

REFERENCES

1. Majorana A, Bardellini E, Conti G, Keller E, Pasini S. Root resorption in dental trauma: 45 cases followed for 5 years. *Dent Traumatol* 2003; 19(5): 262-5.
2. Tronstad L. Root resorption--etiology, terminology and clinical manifestations. *Endod Dent Traumatol* 1988; 4(6): 241-52.
3. Finucane D, Kinirons MJ. External inflammatory and replacement resorption of luxated, and avulsed replanted permanent incisors: a review and case presentation. *Dent Traumatol* 2003; 19(3): 170-4.
4. Ne RF, Witherspoon DE, Gutmann JL. Tooth resorption. *Quintessence Int* 1999; 30(1): 9-25.
5. He J, Jiang J, Safavi KE, Spangberg LS, Zhu Q. Emdogain promotes osteoblast proliferation and differentiation and stimulates osteoprotegerin expression. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 97(2): 239-45.
6. Hoang AM, Oates TW, Cochran DL. In vitro wound healing responses to enamel matrix derivative. *J Periodontol* 2000; 71(8): 1270-7.
7. Jiang J, Fouad AF, Safavi KE, Spangberg LS, Zhu Q. Effects of enamel matrix derivative on gene expression of primary osteoblasts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; 91(1): 95-100.
8. Ninomiya M, Kamata N, Fujimoto R, Ishimoto T, Suryono, Kido J, et al. Application of enamel matrix derivative in autotransplantation of an impacted maxillary premolar: a case report. *J Periodontol* 2002; 73(3): 346-51.
9. Filippi A, Pohl Y, von Arx T. Treatment of replacement resorption with Emdogain--a prospective clinical study. *Dent Traumatol* 2002; 18(3): 138-43.
10. Al-Hezaimi K, Naghshbandi J, Simon JH, Oglesby S, Rotstein I. Successful treatment of a radicular groove by intentional replantation and Emdogain therapy. *Dent Traumatol* 2004; 20(4): 226-8.
11. Hamamoto Y, Kawasaki N, Jarnbring F, Hammarstrom L. Effects and distribution of the enamel matrix derivative Emdogain in the periodontal tissues of rat molars transplanted to the abdominal wall. *Dent Traumatol* 2002; 18(1): 12-23.

12. Hammarstrom L. Enamel matrix, cementum development and regeneration. *J Clin Periodontol* 1997; 24(9 Pt 2): 658-68.
13. Hammarstrom L. The role of enamel matrix proteins in the development of cementum and periodontal tissues. *Ciba Found Symp* 1997; 205: 246-55; discussion 55-60.
14. Robinson C, Brookes SJ, Shore RC, Kirkham J. The developing enamel matrix: nature and function. *Eur J Oral Sci* 1998; 106 Suppl 1: 282-91.
15. Brookes SJ, Robinson C, Kirkham J, Bonass WA. Biochemistry and molecular biology of amelogenin proteins of developing dental enamel. *Arch Oral Biol* 1995; 40(1): 1-14.
16. Lau EC, Mohandas TK, Shapiro LJ, Slavkin HC, Snead ML. Human and mouse amelogenin gene loci are on the sex chromosomes. *Genomics* 1989; 4(2): 162-8.
17. Akane A. Sex determination by PCR analysis of the X-Y amelogenin gene. *Methods Mol Biol* 1998; 98: 245-9.
18. Gestrelus S, Lyngstadaas SP, Hammarstrom L. Emdogain--periodontal regeneration based on biomimicry. *Clin Oral Investig* 2000; 4(2): 120-5.
19. Hammarstrom L, Heijl L, Gestrelus S. Periodontal regeneration in a buccal dehiscence model in monkeys after application of enamel matrix proteins. *J Clin Periodontol* 1997; 24(9 Pt 2): 669-77.
20. Nagano T, Iwata T, Ogata Y, Tanabe T, Gomi K, Fukae M, et al. Effect of heat treatment on bioactivities of enamel matrix derivatives in human periodontal ligament (HPDL) cells. *J Periodontal Res* 2004; 39(4): 249-56.
21. Gestrelus S, Andersson C, Lidstrom D, Hammarstrom L, Somerman M. In vitro studies on periodontal ligament cells and enamel matrix derivative. *J Clin Periodontol* 1997; 24 (9 Pt 2): 685-92.
22. Maycock J, Wood SR, Brookes SJ, Shore RC, Robinson C, Kirkham J. Characterization of a porcine amelogenin preparation, EMDOGAIN, a biological treatment for periodontal disease. *Connect Tissue Res* 2002; 43(2-3): 472-6.
23. Veis A. Amelogenin gene splice products: potential signaling molecules. *Cell Mol Life Sci* 2003; 60(1): 38-55.
24. Veis A, Tompkins K, Alvares K, Wei K, Wang L, Wang XS, et al. Specific amelogenin gene splice products have signaling effects on cells in culture and in implants in vivo. *J Biol Chem* 2000; 275(52): 41263-72.

