshiro MM, Watts GS, Wozniak RJ, Junk DJ, Munoz-Rodriguez JL, Domann FE, et al. Mutant p53 and aberrant cytosine methylation cooperate to silence gene expression. Oncogene. 2003 Jun 5;22(23):3624-34.

49. Holliday R, Pugh JE. DNA modification mechanisms and gene activity during development. Science. 1975 Jan 24;187(4173):226-32.

50. Futscher BW, Oshiro MM, Wozniak RJ, Holtan N, Hanigan CL, Duan H, et al. Role for DNA methylation in the control of cell type specific maspin expression. Nat Genet. 2002 Jun;31(2):175-9.

51. Fujisawa K, Maesawa C, Sato R, Wada K, Ogasawara S, Akiyama Y, et al. Epigenetic status and aberrant expression of the maspin gene in human hepato-biliary tract carcinomas. Lab Invest. 2005 Feb;85(2):214-24.

52. Hendrix MJ. De-mystifying the mechanism(s) of maspin. Nat Med. 2000 Apr;6(4):374-6.

53. Muhonen P, Holthofer H. Epigenetic and microRNA-mediated regulation in diabetes. Nephrol Dial Transplant. 2009 Apr;24(4):1088-96.

54. Levine A, Cantoni GL, Razin A. Methylation in the preinitiation domain suppresses gene transcription by an indirect mechanism. Proc Natl Acad Sci U S A. 1992 Nov 1;89(21):10119-23.

55. Costello JF, Vertino PM. Methylation matters: a new spin on maspin. Nat Genet. 2002 Jun;31(2):123-4.

56. Feinberg AP, Tycko B. The history of cancer epigenetics. Nat Rev Cancer. 2004 Feb;4(2):143-53.

57. Liu L, Wylie RC, Andrews LG, Tollefsbol TO. Aging, cancer and nutrition: the DNA methylation connection. Mech Ageing Dev. 2003 Dec;124(10-12):989-98.

58. Jones PA, Baylin SB. The fundamental role of epigenetic events in cancer. Nat Rev Genet. 2002 Jun;3(6):415-28.

59. Esteller M. Aberrant DNA methylation as a cancer-inducing mechanism. Annu Rev Pharmacol Toxicol. 2005;45:629-56.

60. Maass N, Hojo T, Ueding M, Luttges J, Kloppel G, Jonat W, et al. Expression of the tumor suppressor gene Maspin in human pancreatic cancers. Clin Cancer Res. 2001 Apr;7(4):812-7.

61. Wang MC, Yang YM, Li XH, Dong F, Li Y. Maspin expression and its clinicopathological significance in tumorigenesis and progression of gastric cancer. World J Gastroenterol. 2004 Mar 1;10(5):634-7.

62. Maass N, Biallek M, Rosel F, Schem C, Ohike N, Zhang M, et al. Hypermethylation and histone deacetylation lead to silencing of the maspin gene in human breast cancer. Biochem Biophys Res Commun. 2002 Sep 13;297(1):125-8.

63. Wada K, Maesawa C, Akasaka T, Masuda T. Aberrant expression of the maspin gene associated with epigenetic modification in melanoma cells. J Invest Dermatol. 2004 Mar;122(3):805-11.

64. Primeau M, Gagnon J, Momparler RL. Synergistic antineoplastic action of DNA methylation inhibitor 5-AZA-2'-deoxycytidine and histone deacetylase inhibitor depsipeptide on human breast carcinoma cells. Int J Cancer. 2003 Jan 10;103(2):177-84.

65. Boltze C, Schneider-Stock R, Quednow C, Hinze R, Mawrin C, Hribaschek A, et al. Silencing of the maspin gene by promoter hypermethylation in thyroid cancer. Int J Mol Med. 2003 Oct;12(4):479-84.

66. Sato N, Maitra A, Fukushima N, van Heek NT, Matsubayashi H, Iacobuzio-Donahue CA, et al. Frequent hypomethylation of multiple genes overexpressed in pancreatic ductal adenocarcinoma. Cancer Res. 2003 Jul 15;63(14):4158-66.

