

TABLE E-1 Animal Models and Corresponding Reference Numbers

	Fracture Type		Fixation		
	Open	Closed	None	Internal	External
Mouse	(1-23)	(24-42)	(1-12, 24-26)	(13-16, 27-44)	(17-23, 42)
Rat	(43-102)	(103-152)	(43-56, 103-106)	(57-84, 107-150)	(85-102, 151-152)
Rabbit	(153-202)	(203-205)	(153-166, 203-204)	(167-176)	(177-202, 205)
Sheep	(206-236)		(206-208)	(209-219)	(220-236)
Goat	(237-243)	(244-246)	(237-239)		(240-246)
Dog	(247-272)	273	(247-251)	(252-261, 273)	(262-272)
Monkey	(274-278)		274	(275-278)	
Micropig	(279-283)			(279-280)	(281-283)
Chick	(284-285)		(284-285)		
Axolotl	286		286		

E-References

1. Colnot C, Romero DM, Huang S, Helms JA. Mechanisms of action of demineralized bone matrix in the repair of cortical bone defects. *Clin Orthop Relat Res.* 2005;435:69-78.
2. Gamradt SC, Abe N, Bahamonde ME, Lee YP, Nelson SD, Lyons KM, Lieberman JR. Tracking expression of virally mediated BMP-2 in gene therapy for bone repair. *Clin Orthop Relat Res.* 2006;450:238-45.
3. Lee JY, Musgrave D, Pelinkovic D, Fukushima K, Cummins J, Usas A, Robbins P, Fu FH, Huard J. Effect of bone morphogenetic protein-2-expressing muscle-derived cells on healing of critical-sized bone defects in mice. *J Bone Joint Surg Am.* 2001;83:1032-9.
4. Uusitalo H, Hiltunen A, Ahonen M, Gao TJ, Lefebvre V, Harley V, Kähäri VM, Vuorio E. Accelerated up-regulation of L-Sox5, Sox6, and Sox9 by BMP-2 gene transfer during murine fracture healing. *J Bone Miner Res.* 2001;16:1837-45.
5. Hirata K, Tsukazaki T, Kadowaki A, Furukawa K, Shibata Y, Moriishi T, Okubo Y, Bessho K, Komori T, Mizuno A, Yamaguchi A. Transplantation of skin fibroblasts expressing BMP-2 promotes bone repair more effectively than those expressing Runx2. *Bone.* 2003;32:502-12.
6. Asami K, Nakanishi T, Asahara H, Inoue H, Takigawa M. Expression of neurotrophins and their receptors (TRK) during fracture healing. *Bone.* 2000;26:625-33.
7. Nagashima M, Sakai A, Uchida S, Tanaka S, Tanaka M, Nakamura T. Bisphosphonate (YM529) delays the repair of cortical bone defect after drill-hole injury by reducing terminal differentiation of osteoblasts in the mouse femur. *Bone.* 2005;36:502-11.
8. Meinel L, Fajardo R, Hofmann S, Langer R, Chen J, Snyder B, Vunjak-Novakovic G, Kaplan D. Silk implants for the healing of critical size bone defects. *Bone.* 2005;37:688-98.
9. Yoshimura Y, Nomura S, Kawasaki S, Tsutsumimoto T, Shimizu T, Takaoka K. Colocalization of noggin and bone morphogenetic protein-4 during fracture healing. *J Bone Miner Res.* 2001;16:876-84.
10. Peng H, Usas A, Olshanski A, Ho AM, Gearhart B, Cooper GM, Huard J. VEGF improves, whereas sFlt1 inhibits, BMP2-induced bone formation and bone healing through modulation of angiogenesis. *J Bone Miner Res.* 2005;20:2017-27.
11. Yamagiwa H, Tokunaga K, Hayami T, Hatano H, Uchida M, Endo N, Takahashi HE. Expression of metalloproteinase-13 (Collagenase-3) is induced during fracture healing in mice. *Bone.* 1999;25:197-203.
12. Hansen-Algenstaedt N, Schaefer C, Wolfram L, Joscheck C, Schroeder M, Algenstaedt P, Ruther W. Femur window—a new approach to microcirculation of living bone in situ. *J Orthop Res.* 2005;23:1073-82.
- 13.

- Tiyapatanaputi P, Rubery PT, Carmouche J, Schwarz EM, O'Keefe RJ, Zhang X. A novel murine segmental femoral graft model. *J Orthop Res.* 2004;22:1254-60.
14. Baldik Y, Diwan AD, Appleyard RC, Fang ZM, Wang Y, Murrell GA. Deletion of iNOS gene impairs mouse fracture healing. *Bone.* 2005;37:32-6.
 15. Uusitalo H, Rantakokko J, Ahonen M, Jamsa T, Tuukkanen J, KaHari V, Vuorio E, Aro HT. A metaphyseal defect model of the femur for studies of murine bone healing. *Bone.* 2001;28:423-9.
 16. Skoglund B, Forslund C, Aspenberg P. Simvastatin improves fracture healing in mice. *J Bone Miner Res.* 2002;17:2004-8.
 17. Tay BK, Le AX, Gould SE, Helms JA. Histochemical and molecular analyses of distraction osteogenesis in a mouse model. *J Orthop Res.* 1998;16:636-42.
 18. Flick LM, Weaver JM, Ulrich-Vinther M, Abuzzahab F, Zhang X, Dougall WC, Anderson D, O'Keefe RJ, Schwarz EM. Effects of receptor activator of NFkappaB (RANK) signaling blockade on fracture healing. *J Orthop Res.* 2003;21:676-84.
 19. Fang TD, Nacamuli RP, Song HM, Fong KD, Warren SM, Salim A, Carano RA, Filvaroff EH, Longaker MT. Creation and characterization of a mouse model of mandibular distraction osteogenesis. *Bone.* 2004;34:1004-12.
 20. Carvalho RS, Einhorn TA, Lehmann W, Edgar C, Al-Yamani A, Apazidis A, Pacicca D, Clemens TL, Gerstenfeld LC. The role of angiogenesis in a murine tibial model of distraction osteogenesis. *Bone.* 2004;34:849-61.
 21. Li G, White G, Connolly C, Marsh D. Cell proliferation and apoptosis during fracture healing. *J Bone Miner Res.* 2002;17:791-9.
 22. Cheung KM, Kaluarachi K, Andrew G, Lu W, Chan D, Cheah KS. An externally fixed femoral fracture model for mice. *J Orthop Res.* 2003;21:685-90.