25. Kawase T, Okuda K, Momose M, Kato Y, Yoshie H, Burns DM. Enamel matrix derivative (EMDOGAIN) rapidly stimulates phosphorylation of the MAP kinase family and nuclear accumulation of smad2 in both oral epithelial and fibroblastic human cells. *J Periodontol Res* 2001; 36(6): 367-76.
26. Suzuki S, Nagano T, Yamakoshi Y, Gomi K, Arai T, Fukae M, et al. Enamel matrix derivative gel stimulates signal transduction of BMP and TGF- β . *J Dent Res* 2005; 84(6): 510-4.
27. He J, Jiang J, Safavi KE, Spangberg LS, Zhu Q. Direct contact between enamel matrix derivative (EMD) and osteoblasts is not required for EMD-induced cell proliferation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004; 98(3): 370-5.
28. Heden G, Wennstrom J, Lindhe J. Periodontal tissue alterations following Emdogain treatment of periodontal sites with angular bone defects. A series of case reports. *J Clin Periodontol* 1999; 26(12): 855-60.
29. Heijl L. Periodontal regeneration with enamel matrix derivative in one human experimental defect. A case report. *J Clin Periodontol* 1997; 24(9 Pt 2): 693-6.
30. Venezia E, Goldstein M, Boyan BD, Schwartz Z. The use of enamel matrix derivative in the treatment of periodontal defects: a literature review and meta-analysis. *Crit Rev Oral Biol Med* 2004; 15(6): 382-402.
31. Bratthall G, Lindberg P, Havemose-Poulsen A, Holmstrup P, Bay L, Soderholm G, et al. Comparison of ready-to-use EMDOGAIN-gel and EMDOGAIN in patients with chronic adult periodontitis. *J Clin Periodontol* 2001; 28(10): 923-9.
32. Cornellini R, Scarano A, Piattelli M, Andreana S, Covani U, Quaranta A, et al. Effect of enamel matrix derivative (Emdogain) on bone defects in rabbit tibias. *J Oral Implantol* 2004; 30(2): 69-73.
33. Sculean A, Junker R, Donos N, Windisch P, Brex M, Dunker N. Immunohistochemical evaluation of matrix molecules associated with wound healing following treatment with an enamel matrix protein derivative in humans. *Clin Oral Investig* 2003; 7(3): 167-74.
34. Zetterstrom O, Andersson C, Eriksson L, Fredriksson A, Friskopp J, Heden G, et al. Clinical safety of enamel matrix derivative (EMDOGAIN) in the treatment of periodontal defects. *J Clin Periodontol* 1997; 24(9 Pt 2): 697-704.

35. Nikolopoulos S, Peteinaki E, Castanas E. Immunologic effects of emdogain in humans: one-year results. *Int J Periodontics Restorative Dent* 2002; 22(3): 269-77.
36. Petinaki E, Nikolopoulos S, Castanas E. Low stimulation of peripheral lymphocytes, following in vitro application of Emdogain. *J Clin Periodontol* 1998;25(9):715-20.
37. Cattaneo V, Rota C, Silvestri M, Piacentini C, Forlino A, Gallanti A, et al. Effect of enamel matrix derivative on human periodontal fibroblasts: proliferation, morphology and root surface colonization. An in vitro study. *J Periodontal Res* 2003; 38(6): 568-74.
38. Hoang AM, Klebe RJ, Steffensen B, Ryu OH, Simmer JP, Cochran DL. Amelogenin is a cell adhesion protein. *J Dent Res* 2002; 81(7): 497-500.
39. Schwartz Z, Carnes DL, Jr., Pulliam R, Lohmann CH, Sylvia VL, Liu Y, et al. Porcine fetal enamel matrix derivative stimulates proliferation but not differentiation of pre-osteoblastic 2T9 cells, inhibits proliferation and stimulates differentiation of osteoblast-like MG63 cells, and increases proliferation and differentiation of normal human osteoblast NHOst cells. *J Periodontol* 2000; 71(8): 1287-96.
40. Ohyama M, Suzuki N, Yamaguchi Y, Maeno M, Otsuka K, Ito K. Effect of enamel matrix derivative on the differentiation of C2C12 cells. *J Periodontol* 2002; 73(5): 543-50.
41. Galli C, Macaluso GM, Guizzardi S, Vescovini R, Passeri M, Passeri G. Osteoprotegerin and receptor activator of nuclear factor-kappa B ligand modulation by enamel matrix derivative in human alveolar osteoblasts. *J Periodontol* 2006; 77(7): 1223-8.
42. Itoh N, Kasai H, Ariyoshi W, Harada E, Yokota M, Nishihara T. Mechanisms involved in the enhancement of osteoclast formation by enamel matrix derivative. *J Periodontal Res* 2006; 41(4): 273-9.
43. Sakallioğlu U, Acikgoz G, Ayas B, Kirtiloglu T, Sakallioğlu E. Healing of periodontal defects treated with enamel matrix proteins and root surface conditioning--an experimental study in dogs. *Biomaterials* 2004; 25(10): 1831-40.
44. Sculean A, Donos N, Brex M, Karring T, Reich E. Healing of fenestration-type defects following treatment with guided tissue regeneration or enamel matrix proteins. An experimental study in monkeys. *Clin Oral Investig* 2000; 4(1): 50-6.
45. Sculean A, Donos N, Brex M, Reich E, Karring T. Treatment of intrabony defects with