67. Akiyama Y, Maesawa C, Ogasawara S, Terashima M, Masuda T. Cell-type-specific repression of the maspin gene is disrupted frequently by demethylation at the promoter region in gastric intestinal metaplasia and cancer cells. Am J Pathol. 2003 Nov;163(5):1911-9.

68. Maesawa C, Ogasawara S, Yashima-Abo A, Kimura T, Kotani K, Masuda S, et al. Aberrant maspin expression in gallbladder epithelium is associated with intestinal metaplasia in patients with cholelithiasis. J Clin Pathol. 2006 Mar;59(3):328-30.

69. Sugimoto S, Maass N, Takimoto Y, Sato K, Minei S, Zhang M, et al. Expression and regulation of tumor suppressor gene maspin in human bladder cancer. Cancer Lett. 2004 Jan 20;203(2):209-15.

70. Balkwill F, Charles KA, Mantovani A. Smoldering and polarized inflammation in the initiation and promotion of malignant disease. Cancer Cell. 2005 Mar;7(3):211-7.

71. Dunn GP, Old, L. J. & Schreiber, R. D. The immunobiology of cancer immunosurveillance and immunoediting. Immunity. 2004(21):137-48.

72. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? Lancet. 2001 Feb 17;357(9255):539-45.

73. Burke F, Relf M, Negus R, Balkwill F. A cytokine profile of normal and malignant ovary. Cytokine. 1996 Jul;8(7):578-85.

74. Erdman SE, Sohn JJ, Rao VP, Nambiar PR, Ge Z, Fox JG, et al. CD4+CD25+ regulatory lymphocytes induce regression of intestinal tumors in ApcMin/+ mice. Cancer Res. 2005 May 15;65(10):3998-4004.

75. Engle SJ, Hoying JB, Boivin GP, Ormsby I, Gartside PS, Doetschman T. Transforming growth factor beta1 suppresses nonmetastatic colon cancer

at an early stage of tumorigenesis. Cancer Res. 1999 Jul 15;59(14):3379-86.

76. Berg DJ, Davidson N, Kuhn R, Muller W, Menon S, Holland G, et al. Enterocolitis and colon cancer in interleukin-10-deficient mice are associated with aberrant cytokine production and CD4(+) TH1-like responses. J Clin Invest. 1996 Aug 15;98(4):1010-20.

77. Lin WW, Karin M. A cytokine-mediated link between innate immunity, inflammation, and cancer. J Clin Invest. 2007 May;117(5):1175-83.

78. Attisano L, Wrana JL. Signal transduction by the TGF-beta superfamily. Science. 2002 May 31;296(5573):1646-7.

79. Shi Y, Massague J. Mechanisms of TGF-beta signaling from cell membrane to the nucleus. Cell. 2003 Jun 13;113(6):685-700.

80. Derynck R, Zhang YE. Smad-dependent and Smad-independent pathways in TGF-beta family signalling. Nature. 2003 Oct 9;425(6958):577-84.

81. Massague J. TGF-beta signal transduction. Annu Rev Biochem. 1998;67:753-91.

82. Gordon KJ, Blobe GC. Role of transforming growth factor-beta superfamily signaling pathways in human disease. Biochim Biophys Acta. 2008 Apr;1782(4):197-228.

83. Bierie B, Moses HL. Tumour microenvironment: TGFbeta: the molecular Jekyll and Hyde of cancer. Nat Rev Cancer. 2006 Jul;6(7):506-20.

84. Bierie B, Moses HL. TGF-beta and cancer. Cytokine Growth Factor Rev. 2006 Feb-Apr;17(1-2):29-40.

85. Massague J. TGFbeta in Cancer. Cell. 2008 Jul 25;134(2):215-30.

86. Elliott RL, Blobe GC. Role of transforming growth factor Beta in human cancer. J Clin Oncol. 2005 Mar 20;23(9):2078-93.

87. Jakowlew SB. Transforming growth factor-beta in cancer and metastasis. Cancer Metastasis Rev. 2006 Sep;25(3):435-57.

88. Pardali K, Moustakas A. Actions of TGF-beta as tumor suppressor and pro-metastatic factor in human cancer. Biochim Biophys Acta. 2007 Jan;1775(1):21-62.