 23. Connolly CK, Li G, Bunn JR, Mushipe M, Dickson GR, Marsh DR. A reliable externally fixated murine femoral fracture model that accounts for variation in movement between animals. *J Orthop Res.* 2003;21:843-9.
 24. Chadha HS, Fitzgerald RH Jr, Wiater P, Sud S, Nasser S, Wooley PH. Experimental acute hematogenous osteomyelitis in mice. I. Histopathological and immunological findings. *J Orthop Res.* 1999;17:376-81.
 25. Lu C, Miclau T, Hu D, Hansen E, Tsui K, Puttlitz C, Marcucio RS. Cellular basis for age-related changes in fracture repair. *J Orthop Res.* 2005;23:1300-7.
 26. Toyosawa S, Kanatani N, Shintani S, Kobata M, Yuki M, Kishino M, Ijuhin N, Komori T. Expression of dentin matrix protein 1 (DMP1) during fracture healing. *Bone.* 2004;35:553-61.
 27. Le AX, Miclau T, Hu D, Helms JA. Molecular aspects of healing in stabilized and non-stabilized fractures. *J Orthop Res.* 2001;19:78-84.
 28. Devine MJ, Mierisch CM, Jang E, Anderson PC, Balian G. Transplanted bone marrow cells localize to fracture callus in a mouse model. *J Orthop Res.* 2002;20:1232-9.
 29. Bhandari M, Schemitsch EH. Bone formation following intramedullary femoral reaming is decreased by indomethacin and antibodies to insulin-like growth factors. *J Orthop Trauma.* 2002;16:717-22.
 30. Shen FH, Visger JM, Balian G, Hurwitz SR, Diduch DR. Systemically administered mesenchymal stromal cells transduced with insulin-like growth factor-I localize to a fracture site and potentiate healing. *J Orthop Trauma.* 2002;16:651-9.
 31. Manigrasso MB, O'Connor JP. Characterization of a closed femur fracture model in mice. *J Orthop Trauma.* 2004;18:687-95.
 32. Chhabra A, Zijerdi D, Zhang J, Kline A, Balian G, Hurwitz S. BMP-14 deficiency inhibits long bone fracture healing: a biochemical, histologic, and radiographic assessment. *J Orthop Trauma.* 2005;19:629-34.
 - 33.

- Lehmann W, Schinke T, Schilling AF, Catala-Lehnen P, Gebauer M, Pogoda P, Gerstenfeld LC, Rueger JM, Einhorn TA, Amling M. Absence of mouse pleiotrophin does not affect bone formation in vivo. *Bone*. 2004;35:1247-55.
34. Li M, Healy DR, Li Y, Simmons HA, Crawford DT, Ke HZ, Pan LC, Brown TA, Thompson DD. Osteopenia and impaired fracture healing in aged EP4 receptor knockout mice. *Bone*. 2005;37:46-54.
35. Ohta S, Muramatsu H, Senda T, Zou K, Iwata H, Muramatsu T. Midkine is expressed during repair of bone fracture and promotes chondrogenesis. *J Bone Miner Res*. 1999;14:1132-44.
36. Sakano S, Zhu Y, Sandell LJ. Cartilage-derived retinoic acid-sensitive protein and type II collagen expression during fracture healing are potential targets for Sox9 regulation. *J Bone Miner Res*. 1999;14:1891-901. Erratum in: *J Bone Miner Res*. 2000;15:609.
37. Kon T, Cho TJ, Aizawa T, Yamazaki M, Nooh N, Graves D, Gerstenfeld LC, Einhorn TA. Expression of osteoprotegerin, receptor activator of NF-kappaB ligand (osteoprotegerin ligand) and related proinflammatory cytokines during fracture healing. *J Bone Miner Res*. 2001;16:1004-14.
38. Cho TJ, Gerstenfeld LC, Einhorn TA. Differential temporal expression of members of the transforming growth factor beta superfamily during murine fracture healing. *J Bone Miner Res*. 2002;17:513-20.
39. Gerstenfeld LC, Cho TJ, Kon T, Aizawa T, Tsay A, Fitch J, Barnes GL, Graves DT, Einhorn TA. Impaired fracture healing in the absence of TNF-alpha signaling: the role of TNF-alpha in endochondral cartilage resorption. *J Bone Miner Res*. 2003;18:1584-92.
40. Duvall CL, Taylor WR, Weiss D, Wojtowicz AM, Guldborg RE. Impaired angiogenesis, early callus formation, and late stage remodeling in fracture healing of osteopontin-deficient mice. *J Bone Miner Res*. 2007;22:286-97.
41. Komatsu DE, Bosch-Marce M, Semenza GL, Hadjiargyrou M. Enhanced bone regeneration associated with decreased apoptosis in mice with partial HIF-1alpha deficiency. *J Bone Miner Res*. 2007;22:366-74.
42. Thompson Z, Miclau T, Hu D, Helms JA. A model for intramembranous ossification during fracture healing. *J Orthop Res*. 2002;20:1091-8.
43. Ibiwoye MO, Powell KA, Grabiner MD, Patterson TE, Sakai Y, Zborowski M, Wolfman A, Midura RJ. Bone mass is preserved in a critical-sized osteotomy by low energy pulsed electromagnetic fields as quantitated by in vivo micro-computed tomography. *J Orthop Res*. 2004;22:1086-93.
44. Landry PS, Sadasivan KK, Marino AA, Albright JA. Electromagnetic fields can affect osteogenesis by increasing the rate of differentiation. *Clin Orthop Relat Res*. 1997;338:262-70.
45. Peng H, Usas A, Gearhart B, Olshanski A, Shen HC, Huard J. Converse relationship between in vitro osteogenic differentiation and in vivo bone healing elicited by different populations of muscle-derived cells genetically engineered to express BMP4. *J Bone Miner Res*. 2004;19:630-41.
46. Kaigler D, Wang Z, Horger K, Mooney DJ, Krebsbach PH. VEGF scaffolds enhance angiogenesis and bone regeneration in irradiated osseous defects. *J Bone Miner Res*. 2006;21:735-44.
47. Hsu WK, Sugiyama O, Park SH, Conduah A, Feeley BT, Liu NQ, Krenek L, Virk MS, An DS, Chen IS, Lieberman JR. Lentiviral-mediated BMP-2 gene transfer enhances healing of segmental femoral defects in rats. *Bone*. 2007;40:931-8.