- guided tissue regeneration and enamel-matrix-proteins. An experimental study in monkeys. *J Clin Periodontol* 2000; 27(7): 466-72.
46. Fernandes JM, Rego RO, Spolidorio LC, Marcantonio RA, Marcantonio Junior E, Cirelli JA. Enamel matrix proteins associated with GTR and bioactive glass in the treatment of class III furcation in dogs. *Pesqui Odontol Bras* 2005; 19(3): 169-75.
47. Moses O, Artzi Z, Sculean A, Tal H, Kozlovsky A, Romanos GE, et al. Comparative study of two root coverage procedures: a 24-month follow-up multicenter study. *J Periodontol* 2006; 77(2): 195-202.
48. Sanz M, Tonetti MS, Zabalegui I, Sicilia A, Blanco J, Rebelo H, et al. Treatment of intrabony defects with enamel matrix proteins or barrier membranes: results from a multicenter practice-based clinical trial. *J Periodontol* 2004; 75(5): 726-33.
49. Meyle J, Gonzales JR, Bodeker RH, Hoffmann T, Richter S, Heinz B, et al. A randomized clinical trial comparing enamel matrix derivative and membrane treatment of buccal class II furcation involvement in mandibular molars. Part II: secondary outcomes. *J Periodontol* 2004; 75(9): 1188-95.
50. Sculean A, Donos N, Blaes A, Lauermann M, Reich E, Brex M. Comparison of enamel matrix proteins and bioabsorbable membranes in the treatment of intrabony periodontal defects. A split-mouth study. *J Periodontol* 1999; 70(3): 255-62.
51. Sculean A, Donos N, Miliauskaite A, Arweiler N, Brex M. Treatment of intrabony defects with enamel matrix proteins or bioabsorbable membranes. A 4-year follow-up split-mouth study. *J Periodontol* 2001; 72(12): 1695-701.
52. Sculean A, Pietruska M, Schwarz F, Willershausen B, Arweiler NB, Auschill TM. Healing of human intrabony defects following regenerative periodontal therapy with an enamel matrix protein derivative alone or combined with a bioactive glass. A controlled clinical study. *J Clin Periodontol* 2005; 32(1): 111-7.
53. Silvestri M, Ricci G, Rasperini G, Sartori S, Cattaneo V. Comparison of treatments of infrabony defects with enamel matrix derivative, guided tissue regeneration with a nonresorbable membrane and Widman modified flap. A pilot study. *J Clin Periodontol* 2000; 27(8): 603-10.
54. Filippi A, Pohl Y, von Arx T. Treatment of replacement resorption with Emdogain--preliminary results after 10 months. *Dent Traumatol* 2001; 17(3): 134-8.

55. Caglar E, Tanboga I, Susal S. Treatment of avulsed teeth with Emdogain--a case report. *Dent Traumatol* 2005; 21(1): 51-3.
56. Schjott M, Andreasen JO. Emdogain does not prevent progressive root resorption after replantation of avulsed teeth: a clinical study. *Dent Traumatol* 2005; 21(1): 46-50.
57. St George G, Darbar U, Thomas G. Inflammatory external root resorption following surgical treatment for intra-bony defects: a report of two cases involving Emdogain and a review of the literature. *J Clin Periodontol* 2006; 33(6): 449-54.
58. Aubin JE, Turksen K. Monoclonal antibodies as tools for studying the osteoblast lineage. *Microsc Res Tech* 1996; 33(2): 128-40.
59. Christenson RH. Biochemical markers of bone metabolism: an overview. *Clin Biochem* 1997; 30(8): 573-93.
60. Ducy P, Schinke T, Karsenty G. The osteoblast: a sophisticated fibroblast under central surveillance. *Science* 2000; 289(5484): 1501-4.
61. Karsenty G. Role of Cbfa1 in osteoblast differentiation and function. *Semin Cell Dev Biol* 2000; 11(5): 343-6.
62. Sommerfeldt DW, Rubin CT. Biology of bone and how it orchestrates the form and function of the skeleton. *Eur Spine J* 2001; 10 Suppl 2: S86-95.
63. Schor AM, Canfield AE, Sutton AB, Arciniegas E, Allen TD. Pericyte differentiation. *Clin Orthop Relat Res* 1995(313): 81-91.
64. Manolagas SC. Birth and death of bone cells: basic regulatory mechanisms and implications for the pathogenesis and treatment of osteoporosis. *Endocr Rev* 2000; 21(2): 115-37.
65. Friedenstein AJ, Chailakhyan RK, Latsinik NV, Panasyuk AF, Keiliss-Borok IV. Stromal cells responsible for transferring the microenvironment of the hemopoietic tissues. Cloning in vitro and retransplantation in vivo. *Transplantation* 1974; 17(4): 331-40.
66. Komori T, Yagi H, Nomura S, Yamaguchi A, Sasaki K, Deguchi K, et al. Targeted disruption of Cbfa1 results in a complete lack of bone formation owing to maturational arrest of osteoblasts. *Cell* 1997; 89(5): 755-64.
67. Ducy P, Starbuck M, Priemel M, Shen J, Pinero G, Geoffroy V, et al. A Cbfa1-dependent genetic pathway controls bone formation beyond embryonic development. *Genes Dev* 1999; 13(8): 1025-36.