89. Rahimi RA, Leof EB. TGF-beta signaling: a tale of two responses. J Cell Biochem. 2007 Oct 15;102(3):593-608.

90. Xu J, Lamouille S, Derynck R. TGF-beta-induced epithelial to mesenchymal transition. Cell Res. 2009 Feb;19(2):156-72.

91. Derynck R, Akhurst RJ, Balmain A. TGF-beta signaling in tumor suppression and cancer progression. Nat Genet. 2001 Oct;29(2):117-29.

92. Chen ML, Pittet MJ, Gorelik L, Flavell RA, Weissleder R, von Boehmer H, et al. Regulatory T cells suppress tumor-specific CD8 T cell cytotoxicity through TGF-beta signals in vivo. Proc Natl Acad Sci U S A. 2005 Jan 11;102(2):419-24.

93. Yang X, Letterio JJ, Lechleider RJ, Chen L, Hayman R, Gu H, et al. Targeted disruption of SMAD3 results in impaired mucosal immunity and diminished T cell responsiveness to TGF-beta. EMBO J. 1999 Mar 1;18(5):1280-91.

94. Parsons R, Myeroff LL, Liu B, Willson JK, Markowitz SD, Kinzler KW, et al. Microsatellite instability and mutations of the transforming growth factor beta type II receptor gene in colorectal cancer. Cancer Res. 1995 Dec 1;55(23):5548-50.

95. Kim SJ, Im YH, Markowitz SD, Bang YJ. Molecular mechanisms of inactivation of TGF-beta receptors during carcinogenesis. Cytokine Growth Factor Rev. 2000 Mar-Jun;11(1-2):159-68.

96. Markowitz S, Wang J, Myeroff L, Parsons R, Sun L, Lutterbaugh J, et al. Inactivation of the type II TGF-beta receptor in colon cancer cells with microsatellite instability. Science. 1995 Jun 2;268(5215):1336-8.

97. Jenkins BJ, Grail D, Nheu T, Najdovska M, Wang B, Waring P, et al. Hyperactivation of Stat3 in gp130 mutant mice promotes gastric hyperproliferation and desensitizes TGF-beta signaling. Nat Med. 2005 Aug;11(8):845-52.

98. Kollias G, Douni E, Kassiotis G, Kontoyiannis D. On the role of tumor necrosis factor and receptors in models of multiorgan failure, rheumatoid arthritis, multiple sclerosis and inflammatory bowel disease. Immunol Rev. 1999 Jun;169:175-94.

99. Lejeune FJ, Ruegg C, Lienard D. Clinical applications of TNF-alpha in cancer. Curr Opin Immunol. 1998 Oct;10(5):573-80.

100. Naylor MS, Stamp GW, Foulkes WD, Eccles D, Balkwill FR. Tumor necrosis factor and its receptors in human ovarian cancer. Potential role in disease progression. J Clin Invest. 1993 May;91(5):2194-206.

101. Leek RD, Landers R, Fox SB, Ng F, Harris AL, Lewis CE. Association of tumour necrosis factor alpha and its receptors with thymidine phosphorylase expression in invasive breast carcinoma. Br J Cancer. 1998 Jun;77(12):2246-51.

102. Warzocha K, Salles G, Bienvenu J, Bastion Y, Dumontet C, Renard N, et al. Tumor necrosis factor ligand-receptor system can predict treatment outcome in lymphoma patients. J Clin Oncol. 1997 Feb;15(2):499-508.

103. Malik ST, Griffin DB, Fiers W, Balkwill FR. Paradoxical effects of tumour necrosis factor in experimental ovarian cancer. Int J Cancer. 1989 Nov 15;44(5):918-25.

104. Malik ST, Naylor MS, East N, Oliff A, Balkwill FR. Cells secreting tumour necrosis factor show enhanced metastasis in nude mice. Eur J Cancer. 1990;26(10):1031-4.

105. Roberts RA, Kimber I. Cytokines in non-genotoxic hepatocarcinogenesis. Carcinogenesis. 1999 Aug;20(8):1397-401.

106. Moore RJ, Owens DM, Stamp G, Arnott C, Burke F, East N, et al. Mice deficient in tumor necrosis factor-alpha are resistant to skin carcinogenesis. Nat Med. 1999 Jul;5(7):828-31.