48. Sugimoto M, Hirota S, Sato M, Kawahata H, Tsukamoto I, Yasui N, Kitamura Y, Ochi T, Nomura S. Impaired expression of noncollagenous bone matrix protein mRNAs during fracture healing in ascorbic acid-deficient rats. *J Bone Miner Res*. 1998;13:271-8.
49. Sakai R, Miwa K, Eto Y. Local administration of activin promotes fracture healing in the rat fibula fracture model. *Bone*. 1999;25:191-6.
50. Tamura S, Kataoka H, Matsui Y, Shionoya Y, Ohno K, Michi KI, Takahashi K, Yamaguchi A. The effects of transplantation of osteoblastic cells with bone morphogenetic protein (BMP)/carrier complex on bone repair. *Bone*. 2001;29:169-75.
- 51.

- Follak N, Kloting I, Wolf E, Merk H. Histomorphometric evaluation of the influence of the diabetic metabolic state on bone defect healing depending on the defect size in spontaneously diabetic BB/OK rats. *Bone*. 2004;35:144-52.
- 52.**
Chakkalakal DA, Strates BS, Mashoof AA, Garvin KL, Novak JR, Fritz ED, Mollner TJ, McGuire MH. Repair of segmental bone defects in the rat: an experimental model of human fracture healing. *Bone*. 1999;25:321-32.
- 53.**
McDonald AC, Schuijers JA, Shen PJ, Gundlach AL, Grills BL. Expression of galanin and galanin receptor-1 in normal bone and during fracture repair in the rat. *Bone*. 2003;33:788-97.
- 54.**
Uchida S, Sakai A, Kudo H, Otomo H, Watanuki M, Tanaka M, Nagashima M, Nakamura T. Vascular endothelial growth factor is expressed along with its receptors during the healing process of bone and bone marrow after drill-hole injury in rats. *Bone*. 2003;32:491-501.
- 55.**
Roldan JC, Jepsen S, Miller J, Freitag S, Rueger DC, Acil Y, Terheyden H. Bone formation in the presence of platelet-rich plasma vs. bone morphogenetic protein-7. *Bone*. 2004;34:80-90.
- 56.**
Tanaka M, Sakai A, Uchida S, Tanaka S, Nagashima M, Katayama T, Yamaguchi K, Nakamura T. Prostaglandin E2 receptor (EP4) selective agonist (ONO-4819.CD) accelerates bone repair of femoral cortex after drill-hole injury associated with local upregulation of bone turnover in mature rats. *Bone*. 2004;34:940-8.
- 57.**
Lee FY, Hazan EJ, Gebhardt MC, Mankin HJ. Experimental model for allograft incorporation and allograft fracture repair. *J Orthop Res*. 2000;18:303-6.
- 58.**
Chen X, Kidder LS, Lew WD. Osteogenic protein-1 induced bone formation in an infected segmental defect in the rat femur. *J Orthop Res*. 2002;20:142-50.
- 59.**
Amanat N, Brown R, Bilston LE, Little DG. A single systemic dose of pamidronate improves bone mineral content and accelerates restoration of strength in a rat model of fracture repair. *J Orthop Res*. 2005;23:1029-34.
- 60.**
Chen X, Tsukayama DT, Kidder LS, Bourgeault CA, Schmidt AH, Lew WD. Characterization of a chronic infection in an internally-stabilized segmental defect in the rat femur. *J Orthop Res*. 2005;23:816-23.
- 61.**
Shefelbine SJ, Augat P, Claes L, Beck A. Intact fibula improves fracture healing in a rat tibia osteotomy model. *J Orthop Res*. 2005;23:489-93.
- 62.**
Jackson RA, McDonald MM, Nurcombe V, Little DG, Cool SM. The use of heparan sulfate to augment fracture repair in a rat fracture model. *J Orthop Res*. 2006;24:636-44.
- 63.**
Adili A, Bhandari M, Schemitsch EH. The biomechanical effect of high-pressure irrigation on diaphyseal fracture healing in vivo. *J Orthop Trauma*. 2002;16:413-7.
- 64.**
Utvag SE, Grundnes O, Rindal DB, Reikeras O. Influence of extensive muscle injury on fracture healing in rat tibia. *J Orthop Trauma*. 2003;17:430-5.
- 65.**
Tielinen L, Manninen M, Puolakkainen P, Pihlajamaki H, Pohjonen T, Rautavuori J, Törmälä P. Polylactide pin with transforming growth factor beta 1 in delayed osteotomy fixation. *Clin Orthop Relat Res*. 1998;355:312-22.
- 66.**
Nordstrom P, Pihlajamaki H, Toivonen T, Tormala P, Rokkanen P. Tissue response to polyglycolide and polylevolactide pins in osteotomized cancellous bone. *Clin Orthop Relat Res*. 2001;382:247-57.
- 67.**
Vogelin E, Jones NF, Huang JI, Brekke JH, Lieberman JR. Healing of a critical-sized defect in the rat femur with use of a vascularized periosteal flap, a biodegradable matrix, and bone morphogenetic protein. *J Bone Joint Surg Am*. 2005;87:1323-31.
- 68.**
Chen X, Schmidt AH, Tsukayama DT, Bourgeault CA, Lew WD. Recombinant human osteogenic protein-1 induces bone formation in a chronically infected, internally stabilized segmental defect in the rat femur. *J Bone Joint Surg Am*. 2006;88:1510-23.
- 69.**
Wang FS, Yang KD, Kuo YR, Wang CJ, Sheen-Chen SM, Huang HC, Chen YJ. Temporal and spatial expression of bone morphogenetic proteins in extracorporeal shock wave-promoted healing of segmental defect. *Bone*. 2003;32:387-96.
- 70.**

- Chen YJ, Kuo YR, Yang KD, Wang CJ, Sheen Chen SM, Huang HC, Yang YJ, Yi-Chih S, Wang FS. Activation of extracellular signal-regulated kinase (ERK) and p38 kinase in shock wave-promoted bone formation of segmental defect in rats. *Bone*. 2004;34:466-77.
- 71.**
Wildemann B, Bamdad P, Holmer C, Haas NP, Raschke M, Schmidmaier G. Local delivery of growth factors from coated titanium plates increases osteotomy healing in rats. *Bone*. 2004;34:862-8.