68. Karsenty G. The genetic transformation of bone biology. *Genes Dev* 1999; 13(23): 3037-51.
69. Yamaguchi A, Komori T, Suda T. Regulation of osteoblast differentiation mediated by bone morphogenetic proteins, hedgehogs, and Cbfa1. *Endocr Rev* 2000; 21(4): 393-411.
70. Stein GS, Lian JB, Stein JL, Van Wijnen AJ, Montecino M. Transcriptional control of osteoblast growth and differentiation. *Physiol Rev* 1996; 76(2): 593-629.
71. Marie PJ. Cellular and molecular alterations of osteoblasts in human disorders of bone formation. *Histol Histopathol* 1999; 14(2): 525-38.
72. Mundlos S, Olsen BR. Heritable diseases of the skeleton. Part II: Molecular insights into skeletal development-matrix components and their homeostasis. *Faseb J* 1997; 11(4): 227-33.
73. Robey PG, Fedarko NS, Hefferan TE, Bianco P, Vetter UK, Grzesik W, et al. Structure and molecular regulation of bone matrix proteins. *J Bone Miner Res* 1993; 8 Suppl 2: S483-7.
74. Young MF, Kerr JM, Ibaraki K, Heegaard AM, Robey PG. Structure, expression, and regulation of the major noncollagenous matrix proteins of bone. *Clin Orthop Relat Res* 1992(281): 275-94.
75. Curtis TA, Ashrafi SH, Weber DF. Canalicular communication in the cortices of human long bones. *Anat Rec* 1985; 212(4): 336-44.
76. Jilka RL, Weinstein RS, Bellido T, Parfitt AM, Manolagas SC. Osteoblast programmed cell death (apoptosis): modulation by growth factors and cytokines. *J Bone Miner Res* 1998; 13(5): 793-802.
77. Lynch MP, Capparelli C, Stein JL, Stein GS, Lian JB. Apoptosis during bone-like tissue development in vitro. *J Cell Biochem* 1998; 68(1): 31-49.
78. Billiau A, Edy VG, Heremans H, Van Damme J, Desmyter J, Georgiades JA, et al. Human interferon: mass production in a newly established cell line, MG-63. *Antimicrob Agents Chemother* 1977; 12(1): 11-5.
79. Boyan BD, Batzer R, Kieswetter K, Liu Y, Cochran DL, Szmuckler-Moncler S, et al. Titanium surface roughness alters responsiveness of MG63 osteoblast-like cells to 1 alpha,25-(OH)2D3. *J Biomed Mater Res* 1998; 39(1): 77-85.