107. Robertson FM, Ross MS, Tober KL, Long BW, Oberyszyn TM. Inhibition of pro-inflammatory cytokine gene expression and papilloma growth during murine multistage carcinogenesis by pentoxifylline. Carcinogenesis. 1996 Aug;17(8):1719-28.

108. Voronov E, Shouval DS, Krelin Y, Cagnano E, Benharroch D, Iwakura Y, et al. IL-1 is required for tumor invasiveness and angiogenesis. Proc Natl Acad Sci U S A. 2003 Mar 4;100(5):2645-50.

109. Dinarello CA. Interleukin-1 and interleukin-1 antagonism. Blood. 1991 Apr 15;77(8):1627-52.

110. Dinarello CA. Biologic basis for interleukin-1 in disease. Blood. 1996 Mar 15;87(6):2095-147.

111. Endres S, Cannon JG, Ghorbani R, Dempsey RA, Sisson SD, Lonnemann G, et al. In vitro production of IL 1 beta, IL 1 alpha, TNF and IL2 in healthy subjects: distribution, effect of cyclooxygenase inhibition and evidence of independent gene regulation. Eur J Immunol. 1989 Dec;19(12):2327-33.

112. Vidal-Vanaclocha F, Fantuzzi G, Mendoza L, Fuentes AM, Anasagasti MJ, Martin J, et al. IL-18 regulates IL-1beta-dependent hepatic melanoma metastasis via vascular cell adhesion molecule-1. Proc Natl Acad Sci U S A. 2000 Jan 18;97(2):734-9.

113. Tricot G. New insights into role of microenvironment in multiple myeloma. Lancet. 2000 Jan 22;355(9200):248-50.

114. Balkwill F. Cancer and the chemokine network. Nat Rev Cancer. 2004 Jul;4(7):540-50.

115. Muller A, Homey B, Soto H, Ge N, Catron D, Buchanan ME, et al. Involvement of chemokine receptors in breast cancer metastasis. Nature. 2001 Mar 1;410(6824):50-6.

116. Burger JA, Kipps TJ. CXCR4: a key receptor in the crosstalk between tumor cells and their microenvironment. Blood. 2006 Mar 1;107(5):1761-7.

117. Karin M. Nuclear factor-kappaB in cancer development and progression. Nature. 2006 May 25;441(7092):431-6.

118. Huber MA, Azoitei N, Baumann B, Grunert S, Sommer A, Pehamberger H, et al. NF-kappaB is essential for epithelial-mesenchymal transition and metastasis in a model of breast cancer progression. J Clin Invest. 2004 Aug;114(4):569-81.

119. Luo JL, Tan W, Ricono JM, Korchynskyi O, Zhang M, Gonias SL, et al. Nuclear cytokine-activated IKKalpha controls prostate cancer metastasis by repressing Maspin. Nature. 2007 Apr 5;446(7136):690-4.

120. Steeg PS. Metastasis suppressors alter the signal transduction of cancer cells. Nat Rev Cancer. 2003 Jan;3(1):55-63.

121. Livak KJ, Schmittgen TD. Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. Methods. 2001 Dec;25(4):402-8.

122. Vichai V, Kirtikara K. Sulforhodamine B colorimetric assay for cytotoxicity screening. Nat Protoc. 2006;1(3):1112-6.

123. Ngamkitidechakul C, Warejcka DJ, Burke JM, O'Brien WJ, Twining SS. Sufficiency of the reactive site loop of maspin for induction of cell-matrix adhesion and inhibition of cell invasion. Conversion of ovalbumin to a maspin-like molecule. J Biol Chem. 2003 Aug 22;278(34):31796-806.

124. Frommer M, McDonald LE, Millar DS, Collis CM, Watt F, Grigg GW, et al. A genomic sequencing protocol that yields a positive display of 5-methylcytosine residues in individual DNA strands. Proc Natl Acad Sci U S A. 1992 Mar 1;89(5):1827-31.