- 72.**
Komatsubara S, Mori S, Mashiba T, Nonaka K, Seki A, Akiyama T, Miyamoto K, Cao Y, Manabe T, Norimatsu H. Human parathyroid hormone (1-34) accelerates the fracture healing process of woven to lamellar bone replacement and new cortical shell formation in rat femora. *Bone*. 2005;36:678-87.
- 73.**
Cao Y, Mori S, Mashiba T, Kaji Y, Manabe T, Iwata K, Miyamoto K, Komatsubara S, Yamamoto T. 1Alpha,25-dihydroxy-2beta(3-hydroxypropoxy)vitamin D3 (ED-71) suppressed callus remodeling but did not interfere with fracture healing in rat femora. *Bone*. 2007;40:132-9.
- 74.**
Li J, Mori S, Kaji Y, Mashiba T, Kawanishi J, Norimatsu H. Effect of bisphosphonate (incadronate) on fracture healing of long bones in rats. *J Bone Miner Res*. 1999;14:969-79.
- 75.**
Li J, Mori S, Kaji Y, Kawanishi J, Akiyama T, Norimatsu H. Concentration of bisphosphonate (incadronate) in callus area and its effects on fracture healing in rats. *J Bone Miner Res*. 2000;15:2042-51.
- 76.**
Li C, Mori S, Li J, Kaji Y, Akiyama T, Kawanishi J, Norimatsu H. Long-term effect of incadronate disodium (ym-175) on fracture healing of femoral shaft in growing rats. *J Bone Miner Res*. 2001;16:429-36.
- 77.**
Zhu W, Diwan AD, Lin JH, Murrell GA. Nitric oxide synthase isoforms during fracture healing. *J Bone Miner Res*. 2001;16:535-40.
- 78.**
Zhu W, Murrell GA, Lin J, Gardiner EM, Diwan AD. Localization of nitric oxide synthases during fracture healing. *J Bone Miner Res*. 2002;17:1470-7.
- 79.**
Cao Y, Mori S, Mashiba T, Westmore MS, Ma L, Sato M, Akiyama T, Shi L, Komatsubara S, Miyamoto K, Norimatsu H. Raloxifene, estrogen, and alendronate affect the processes of fracture repair differently in ovariectomized rats. *J Bone Miner Res*. 2002;17:2237-46.
- 80.**
Chen YJ, Kuo YR, Yang KD, Wang CJ, Huang HC, Wang FS. Shock wave application enhances pertussis toxin protein-sensitive bone formation of segmental femoral defect in rats. *J Bone Miner Res*. 2003;18:2169-79.
- 81.**
Ekholm EC, Ravanti L, Kahari V, Paavolainen P, Penttinen RP. Expression of extracellular matrix genes: transforming growth factor (TGF)-beta1 and ras in tibial fracture healing of lathyrictic rats. *Bone*. 2000;27:551-7.
- 82.**
Utvag SE, Rindal DB, Reikeras O. Effects of torsional rigidity on fracture healing: strength and mineralization in rat femora. *J Orthop Trauma*. 1999;13:212-9.
- 83.**
Namkung-Matthai H, Appleyard R, Jansen J, Hao Lin J, Maastricht S, Swain M, Mason RS, Murrell GA, Diwan AD, Diamond T. Osteoporosis influences the early period of fracture healing in a rat osteoporotic model. *Bone*. 2001;28:80-6.
- 84.**
Little DG, McDonald M, Bransford R, Godfrey CB, Amanat N. Manipulation of the anabolic and catabolic responses with OP-1 and zoledronic acid in a rat critical defect model. *J Bone Miner Res*. 2005;20:2044-52.
- 85.**
Smith-Adaline EA, Volkman SK, Ignelzi MA Jr, Slade J, Platte S, Goldstein SA. Mechanical environment alters tissue formation patterns during fracture repair. *J Orthop Res*. 2004;22:1079-85.
- 86.**
Borrelli J Jr, Tinsley K, Ricci WM, Burns M, Karl IE, Hotchkiss R. Induction of chondrocyte apoptosis following impact load. *J Orthop Trauma*. 2003;17:635-41.
- 87.**
Baldik Y, Talu U, Altinel L, Bilge H, Demiryont M, Aykac-Toker G. Bone healing regulated by nitric oxide: an experimental study in rats. *Clin Orthop Relat Res*. 2002;404:343-52.
- 88.**
Oakes DA, Lee CC, Lieberman JR. An evaluation of human demineralized bone matrices in a rat femoral defect model. *Clin Orthop Relat Res*. 2003;413:281-90.
- 89.**

- Chen H, Frankenburg EP, Goldstein SA, McCauley LK. Combination of local and systemic parathyroid hormone enhances bone regeneration. *Clin Orthop Relat Res.* 2003;416:291-302.
- 90.**
Aronson J. Modulation of distraction osteogenesis in the aged rat by fibroblast growth factor. *Clin Orthop Relat Res.* 2004;425:264-83.
- 91.**
Mark H, Nilsson A, Nannmark U, Rydevik B. Effects of fracture fixation stability on ossification in healing fractures. *Clin Orthop Relat Res.* 2004;419:245-50.
- 92.**
Lane JM, Yasko AW, Tomin E, Cole BJ, Waller S, Browne M, Turek T, Gross J. Bone marrow and recombinant human bone morphogenetic protein-2 in osseous repair. *Clin Orthop Relat Res.* 1999;361:216-27.
- 93.**
Takamine Y, Tsuchiya H, Kitakoji T, Kurita K, Ono Y, Ohshima Y, Kitoh H, Ishiguro N, Iwata H. Distraction osteogenesis enhanced by osteoblastlike cells and collagen gel. *Clin Orthop Relat Res.* 2002;399:240-6.
- 94.**
Millett PJ, Allen MJ, Bostrom MP. Effects of alendronate on particle-induced osteolysis in a rat model. *J Bone Joint Surg Am.* 2002;84:236-49.
- 95.**
Betz OB, Betz VM, Nazarian A, Pilapil CG, Vrahas MS, Bouxsein ML, Gerstenfeld LC, Einhorn TA, Evans CH. Direct percutaneous gene delivery to enhance healing of segmental bone defects. *J Bone Joint Surg Am.* 2006;88:355-65.
- 96.**
Meinel L, Betz O, Fajardo R, Hofmann S, Nazarian A, Cory E, Hilbe M, McCool J, Langer R, Vunjak-Novakovic G, Merkle HP, Rechenberg B, Kaplan DL, Kirker-Head C. Silk based biomaterials to heal critical sized femur defects. *Bone.* 2006;39:922-31.