80. Lincks J, Boyan BD, Blanchard CR, Lohmann CH, Liu Y, Cochran DL, et al. Response of MG63 osteoblast-like cells to titanium and titanium alloy is dependent on surface roughness and composition. *Biomaterials* 1998; 19(23): 2219-32.
81. Lohmann CH, Sagun R, Jr., Sylvia VL, Cochran DL, Dean DD, Boyan BD, et al. Surface roughness modulates the response of MG63 osteoblast-like cells to 1,25-(OH)(2)D(3) through regulation of phospholipase A(2) activity and activation of protein kinase A. *J Biomed Mater Res* 1999; 47(2): 139-51.
82. Martin JY, Schwartz Z, Hummert TW, Schraub DM, Simpson J, Lankford J, Jr., et al. Effect of titanium surface roughness on proliferation, differentiation, and protein synthesis of human osteoblast-like cells (MG63). *J Biomed Mater Res* 1995; 29(3): 389-401.
83. Viridi AS, Cook LJ, Oreffo RO, Triffitt JT. Modulation of bone morphogenetic protein-2 and bone morphogenetic protein-4 gene expression in osteoblastic cell lines. *Cell Mol Biol* 1998; 44(8): 1237-46.
84. Kue R, Sohrabi A, Nagle D, Frondoza C, Hungerford D. Enhanced proliferation and osteocalcin production by human osteoblast-like MG63 cells on silicon nitride ceramic discs. *Biomaterials* 1999; 20(13): 1195-201.
85. Lajeunesse D, Frondoza C, Schoffield B, Sacktor B. Osteocalcin secretion by the human osteosarcoma cell line MG-63. *J Bone Miner Res* 1990; 5(9): 915-22.
86. Lam J, Nelson CA, Ross FP, Teitelbaum SL, Fremont DH. Crystal structure of the TRANCE/RANKL cytokine reveals determinants of receptor-ligand specificity. *J Clin Invest* 2001; 108(7): 971-9.
87. Drake FH, Dodds RA, James IE, Connor JR, Debouck C, Richardson S, et al. Cathepsin K, but not cathepsins B, L, or S, is abundantly expressed in human osteoclasts. *J Biol Chem* 1996; 271(21): 12511-6.
88. Loveridge N. Bone: more than a stick. *J Anim Sci* 1999; 77 Suppl 2: 190-6.
89. Chambers TJ. Regulation of the differentiation and function of osteoclasts. *J Pathol* 2000; 192(1): 4-13.
90. Gowen M, Lazner F, Dodds R, Kapadia R, Feild J, Tavarria M, et al. Cathepsin K knockout mice develop osteopetrosis due to a deficit in matrix degradation but not demineralization. *J Bone Miner Res* 1999; 14(10): 1654-63.

91. Stenbeck G. Formation and function of the ruffled border in osteoclasts. *Semin Cell Dev Biol* 2002; 13(4): 285-92.
92. Tanaka S, Takahashi N, Udagawa N, Tamura T, Akatsu T, Stanley ER, et al. Macrophage colony-stimulating factor is indispensable for both proliferation and differentiation of osteoclast progenitors. *J Clin Invest* 1993; 91(1): 257-63.
93. Felix R, Hofstetter W, Wetterwald A, Cecchini MG, Fleisch H. Role of colony-stimulating factor-1 in bone metabolism. *J Cell Biochem* 1994; 55(3): 340-9.
94. Hsu H, Lacey DL, Dunstan CR, Solovyev I, Colombero A, Timms E, et al. Tumor necrosis factor receptor family member RANK mediates osteoclast differentiation and activation induced by osteoprotegerin ligand. *Proc Natl Acad Sci U S A* 1999; 96(7): 3540-5.
95. Lacey DL, Timms E, Tan HL, Kelley MJ, Dunstan CR, Burgess T, et al. Osteoprotegerin ligand is a cytokine that regulates osteoclast differentiation and activation. *Cell* 1998; 93(2): 165-76.
96. Simonet WS, Lacey DL, Dunstan CR, Kelley M, Chang MS, Luthy R, et al. Osteoprotegerin: a novel secreted protein involved in the regulation of bone density. *Cell* 1997; 89(2): 309-19.
97. Yasuda H, Shima N, Nakagawa N, Yamaguchi K, Kinosaki M, Mochizuki S, et al. Osteoclast differentiation factor is a ligand for osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical to TRANCE/RANKL. *Proc Natl Acad Sci U S A* 1998; 95(7): 3597-602.
98. Itonaga I, Sabokbar A, Sun SG, Kudo O, Danks L, Ferguson D, et al. Transforming growth factor-beta induces osteoclast formation in the absence of RANKL. *Bone* 2004; 34(1): 57-64.
99. Roodman GD. Advances in bone biology: the osteoclast. *Endocr Rev* 1996; 17(4): 308-32.
100. Bellido T, Jilka RL, Boyce BF, Girasole G, Broxmeyer H, Dalrymple SA, et al. Regulation of interleukin-6, osteoclastogenesis, and bone mass by androgens. The role of the androgen receptor. *J Clin Invest* 1995; 95(6): 2886-95.
101. Buxton EC, Yao W, Lane NE. Changes in serum receptor activator of nuclear factor-kappaB ligand, osteoprotegerin, and interleukin-6 levels in patients with glucocorticoid-