125. Grunau C, Clark SJ, Rosenthal A. Bisulfite genomic sequencing: systematic investigation of critical experimental parameters. Nucleic Acids Res. 2001 Jul 1;29(13):E65-5.

126. Horswill MA, Narayan M, Warejcka DJ, Cirillo LA, Twining SS. Epigenetic silencing of maspin expression occurs early in the conversion of keratocytes to fibroblasts. Exp Eye Res. 2008 Apr;86(4):586-600.

127. Zhang Y, Rodhe C, Tierling S, Stamerjohanns H, Reinhardt R. DNA Methylation Analysis by bisulfite Conversion, Cloning, and Sequencing of Individual Clones. Tost J, editor.; 2008.

128. Maass N, Hojo T, Rosel F, Ikeda T, Jonat W, Nagasaki K. Down regulation of the tumor suppressor gene maspin in breast carcinoma is associated with a higher risk of distant metastasis. Clin Biochem. 2001 Jun;34(4):303-7.

129. Coussens LM, Werb Z. Inflammation and cancer. Nature. 2002 Dec 19-26;420(6917):860-7.

130. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature. 2008 Jul 24;454(7203):436-44.

131. Wang SE, Narasanna A, Whitell CW, Wu FY, Friedman DB, Arteaga CL. Convergence of p53 and transforming growth factor beta (TGFbeta) signaling on activating expression of the tumor suppressor gene maspin in mammary epithelial cells. J Biol Chem. 2007 Feb 23;282(8):5661-9.

132. Nuovo GJ. In situ detection of PCR-amplified metalloproteinase cDNAs, their inhibitors and human papillomavirus transcripts in cervical carcinoma cell lines. Int J Cancer. 1997 Jun 11;71(6):1056-60.

133. Sheng S. The promise and challenge toward the clinical application of maspin in cancer. Front Biosci. 2004 Sep 1;9:2733-45.

134. Rosen EM, Goldberg ID, Liu D, Setter E, Donovan MA, Bhargava M, et al. Tumor necrosis factor stimulates epithelial tumor cell motility. Cancer Res. 1991 Oct 1;51(19):5315-21.

APPENDICES

APPENDIX A

List of chemicals and materials used in this study

Name of chemicals and materials	Company
Absolute ethanol	Merck, Germany
Acetone	Merck, Germany
40%Acrylamide/Bis solution	BIO-RAD, USA
Agarose	Vivantis, USA
Ammonium persulfate	Pierce, USA
VisiGlo™ HRP Plus Chemiluminescent Substrate kit	Amresco, USA
Antibiotic antimycotic solution	Invitrogen, USA
Boric acid	USB, USA
Bovine serum albumin	Pierce, USA
Bromphenol blue	Sigma-Aldrich, USA
Cell culture 25 and 75 cm^3 flask and well plates	Corning, USA
CHAPS	Fluka, Switzerland
Complete proteinase inhibitor cocktail, Mini, EDTA –free	Roche, Germany
Competent cell DH5 alpha	RBC Bioscience, Taiwan
Coomassie brilliant blue R250	BIO-RAD, USA
CyQUANT®Cell Proliferation Assay Kit	Invitrogen, USA
Developer	AGFA, Belgium

Name of chemicals and materials	Company
Diethylpyrocarbonate (DEPC)	Amresco, USA
Dimethyl sulfoxide (DMSO)	Amresco, USA
Dithiotheritol (DTT)	USB, USA
dNTP Mix	Vivantis, USA
Dulbeco's Modified Eagel's Medium (DMEM)	GIBCO, USA
Ethylenediaminetetraacetic acid (EDTA)	Fluka, Switzerland
Ethidium bromide	Vivantis, USA
EZ DNA Methylation-Gold Kit™	ZYMO Research, USA
Fetal bovine serum (FBS)	HyClone, USA
Film	Kodak, USA
Fixative	AGFA, Belgium
Glycerol anhydrous	Fluka, Switzerland
Glycine	Vivantis, USA
HEPES	Invitrogen, USA
Hydrochloric acid	Merck, Germany
Human Interleukin-1β	Roche, Germany
Human Transforming Growth Factor-β1	Roche, Germany
Human Tumor Necrosis Factor-α	Roche, Germany
Isopropyl-β-D-thio-galactoside (IPTG)	Bio Basic Inc., Canada
Isopropyl alcohol	Sigma-Aldrich, USA
LB Broth	Criterion, USA
LB Agar	Criterion, USA