- 97.**
Loboa EG, Fang TD, Warren SM, Lindsey DP, Fong KD, Longaker MT, Carter DR. Mechanobiology of mandibular distraction osteogenesis: experimental analyses with a rat model. *Bone.* 2004;34:336-43.
- 98.**
Sato M, Yasui N, Nakase T, Kawahata H, Sugimoto M, Hirota S, Kitamura Y, Nomura S, Ochi T. Expression of bone matrix proteins mRNA during distraction osteogenesis. *J Bone Miner Res.* 1998;13:1221-31.
- 99.**
Sato M, Ochi T, Nakase T, Hirota S, Kitamura Y, Nomura S, Yasui N. Mechanical tension-stress induces expression of bone morphogenetic protein (BMP)-2 and BMP-4, but not BMP-6, BMP-7, and GDF-5 mRNA, during distraction osteogenesis. *J Bone Miner Res.* 1999;14:1084-95.
- 100.**
Richards M, Kozloff KM, Goulet JA, Goldstein SA. Increased distraction rates influence precursor tissue composition without affecting bone regeneration. *J Bone Miner Res.* 2000;15:982-9.
- 101.**
Fang TD, Salim A, Xia W, Nacamuli RP, Guccione S, Song HM, Carano RA, Filvaroff EH, Bednarski MD, Giaccia AJ, Longaker MT. Angiogenesis is required for successful bone induction during distraction osteogenesis. *J Bone Miner Res.* 2005;20:1114-24.
- 102.**
Harrison LJ, Cunningham JL, Stromberg L, Goodship AE. Controlled induction of a pseudoarthrosis: a study using a rodent model. *J Orthop Trauma.* 2003;17:11-21.
- 103.**
Tami AE, Nasser P, Schaffler MB, Knothe Tate ML. Noninvasive fatigue fracture model of the rat ulna. *J Orthop Res.* 2003;21:1018-24.
- 104.**
Rundle CH, Miyakoshi N, Ramirez E, Wergedal JE, Lau KH, Baylink DJ. Expression of the fibroblast growth factor receptor genes in fracture repair. *Clin Orthop Relat Res.* 2002;403:253-63.
- 105.**
Walsh WR, Sherman P, Howlett CR, Sonnabend DH, Ehrlich MG. Fracture healing in a rat osteopenia model. *Clin Orthop Relat Res.* 1997;342:218-27.
- 106.**
Holzer G, Majeska RJ, Lundy MW, Hartke JR, Einhorn TA. Parathyroid hormone enhances fracture healing. A preliminary report. *Clin Orthop Relat Res.* 1999;366:258-63.
- 107.**
Nakajima F, Ogasawara A, Goto K, Moriya H, Ninomiya Y, Einhorn TA, Yamazaki M. Spatial and temporal gene expression in chondrogenesis during fracture healing and the effects of basic fibroblast growth factor. *J Orthop Res.* 2001;19:935-44.
- 108.**

- Delgado-Martinez AD, Martinez ME, Carrascal MT, Rodriguez-Avial M, Munuera L. Effect of 25-OH-vitamin D on fracture healing in elderly rats. *J Orthop Res.* 1998;16:650-3.
- 109.**
Probst A, Jansen H, Ladas A, Spiegel HU. Callus formation and fixation rigidity: a fracture model in rats. *J Orthop Res.* 1999;17:256-60.
- 110.**
Hankemeier S, Grassel S, Plenz G, Spiegel HU, Bruckner P, Probst A. Alteration of fracture stability influences chondrogenesis, osteogenesis and immigration of macrophages. *J Orthop Res.* 2001;19:531-8.
- 111.**
Ford JL, Robinson DE, Scammell BE. The fate of soft callus chondrocytes during long bone fracture repair. *J Orthop Res.* 2003;21:54-61.
- 112.**
Kokubu T, Hak DJ, Hazelwood SJ, Reddi AH. Development of an atrophic nonunion model and comparison to a closed healing fracture in rat femur. *J Orthop Res.* 2003;21:503-10.
- 113.**
Li RH, Bouxsein ML, Blake CA, D'Augusta D, Kim H, Li XJ, Wozney JM, Seeherman HJ. rhBMP-2 injected in a calcium phosphate paste (alpha-BSM) accelerates healing in the rabbit ulnar osteotomy model. *J Orthop Res.* 2003;21:997-1004.
- 114.**
Makino T, Hak DJ, Hazelwood SJ, Curtiss S, Reddi AH. Prevention of atrophic nonunion development by recombinant human bone morphogenetic protein-7. *J Orthop Res.* 2004;23:632-8.
- 115.**
Schmidmaier G, Wildemann B, Ostapowicz D, Kandziora F, Stange R, Haas NP, Raschke M. Long-term effects of local growth factor (IGF-I and TGF-beta 1) treatment on fracture healing. A safety study for using growth factors. *J Orthop Res.* 2004;22:514-9.
- 116.**
Wang H, Li X, Tomin E, Doty SB, Lane JM, Carney DH, Ryaby JT. Thrombin peptide (TP508) promotes fracture repair by up-regulating inflammatory mediators, early growth factors, and increasing angiogenesis. *J Orthop Res.* 2005;23:671-9.
- 117.**
Claes L, Maurer-Klein N, Henke T, Gerngross H, Melnyk M, Augat P. Moderate soft tissue trauma delays new bone formation only in the early phase of fracture healing. *J Orthop Res.* 2006;24:1178-85.
- 118.**
Hak DJ, Stewart RL, Hazelwood SJ. Effect of low molecular weight heparin on fracture healing in a stabilized rat femur fracture model. *J Orthop Res.* 2006;24:645-52.
- 119.**
Wheeler DL, Eschbach EJ, Montfort MJ, Maheshwari P, McLoughlin SW. Mechanical strength of fracture callus in osteopenic bone at different phases of healing. *J Orthop Trauma.* 2000;14:86-92.
- 120.**
Tyndall WA, Beam HA, Zarro C, O'Connor JP, Lin SS. Decreased platelet derived growth factor expression during fracture healing in diabetic animals. *Clin Orthop Relat Res.* 2003;408:319-30.
- 121.**
Haleem AA, Rouse MS, Lewallen DG, Hanssen AD, Steckelberg JM, Patel R. Gentamicin and vancomycin do not impair experimental fracture healing. *Clin Orthop Relat Res.* 2004;427:22-4.