- induced osteoporosis treated with human parathyroid hormone (1-34). *J Clin Endocrinol Metab* 2004; 89(7): 3332-6.
102. Benford HL, McGowan NW, Helfrich MH, Nuttall ME, Rogers MJ. Visualization of bisphosphonate-induced caspase-3 activity in apoptotic osteoclasts in vitro. *Bone* 2001; 28(5): 465-73.
103. Nishikawa M, Akatsu T, Katayama Y, Yasutomo Y, Kado S, Kugal N, et al. Bisphosphonates act on osteoblastic cells and inhibit osteoclast formation in mouse marrow cultures. *Bone* 1996; 18(1): 9-14.
104. Troen BR. Molecular mechanisms underlying osteoclast formation and activation. *Exp Gerontol* 2003; 38(6): 605-14.
105. Suda T, Takahashi N, Martin TJ. Modulation of osteoclast differentiation. *Endocr Rev* 1992; 13(1): 66-80.
106. Pittenger MF, Mackay AM, Beck SC, Jaiswal RK, Douglas R, Mosca JD, et al. Multilineage potential of adult human mesenchymal stem cells. *Science* 1999; 284(5411): 143-7.
107. Feng X. Regulatory roles and molecular signaling of TNF family members in osteoclasts. *Gene* 2005; 350(1): 1-13.
108. Caplan AI. Mesenchymal stem cells. *J Orthop Res* 1991; 9(5): 641-50.
109. Yao GQ, Sun B, Hammond EE, Spencer EN, Horowitz MC, Insogna KL, et al. The cell-surface form of colony-stimulating factor-1 is regulated by osteotropic agents and supports formation of multinucleated osteoclast-like cells. *J Biol Chem* 1998; 273(7): 4119-28.
110. Wong BR, Rho J, Arron J, Robinson E, Orlinick J, Chao M, et al. TRANCE is a novel ligand of the tumor necrosis factor receptor family that activates c-Jun N-terminal kinase in T cells. *J Biol Chem* 1997; 272(40): 25190-4.
111. Burgess TL, Qian Y, Kaufman S, Ring BD, Van G, Capparelli C, et al. The ligand for osteoprotegerin (OPGL) directly activates mature osteoclasts. *J Cell Biol* 1999; 145(3): 527-38.
112. Aubin JE, Bonnellye E. Osteoprotegerin and its ligand: a new paradigm for regulation of osteoclastogenesis and bone resorption. *Osteoporos Int* 2000; 11(11): 905-13.

113. Hofbauer LC, Khosla S, Dunstan CR, Lacey DL, Boyle WJ, Riggs BL. The roles of osteoprotegerin and osteoprotegerin ligand in the paracrine regulation of bone resorption. *J Bone Miner Res* 2000; 15(1): 2-12.
114. Hofbauer LC, Neubauer A, Heufelder AE. Receptor activator of nuclear factor-kappaB ligand and osteoprotegerin: potential implications for the pathogenesis and treatment of malignant bone diseases. *Cancer* 2001; 92(3): 460-70.
115. Yasuda H, Shima N, Nakagawa N, Mochizuki SI, Yano K, Fujise N, et al. Identity of osteoclastogenesis inhibitory factor (OCIF) and osteoprotegerin (OPG): a mechanism by which OPG/OCIF inhibits osteoclastogenesis in vitro. *Endocrinology* 1998; 139(3): 1329-37.
116. Tsuda E, Goto M, Mochizuki S, Yano K, Kobayashi F, Morinaga T, et al. Isolation of a novel cytokine from human fibroblasts that specifically inhibits osteoclastogenesis. *Biochem Biophys Res Commun* 1997; 234(1): 137-42.
117. Bucay N, Sarosi I, Dunstan CR, Morony S, Tarpley J, Capparelli C, et al. osteoprotegerin-deficient mice develop early onset osteoporosis and arterial calcification. *Genes Dev* 1998; 12(9): 1260-8.
118. Bonewald LF, Dallas SL. Role of active and latent transforming growth factor beta in bone formation. *J Cell Biochem* 1994; 55(3): 350-7.
119. Lemaire V, Tobin FL, Greller LD, Cho CR, Suva LJ. Modeling the interactions between osteoblast and osteoclast activities in bone remodeling. *J Theor Biol* 2004; 229(3): 293-309.
120. Alliston T, Choy L, Ducy P, Karsenty G, Derynck R. TGF-beta-induced repression of CBFA1 by Smad3 decreases cbfa1 and osteocalcin expression and inhibits osteoblast differentiation. *Embo J* 2001; 20(9): 2254-72.
121. Takai H, Kanematsu M, Yano K, Tsuda E, Higashio K, Ikeda K, et al. Transforming growth factor-beta stimulates the production of osteoprotegerin/osteoclastogenesis inhibitory factor by bone marrow stromal cells. *J Biol Chem* 1998; 273(42): 27091-6.
122. Itoh K, Udagawa N, Katagiri T, Iemura S, Ueno N, Yasuda H, et al. Bone morphogenetic protein 2 stimulates osteoclast differentiation and survival supported by receptor activator of nuclear factor-kappaB ligand. *Endocrinology* 2001; 142(8): 3656-62.