Name of chemicals and materials	Company
Leibovitz's L-15	Invitrogen, USA
MultiScreen-MIC 96-well Plate	Millipore, USA
Mammalian Protein Extraction Buffer	GE Healthcare, USA
Matrigel	BD Biosciences, USA
Maxima^{TM} SYBR Green qPCR Master Mix (2X)	Fermentas, Canada
Mercaptoethanol	Sigma-Aldrich, USA
Methanol	Merck, German
M-MuLV Reverse transcriptase	Fermentas, Canada
Mouse monoclonal anti-human Maspin antibody	BD Biosciences, USA
Mouse monoclonal anti beta Actin (HRP conjugated)	Abcam, USA
Non-fat dry milk	BIO-RAD, USA
Nitrocellulose membrane	GE Healthcare, USA
Oligo-(dT)$_{18}$ primers	Bio Basic Inc., Thailand
Potassium chloride	BDH, England
Potassium dihydrogen phosphate	BDH, England
Potassium phosphate	BDH, England
Precision Plus Protein^{TM}Standards Dual Color	BIO-RAD, USA
Primers	Bio Basic Inc., Thailand
Protein assay kit	BIO-RAD, USA
Protein loading marker	Fermentas, Canada
pTG19-T PCR Cloning Vector	Vivantis, USA
QIAprep Spin Miniprep kit	Qiagen, USA

Name of chemicals and materials	Company
QIAquick Gel Extraction kit	Qiagen, USA
RevertAid^{TM} First Stand cDNA Synthesis Kit	Fermentas, Canada
Ribonuclease inhibitor	Fermentas, Canada
RNase Away	Molecular Bio Products, USA
Sodium chloride	BDH chemical, England
Sodium dodecyl sulfate	Sigma-Aldrich, USA
Sodium hydroxide	BDH, England
Sodium hydrogen carbonate	Merck, Germany
Standard 100-base pairs DNA ladder	RBC Bioscience
Sulforhodamine B	Sigma-Aldrich, USA
T4 DNA Ligation kit	Vivantis, USA
Taq DNA Polymerase	Vivantis, USA
TEMED	USB, USA
Thiourea	USB, USA
Tricholoroacetic acid	BDH chemical, England
Tris	Research Organics, USA
Trisodium citrate	Merck, Germany
Trizol reagent	Invitrogen, USA
Trypan Blue	Sigma-Aldrich, USA
Trypsin	Invitrogen,USA
Tween 20	USB, USA

Name of chemicals and materials	Company
Urea	Research Organics, USA
Vacuum Filter/Storage Bottle	Corning, USA
Xgal	Bio Basic Inc., Canada
Xylene cyanol	Amresco, USA

APPENDIX B

List of instrument used in this study

Instrument	Company
Autoclave	Tomy autoclave SS-240
Automatic pipette	Gilson
Carbon dioxide incubator	Thermoscientific
Centrifuge	KUBOTA CORPORATION
Micro-plate spectrophotometer	Bio-Tek Instrument
Film cassette	Amersham Biosciences
Freezer (-80°c)	Forma Scientific
Freezer (-20°c)	Sanyo
Glassware	Pyrex and Scott duran
Gel Documentation System	Synergy G:Box ChemiHR
GeneQuant pro	Amersham Biosciences
Hot air oven	Haraeus
Inverted microscope	NIKON
Laminar flow biological cabinet	NU AIRE
Liquid nitrogen tank	International Cryogenics, Inc.
Magnetic stirrer	Thermolyne
Microcentrifuge 5402, bench top	Eppendrof
Microwave	LG

Instrument	**Company**
Mupid®-exU Gel Electrophoresis	Advance, Japan
Mini Trans-Blot Electrophoretic Transfer	Bio-Rad
Power supply	Bio-Rad
Shaker incubator	Amerex Instruments Inc.
iCycler thermal cycle	Bio-Rad
Vertical Mini Gel Electrophoresis	Bio-Rad
Vortex	Scientific industries
7500 Fast Real-Time PCR System	Applied Biosystems