- 122.**
Oztuna V, Ersoz G, Ayan I, Eskandari MM, Colak M, Polat A. Early internal fracture fixation prevents bacterial translocation. *Clin Orthop Relat Res.* 2006;446:253-8.
- 123.**
Madsen JE, Hukkanen M, Aune AK, Basran I, Moller JF, Polak JM, Nordsletten L. Fracture healing and callus innervation after peripheral nerve resection in rats. *Clin Orthop Relat Res.* 1998;351:230-40.
- 124.**
Einhorn TA, Majeska RJ, Mohaideen A, Kagel EM, Bouxsein ML, Turek TJ, Wozney JM. A single percutaneous injection of recombinant human bone morphogenetic protein-2 accelerates fracture repair. *J Bone Joint Surg Am.* 2003;85:1425-35.
- 125.**
Brown KM, Saunders MM, Kirsch T, Donahue HJ, Reid JS. Effect of COX-2-specific inhibition on fracture-healing in the rat femur. *J Bone Joint Surg Am.* 2004;86:116-23.
- 126.**
Alkhiary YM, Gerstenfeld LC, Krall E, Westmore M, Sato M, Mitlak BH, Einhorn TA. Enhancement of experimental fracture-healing by systemic administration of recombinant human parathyroid hormone (PTH 1-34). *J Bone Joint Surg Am.* 2005;87:731-41.
- 127.**

- Gerstenfeld LC, Al-Ghawas M, Alkhiary YM, Cullinane DM, Krall EA, Fitch JL, Webb EG, Thiede MA, Einhorn TA. Selective and nonselective cyclooxygenase-2 inhibitors and experimental fracture-healing. Reversibility of effects after short-term treatment. *J Bone Joint Surg Am.* 2007;89:114-25.
- 128.**
Simon AM, O'Connor JP. Dose and time-dependent effects of cyclooxygenase-2 inhibition on fracture-healing. *J Bone Joint Surg Am.* 2007;89:500-11.
- 129.**
Rundle CH, Miyakoshi N, Kasukawa Y, Chen ST, Sheng MH, Wergedal JE, Lau KH, Baylink DJ. In vivo bone formation in fracture repair induced by direct retroviral-based gene therapy with bone morphogenetic protein-4. *Bone.* 2003;32:591-601.
- 130.**
Voggenreiter G, Siozos P, Hunkemoller E, Heute S, Schwarz M, Obertacke U. Immunosuppression with FK506 has no influence on fracture healing in the rat. *Bone.* 2005;37:227-33.
- 131.**
Azuma Y, Ito M, Harada Y, Takagi H, Ohta T, Jingushi S. Low-intensity pulsed ultrasound accelerates rat femoral fracture healing by acting on the various cellular reactions in the fracture callus. *J Bone Miner Res.* 2001;16:671-80.
- 132.**
Hadjjiargyrou M, Rightmire EP, Ando T, Lombardo FT. The E11 osteoblastic lineage marker is differentially expressed during fracture healing. *Bone.* 2001;29:149-54.
- 133.**
Hausman MR, Schaffler MB, Majeska RJ. Prevention of fracture healing in rats by an inhibitor of angiogenesis. *Bone.* 2001;29:560-4.
- 134.**
Nakajima A, Nakajima F, Shimizu S, Ogasawara A, Wanaka A, Moriya H, Einhorn TA, Yamazaki M. Spatial and temporal gene expression for fibroblast growth factor type I receptor (FGFR1) during fracture healing in the rat. *Bone.* 2001;29:458-66.
- 135.**
Schmidmaier G, Wildemann B, Bail H, Lucke M, Fuchs T, Stemberger A, Flyvbjerg A, Haas NP, Raschke M. Local application of growth factors (insulin-like growth factor-1 and transforming growth factor-beta1) from a biodegradable poly(D,L-lactide) coating of osteosynthetic implants accelerates fracture healing in rats. *Bone.* 2001;28:341-50.
- 136.**
Schmidmaier G, Wildemann B, Cromme F, Kandziora F, Haas NP, Raschke M. Bone morphogenetic protein-2 coating of titanium implants increases biomechanical strength and accelerates bone remodeling in fracture treatment: a biomechanical and histological study in rats. *Bone.* 2002;30:816-22.
- 137.**
Schmidmaier G, Wildemann B, Heeger J, Gabelein T, Flyvbjerg A, Bail HJ, Raschke M. Improvement of fracture healing by systemic administration of growth hormone and local application of insulin-like growth factor-1 and transforming growth factor-beta1. *Bone.* 2002;31:165-72.
- 138.**
Pacicca DM, Patel N, Lee C, Salisbury K, Lehmann W, Carvalho R, Gerstenfeld LC, Einhorn TA. Expression of angiogenic factors during distraction osteogenesis. *Bone.* 2003;33:889-98.
- 139.**
Nakazawa T, Nakajima A, Shiomi K, Moriya H, Einhorn TA, Yamazaki M. Effects of low-dose, intermittent treatment with recombinant human parathyroid hormone (1-34) on chondrogenesis in a model of experimental fracture healing. *Bone.* 2005;37:711-9.
- 140.**
Rundle CH, Wang H, Yu H, Chadwick RB, Davis EI, Wergedal JE, Lau KH, Mohan S, Ryaby JT, Baylink DJ. Microarray analysis of gene expression during the inflammation and endochondral bone formation stages of rat femur fracture repair. *Bone.* 2006;38:521-9.
- 141.**
Diwan AD, Wang MX, Jang D, Zhu W, Murrell GA. Nitric oxide modulates fracture healing. *J Bone Miner Res.* 2000;15:342-51.
- 142.**
Hadjjiargyrou M, Ahrens W, Rubin CT. Temporal expression of the chondrogenic and angiogenic growth factor CYR61 during fracture repair. *J Bone Miner Res.* 2000;15:1014-23.
- 143.**
Li M, Ke HZ, Qi H, Healy DR, Li Y, Crawford DT, Paralkar VM, Owen TA, Cameron KO, Lefker BA, Brown TA, Thompson DD. A novel, non-prostanoid EP2 receptor-selective prostaglandin E2 agonist stimulates local bone formation and enhances fracture healing. *J Bone Miner Res.* 2003;18:2033-42.
- 144.**

- Onishi T, Ishidou Y, Nagamine T, Yone K, Imamura T, Kato M, Sampath TK, ten Dijke P, Sakou T. Distinct and overlapping patterns of localization of bone morphogenetic protein (BMP) family members and a BMP type II receptor during fracture healing in rats. *Bone*. 1998;22:605-12.