123. Katagiri T, Takahashi N. Regulatory mechanisms of osteoblast and osteoclast differentiation. *Oral Dis* 2002; 8(3): 147-59.
124. Falany ML, Thames AM, 3rd, McDonald JM, Blair HC, McKenna MA, Moore RE, et al. Osteoclasts secrete the chemotactic cytokine mim-1. *Biochem Biophys Res Commun* 2001; 281(1): 180-5.
125. Parfitt AM. Osteonal and hemi-osteonal remodeling: the spatial and temporal framework for signal traffic in adult human bone. *J Cell Biochem* 1994; 55(3): 273-86.
126. Lindsay R, Hart DM, Forrest C, Baird C. Prevention of spinal osteoporosis in oophorectomised women. *Lancet* 1980; 2(8205): 1151-4.
127. Hill PA. Bone remodelling. *Br J Orthod* 1998; 25(2): 101-7.
128. Madras N, Gibbs AL, Zhou Y, Zandstra PW, Aubin JE. Modeling stem cell development by retrospective analysis of gene expression profiles in single progenitor-derived colonies. *Stem Cells* 2002; 20(3): 230-40.
129. Vaes G. Cellular biology and biochemical mechanism of bone resorption. A review of recent developments on the formation, activation, and mode of action of osteoclasts. *Clin Orthop Relat Res* 1988(231): 239-71.
130. Rodan GA, Martin TJ. Role of osteoblasts in hormonal control of bone resorption--a hypothesis. *Calcif Tissue Int* 1981; 33(4): 349-51.
131. Tan KB, Harrop J, Reddy M, Young P, Terrett J, Emery J, et al. Characterization of a novel TNF-like ligand and recently described TNF ligand and TNF receptor superfamily genes and their constitutive and inducible expression in hematopoietic and non-hematopoietic cells. *Gene* 1997; 204(1-2): 35-46.
132. Kwon BS, Wang S, Udagawa N, Haridas V, Lee ZH, Kim KK, et al. TR1, a new member of the tumor necrosis factor receptor superfamily, induces fibroblast proliferation and inhibits osteoclastogenesis and bone resorption. *Faseb J* 1998; 12(10): 845-54.
133. Yun TJ, Chaudhary PM, Shu GL, Frazer JK, Ewings MK, Schwartz SM, et al. OPG/FDCR-1, a TNF receptor family member, is expressed in lymphoid cells and is up-regulated by ligating CD40. *J Immunol* 1998; 161(11): 6113-21.
134. Leeming DJ, Alexandersen P, Karsdal MA, Qvist P, Schaller S, Tanko LB. An update on biomarkers of bone turnover and their utility in biomedical research and clinical practice. *Eur J Clin Pharmacol* 2006.

135. Mizuno A, Murakami A, Nakagawa N, Yasuda H, Tsuda E, Morinaga T, et al. Structure of the mouse osteoclastogenesis inhibitory factor (OCIF) gene and its expression in embryogenesis. *Gene* 1998; 215(2): 339-43.
136. Hakeda Y, Kobayashi Y, Yamaguchi K, Yasuda H, Tsuda E, Higashio K, et al. Osteoclastogenesis inhibitory factor (OCIF) directly inhibits bone-resorbing activity of isolated mature osteoclasts. *Biochem Biophys Res Commun* 1998; 251(3): 796-801.
137. Wittrant Y, Theoleyre S, Chipoy C, Padrines M, Blanchard F, Heymann D, et al. RANKL/RANK/OPG: new therapeutic targets in bone tumours and associated osteolysis. *Biochim Biophys Acta* 2004; 1704(2): 49-57.
138. Terpos E, Szydlo R, Apperley JF, Hatjiharissi E, Politou M, Meletis J, et al. Soluble receptor activator of nuclear factor kappaB ligand-osteoprotegerin ratio predicts survival in multiple myeloma: proposal for a novel prognostic index. *Blood* 2003; 102(3): 1064-9.
139. Theill LE, Boyle WJ, Penninger JM. RANK-L and RANK: T cells, bone loss, and mammalian evolution. *Annu Rev Immunol* 2002; 20: 795-823.
140. Boyle WJ, Simonet WS, Lacey DL. Osteoclast differentiation and activation. *Nature* 2003; 423(6937): 337-42.
141. Anderson DM, Maraskovsky E, Billingsley WL, Dougall WC, Tometsko ME, Roux ER, et al. A homologue of the TNF receptor and its ligand enhance T-cell growth and dendritic-cell function. *Nature* 1997; 390(6656): 175-9.
142. Roux S, Mariette X. The high rate of bone resorption in multiple myeloma is due to RANK (receptor activator of nuclear factor-kappaB) and RANK Ligand expression. *Leuk Lymphoma* 2004; 45(6): 1111-8.
143. Huang L, Cheng YY, Chow LT, Zheng MH, Kumta SM. Tumour cells produce receptor activator of NF-kappaB ligand (RANKL) in skeletal metastases. *J Clin Pathol* 2002; 55(11): 877-8.
144. Gravallesse EM, Manning C, Tsay A, Naito A, Pan C, Amento E, et al. Synovial tissue in rheumatoid arthritis is a source of osteoclast differentiation factor. *Arthritis Rheum* 2000; 43(2): 250-8.
145. Nakashima T, Kobayashi Y, Yamasaki S, Kawakami A, Eguchi K, Sasaki H, et al. Protein expression and functional difference of membrane-bound and soluble receptor