APPENDIX C

Preparation of some reagents and buffers

A. Mammalian Cell Culture media

1. DMEM serum free medium with phenol red

DMEM	13.5	g
HEPES	2.603	g
$NaHCO_3$	3.7	g

Add deionized water to 1000 mL and steriled by vacuum filter (membrane pore sized 0.2 μm) and stored at 4°C

2. DMEM with 10% fetal bovine serum

DMEM without serum free	89	mL
Fetal bovine serum	10	mL
10X Antibiotic antimycotic solution	1	mL

Stored at 4°C

3. Leibovitz's L-15 serum free medium

Leibovitz's L-15	13.7	g

Add deionized water to 1000 mL and steriled by vacuum filter (membrane pore sized 0.2 μm) and stored at 4°C

4. Leibovitz's L-15 with 10% fetal bovine serum

Leibovitz's L-15 without serum free	89	mL
Fetal bovine serum	10	mL
10X Antibiotic antimycotic solution	1	mL

Stored at 4°C

5. Freezing medium (10%DMSO in 25%FBS-DMEM)

Incomplete DMEM	65	mL
Fetal bovine serum	25	mL
DMSO (Hybrimax)	10	mL

Prepared freshly

6. Trypan blue (0.4%)

Trypan blue powder	0.4	g
1XPBS pH 7.2	100	mL

Filtrated by Whatman filter paper No. 1 and stored at room temperature.

7. 2mM EDTA- PBS buffer

Ethylenediaminetetraacetic acid	0.12	g
1XPBS pH 7.2	200	mL

Steriled by autoclaving

B. Bacteria culture

1. LB Broth

LB Broth powder	20	g
Deionized water	500	mL
Steriled by autoclaving		
Add 200 mg/mL ampicillin	250	µL

Stored at room temperature

2. LB Agar

LB Agar powder	5	g
Deionized water	200	mL
Steriled by autoclaving		
Add 200 mg/mL ampicillin	250	µL

Stored at 4°C

3. 1 M IPTG

IPTG	1	g
Deionized water	4.2	mL
Sterile by filtration		

Stored in the freezer

4. 20 mg/mL Xgal

Xgal	100	mg
DMSO	5	mL
Wrapped in foil		

Stored in the freezer

C. Matrigel Invasion assay

Prepare Matrigel

Dilute stock Matrigel with cool DMEM serum free medium to 5 µg/50µL using cool pipette tip

D. Protein electrophoresis and Western blot analysis

Whole cell lysis buffer

1. CHAPS lysis buffer without proteinase inhibitors

CHAPS	0.4	g
DTT	61.6	mg
Thiourea	1.5	g
Urea	4.2	g
Deionized water	10	mL

2. CHAPS lysis buffer with proteinase inhibitors

CHAPS lysis buffer without proteinase inhibitors	10	mL
Complete Protease Inhibitor Cocktail	1	tablet

Aliquot 1 mL

Stored at -20°C

3. Mammalian Protein Extraction Buffer with proteinase inhibitors

Mammalian Protein Extraction Buffer	10	mL
Complete Protease Inhibitor Cocktail	1	tablet

Aliquot 1 mL

Stored at -20°C

4. Separating gel buffer (1.5M Tris HCl pH 8.8)

Tris base	18.15	g
Deionized water	80	mL

Adjusted pH to 8.8 by HCl

Add deionized water to 100 mL and vacuum-filtrated using 0.2 μm Millipore membrane filter and stored at 4°C

5. Stacking gel buffer (0.5M Tris HCl pH 6.8)

Tris base	6.0	g
Deionized water	80	mL

Adjusted pH to 6.8 by HCl adjusted final volume to 100 mL, and vacuum-filtrated using 0.2 µm Millipore membrane filter and stored at 4°C

6. 5x non-reducing buffer

1 M Tris HCl pH 6.8	5	mL
Glycerol anhydrous	2.5	mL
Sodium dodecyl sulfate	1	g
Deionized water	2.5	mL
1% Bromphenol blue	0.05	g