- 145.**
Li J, Ahmad T, Spetea M, Ahmed M, Kreicbergs A. Bone reinnervation after fracture: a study in the rat. *J Bone Miner Res*. 2001;16:1505-10.
- 146.**
Ulrich-Vinther M, Schwarz EM, Pedersen FS, Soballe K, Andreassen TT. Gene therapy with human osteoprotegerin decreases callus remodeling with limited effects on biomechanical properties. *Bone*. 2005;37:751-8.
- 147.**
Gandhi A, Beam HA, O'Connor JP, Parsons JR, Lin SS. The effects of local insulin delivery on diabetic fracture healing. *Bone*. 2005;37:482-90.
- 148.**
Gandhi A, Dumas C, O'Connor JP, Parsons JR, Lin SS. The effects of local platelet rich plasma delivery on diabetic fracture healing. *Bone*. 2006;38:540-6. Erratum in: *Bone*. 2006;38:957.
- 149.**
Andreassen TT, Ejersted C, Oxlund H. Intermittent parathyroid hormone (1-34) treatment increases callus formation and mechanical strength of healing rat fractures. *J Bone Miner Res*. 1999;14:960-8.
- 150.**
Amanat N, McDonald M, Godfrey C, Bilston L, Little D. Optimal timing of a single dose of zoledronic acid to increase strength in rat fracture repair. *J Bone Miner Res*. 2007;22:867-76.
- 151.**
Boes M, Kain M, Kakar S, Nicholls F, Cullinane D, Gerstenfeld L, Einhorn TA, Tornetta P 3rd. Osteogenic effects of traumatic brain injury on experimental fracture-healing. *J Bone Joint Surg Am*. 2006;88:738-43. Erratum in: *J Bone Joint Surg Am*. 2006;88:1602.
- 152.**
Huddleston PM, Steckelberg JM, Hanssen AD, Rouse MS, Bolander ME, Patel R. Ciprofloxacin inhibition of experimental fracture healing. *J Bone Joint Surg Am*. 2000;82:161-73.
- 153.**
Lill CA, Hessel J, Schlegel U, Eckhardt C, Goldhahn J, Schneider E. Biomechanical evaluation of healing in a non-critical defect in a large animal model of osteoporosis. *J Orthop Res*. 2003;21:836-42.
- 154.**
Bertone AL, Pittman DD, Bouxsein ML, Li J, Clancy B, Seeherman HJ. Adenoviral-mediated transfer of human BMP-6 gene accelerates healing in a rabbit ulnar osteotomy model. *J Orthop Res*. 2004;22:1261-70.
- 155.**
Okubo Y, Bessho K, Fujimura K, Kusumoto K, Ogawa Y, Iizuka T. Osteogenesis by recombinant human bone morphogenetic protein-2 at skeletal sites. *Clin Orthop Relat Res*. 2000;375:295-301.
- 156.**
Lee EW, Dirschl DR, Duff G, Dahners LE, Miclau T. High-pressure pulsatile lavage irrigation of fresh intraarticular fractures: effectiveness at removing particulate matter from bone. *J Orthop Trauma*. 2002;16:162-5.
- 157.**
Wang J. Spatial orientation of the microscopic elements of cortical repair bone. *Clin Orthop Relat Res*. 2000;374:265-77.
- 158.**
Vonau RL, Bostrom MP, Aspenberg P, Sams AE. Combination of growth factors inhibits bone ingrowth in the bone harvest chamber. *Clin Orthop Relat Res*. 2001;386:243-51.
- 159.**
Zegzula HD, Buck DC, Brekke J, Wozney JM, Hollinger JO. Bone formation with use of rhBMP-2 (recombinant human bone morphogenetic protein-2). *J Bone Joint Surg Am*. 1997;79:1778-90.
- 160.**
Bouxsein ML, Turek TJ, Blake CA, D'Augusta D, Li X, Stevens M, Seeherman HJ, Wozney JM. Recombinant human bone morphogenetic protein-2 accelerates healing in a rabbit ulnar osteotomy model. *J Bone Joint Surg Am*. 2001;83:1219-30.
- 161.**
De Man FH, Tigchelaar W, Marti RK, Van Noorden CJ, Van der Vis HM. Effects of mechanical compression of a fibrous tissue interface on bone with or without high-density polyethylene particles in a rabbit model of prosthetic loosening. *J Bone Joint Surg Am*. 2005;87:1522-33.
- 162.**
Seeherman HJ, Azari K, Bidic S, Rogers L, Li XJ, Hollinger JO, Wozney JM. rhBMP-2 delivered in calcium phosphate cement accelerates bridging of critical-sized defects in rabbit radii. *J Bone Joint Surg Am*. 2006;88:1553-65.
- 163.**

- Laffargue P, Hildebrand HF, Rtaimate M, Frayssinet P, Amoureux JP, Marchandise X. Evaluation of human recombinant bone morphogenetic protein-2-loaded tricalcium phosphate implants in rabbits' bone defects. *Bone*. 1999;25(2 Suppl):55S-58S.
- 164.**
Sebecic B, Nikolic V, Sikiric P, Seiwerth S, Sosa T, Patrlj L, Grabarević Z, Rucman R, Petek M, Konjevoda P, Jadrijević S, Perović D, Slaj M. Osteogenic effect of a gastric pentadecapeptide, BPC-157, on the healing of segmental bone defect in rabbits: a comparison with bone marrow and autologous cortical bone implantation. *Bone*. 1999;24:195-202.
- 165.**
Luppen CA, Blake CA, Ammirati KM, Stevens ML, Seeherman HJ, Wozney JM, Bouxsein ML. Recombinant human bone morphogenetic protein-2 enhances osteotomy healing in glucocorticoid-treated rabbits. *J Bone Miner Res*. 2002;17:301-10.
- 166.**
Geiger F, Bertram H, Berger I, Lorenz H, Wall O, Eckhardt C, Simank HG, Richter W. Vascular endothelial growth factor gene-activated matrix (VEGF165-GAM) enhances osteogenesis and angiogenesis in large segmental bone defects. *J Bone Miner Res*. 2005;20:2028-35.
- 167.**
Caprise PA Jr, Miclau T, Dahners LE, Dirschl DR. High-pressure pulsatile lavage irrigation of contaminated fractures: effects on fracture healing. *J Orthop Res*. 2002;20:1205-9.