- activator of NF-kappaB ligand: modulation of the expression by osteotropic factors and cytokines. *Biochem Biophys Res Commun* 2000; 275(3): 768-75.
146. Fata JE, Kong YY, Li J, Sasaki T, Irie-Sasaki J, Moorehead RA, et al. The osteoclast differentiation factor osteoprotegerin-ligand is essential for mammary gland development. *Cell* 2000; 103(1): 41-50.
147. Arai F, Miyamoto T, Ohneda O, Inada T, Sudo T, Brasel K, et al. Commitment and differentiation of osteoclast precursor cells by the sequential expression of c-Fms and receptor activator of nuclear factor kappaB (RANK) receptors. *J Exp Med* 1999; 190(12): 1741-54.
148. Yamane T, Kunisada T, Yamazaki H, Nakano T, Orkin SH, Hayashi SI. Sequential requirements for SCL/tal-1, GATA-2, macrophage colony-stimulating factor, and osteoclast differentiation factor/osteoprotegerin ligand in osteoclast development. *Exp Hematol* 2000; 28(7): 833-40.
149. Nakagawa N, Kinoshita M, Yamaguchi K, Shima N, Yasuda H, Yano K, et al. RANK is the essential signaling receptor for osteoclast differentiation factor in osteoclastogenesis. *Biochem Biophys Res Commun* 1998; 253(2): 395-400.
150. Li J, Sarosi I, Yan XQ, Morony S, Capparelli C, Tan HL, et al. RANK is the intrinsic hematopoietic cell surface receptor that controls osteoclastogenesis and regulation of bone mass and calcium metabolism. *Proc Natl Acad Sci U S A* 2000; 97(4): 1566-71.
151. Dougall WC, Glaccum M, Charrier K, Rohrbach K, Brasel K, De Smedt T, et al. RANK is essential for osteoclast and lymph node development. *Genes Dev* 1999; 13(18): 2412-24.
152. Maddi A, Hai H, Ong ST, Sharp L, Harris M, Meghji S. Long wave ultrasound may enhance bone regeneration by altering OPG/RANKL ratio in human osteoblast-like cells. *Bone* 2006; 39(2): 283-8.
153. Carinci F, Piattelli A, Guida L, Perrotti V, Laino G, Oliva A, et al. Effects of Emdogain on osteoblast gene expression. *Oral Dis* 2006; 12(3): 329-42.
154. Otsuka T, Kasai H, Yamaguchi K, Nishihara T. Enamel matrix derivative promotes osteoclast cell formation by RANKL production in mouse marrow cultures. *J Dent* 2005; 33(9): 749-55.

155. Centrella M, McCarthy TL, Canalis E. Transforming growth factor-beta and remodeling of bone. *J Bone Joint Surg Am* 1991; 73(9): 1418-28.
156. Erlebacher A, Filvaroff EH, Ye JQ, Derynck R. Osteoblastic responses to TGF-beta during bone remodeling. *Mol Biol Cell* 1998; 9(7): 1903-18.
157. Martin TJ, Sims NA. Osteoclast-derived activity in the coupling of bone formation to resorption. *Trends Mol Med* 2005; 11(2): 76-81.
158. Hughes DE, Dai A, Tiffée JC, Li HH, Mundy GR, Boyce BF. Estrogen promotes apoptosis of murine osteoclasts mediated by TGF-beta. *Nat Med* 1996; 2(10): 1132-6.
159. Shinar DM, Rodan GA. Biphasic effects of transforming growth factor-beta on the production of osteoclast-like cells in mouse bone marrow cultures: the role of prostaglandins in the generation of these cells. *Endocrinology* 1990; 126(6): 3153-8.
160. Koseki T, Gao Y, Okahashi N, Murase Y, Tsujisawa T, Sato T, et al. Role of TGF-beta family in osteoclastogenesis induced by RANKL. *Cell Signal* 2002; 14(1): 31-6.
161. Takayanagi K, Osawa G, Nakaya H, Cochran DL, Kamoi K, Oates TW. Effects of enamel matrix derivative on bone-related mRNA expression in human periodontal ligament cells in vitro. *J Periodontol* 2006; 77(5): 891-8.