Mixed well, aliquot and stored at -20°C

7. 5x Reducing buffer

5x non-reducing buffer	750	µL
2-Mercaptoethanol	250	µL

Mixed well, aliquot and stored at -20°C

8. 10X Running buffer

Tris base	30.28	g
Glycine	144.13	g
Sodium dodecyl sulfate	10	g
Deionized water	1000	mL

Mixed well, prepare before use

9. 1X Running buffer

10XRunning buffer	100	mL
Deionized water	900	mL

Mix well, stored at room temperature

10. 30% Polyacrylamide solution (30.8% acrylamide, 2.7% bis-acrylamide)

Acrylamide	60	g
Bis-acrylamide	1.6	g
Deionized water	200	mL

Filtrated through 0.2 μm Millipore membrane and stored at 4°C in dark

11. 10% APS

Ammonium persulfate	0.1	g
Deionized water	1	mL

Mix well, aliquot and stored at -20°C

12. 10% SDS

SDS	1	g
Deionized water	10	mL

Mix well, stored at room temperature

13. Polyacrylamide gels

Solution	Separating gel			4% Stacking gel
	12.5%	10%	7.5%	
Deionized water	3.2 mL	4 mL	4.85mL	1.5 mL
30% polyacrylamide solution	4.2 mL	3.3 mL	2.5 mL	332.5 µL
4X Separating gel buffer	2.5 mL	2.5 mL	2.5 mL	-
4X Stacking gel buffer	-	-	-	625 µL
10% SDS (in distilled water)	100 µL	100 µL	100 µL	25 µL
10% APS (in distilled water)	50 µL	50 µL	50 µL	12.5 µL
TEMED	10 µL	10 µL	10 µL	5 µL

14. 1xBlotting buffer

10XRunning buffer	100	mL
Deionized water	700	mL
Mixed well		
Methanol	200	mL

Mix well, stored at room temperature

15. 0.025% Coomassie brilliant blue R250

Coomassie brilliant blue R250	0.125	g
Methanol	200	mL
Acetic acid	35	mL

Adjusted volume to 500 mL by Deionized water and stored at room temperature

16. Destaining gel solution I (40% methanol, 7% acetic acid)

Methanol	400	mL
Acetic acid	70	mL

Adjusted volume to 1000 mL with Deionized water and stored at room temperature

17. Destaining gel solution II (5% methanol, 7% acetic acid)

Methanol	50	mL
Acetic acid	70	mL

Adjusted volume to 1000 mL with Deionized water and stored at room temperature

E. Agarsoe gel electrophoresis

1. 1.5% agarose gel

Agarose gel	1.5	g
0.5X TBE buffer	100	mL

Heated until dissolved

2. 10X TBE buffer

Tris (anhydroxymethyl) aminomethane	108	g
Boric acid	55	g
EDTA	9.5	g
Deionized water	1000	mL

Mix well, stored at room temperature

3. 0.5X TBE buffer

10X TBE buffer	50	mL
Deionized water	950	mL

Mix well, stored at room temperature

4. 0.5 mg/mL Ethidium bromide

10 mg/mL Ethidium bromide	25	µL
1X TBE buffer	500	mL

Mix well, stored at room temperature

5. DEPC treated water

Deionized water	1000	mL
DEPC	0.1	mL

6. 6X DNA loading dye

Xylene cyanol FF	25	mg
Bromophenol blue	25	mg
Deionized water	7	mL
Glycerol	3	

CURRICULUM VITAE

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Poster presentation

A. Lekawipat, K. Chairatvit, and A. Wongnoppavich. Effect of proinflammatory cytokines on expression of tumor suppressor Maspin in cancer cell line. The RGJ Seminar Series LXXIV. 16thSeptember, 2010.Chiang Mai, Thailand.

Oral presentation

A. Lekawipat, K. Chairatvit, and A. Wongnoppavich, Effect of pro-inflammatory cytokines on expression of tumor suppressor Maspin in human cervical cancer cell. The 36th CONGRESS on SCIENCE and TECHNOLOGY of THAILAND (STT36). October 26th-28th 2010, Bangkok, Thailand.