- 168.**
Gerstenfeld LC, Thiede M, Seibert K, Mielke C, Phippard D, Svagr B, Cullinane D, Einhorn TA. Differential inhibition of fracture healing by non-selective and cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs. *J Orthop Res*. 2003;21:670-5.
- 169.**
Southwood LL, Frisbie DD, Kawcak CE, Ghivizzani SC, Evans CH, McIlwraith CW. Evaluation of Ad-BMP-2 for enhancing fracture healing in an infected defect fracture rabbit model. *J Orthop Res*. 2004;22:66-72.
- 170.**
Dirschl DR, Duff GP, Dahners LE, Edin M, Rahn BA, Miclau T. High pressure pulsatile lavage irrigation of intraarticular fractures: effects on fracture healing. *J Orthop Trauma*. 1998;12:460-3.
- 171.**
Reynders P, Becker JH, Broos P. Osteogenic ability of free periosteal autografts in tibial fractures with severe soft tissue damage: an experimental study. *J Orthop Trauma*. 1999;13:121-8.
- 172.**
Polzin B, Ellis T, Dirschl DR. Effects of varying pulsatile lavage pressure on cancellous bone structure and fracture healing. *J Orthop Trauma*. 2006;20:261-6.
- 173.**
Lattermann C, Baltzer AW, Zelle BA, Whalen JD, Niyibizi C, Robbins PD, Evans CH, Gruen GS. Feasibility of percutaneous gene transfer to an atrophic nonunion in a rabbit. *Clin Orthop Relat Res*. 2004;425:237-43.
- 174.**
Christodoulou A, Givissis P, Mavromatis I, Karkavelas G, Pournaras J. Fracture callus engulfing a peripheral nerve does not affect its function: an experimental study in rabbits. *Clin Orthop Relat Res*. 2005;433:195-204.
- 175.**
Balint L, Park SH, Bellyei A, Luck JV Jr, Sarmiento A, Lovasz G. Repair of steps and gaps in articular fracture models. *Clin Orthop Relat Res*. 2005;430:208-18.
- 176.**
Raikin SM, Landsman JC, Alexander VA, Froimson MI, Plaxton NA. Effect of nicotine on the rate and strength of long bone fracture healing. *Clin Orthop Relat Res*. 1998;353:231-7.
- 177.**
DeCoster TA, Simpson AH, Wood M, Li G, Kenwright J. Biologic model of bone transport distraction osteogenesis and vascular response. *J Orthop Res*. 1999;17:238-45.
- 178.**
Park SH, Silva M. Neuromuscular electrical stimulation enhances fracture healing: results of an animal model. *J Orthop Res*. 2004;22:382-7.
- 179.**
Meffert RH, Inoue N, Tis JE, Brug E, Chao EY. Distraction osteogenesis after acute limb-shortening for segmental tibial defects. Comparison of a monofocal and a bifocal technique in rabbits. *J Bone Joint Surg Am*. 2000;82:799-808.
- 180.**
Park SH, Silva M, Bahk WJ, McKellop H, Lieberman JR. Effect of repeated irrigation and debridement on fracture healing in an animal model. *J Orthop Res*. 2002;20:1197-204.
- 181.**

- Li G, Ryaby JT, Carney DH, Wang H. Bone formation is enhanced by thrombin-related peptide TP508 during distraction osteogenesis. *J Orthop Res.* 2005;23:196-202.
- 182.**
Mori S, Akagi M, Kikuyama A, Yasuda Y, Hamanishi C. Axial shortening during distraction osteogenesis leads to enhanced bone formation in a rabbit model through the HIF-1 α /vascular endothelial growth factor system. *J Orthop Res.* 2006;24:653-63.
- 183.**
Park SH, O'Connor K, Sung R, McKellop H, Sarmiento A. Comparison of healing process in open osteotomy model and closed fracture model. *J Orthop Trauma.* 1999;13:114-20.
- 184.**
Fredericks DC, Piehl DJ, Baker JT, Abbott J, Nepola JV. Effects of pulsed electromagnetic field stimulation on distraction osteogenesis in the rabbit tibial leg lengthening model. *J Pediatr Orthop.* 2003;23:478-83.
- 185.**
Uglow MG, Peat RA, Hile MS, Bilston LE, Smith EJ, Little DG. Low-intensity ultrasound stimulation in distraction osteogenesis in rabbits. *Clin Orthop Relat Res.* 2003;417:303-12.
- 186.**
Kokoroghiannis C, Papaioannou N, Lyritis G, Katsiri M, Kalogera P. Calcitonin administration in a rabbit distraction osteogenesis model. *Clin Orthop Relat Res.* 2003;415:286-92.
- 187.**
Taylor KF, Rafiee B, Inoue N, McHale KA, Howard RS, Chao EY. Linear increase in axial stiffness of regenerate callus during limb lengthening. *Clin Orthop Relat Res.* 2005;435:239-44.
- 188.**
Sailhan F, Chotel F, Chousta A, Viguier E, Boivin G. Unexpected absence of effect of rhBMP-7 on distraction osteogenesis. *Clin Orthop Relat Res.* 2007;457:227-34.
- 189.**
Taylor KF, Rafiee B, Tis JE, Inoue N. Low-intensity pulsed ultrasound does not enhance distraction callus in a rabbit model. *Clin Orthop Relat Res.* 2007;459:237-45.
- 190.**
Waanders NA, Richards M, Steen H, Kuhn JL, Goldstein SA, Goulet JA. Evaluation of the mechanical environment during distraction osteogenesis. *Clin Orthop Relat Res.* 1998;349:225-34.
- 191.**
Kanbe K, Hasegawa A, Takagishi K, Shirakura K, Nagase M, Yanagawa T, Tomiyoshi K. Analysis of muscle bioenergetic metabolism in rabbit leg lengthening. *Clin Orthop Relat Res.* 1998;351:214-21.
- 192.**
Richards M, Goulet JA, Weiss JA, Waanders NA, Schaffler MB, Goldstein SA. Bone regeneration and fracture healing. Experience with distraction osteogenesis model. *Clin Orthop Relat Res.* 1998;355 Suppl:S191-204.
- 193.**
Jarka DE, Nicholas RW, Aronson J. Effect of methotrexate on distraction osteogenesis. *Clin Orthop Relat Res.* 1998;354:209-15.
- 194.**
Meffert RH, Tis JE, Inoue N, McCarthy EF, Brug E, Chao EY. Primary resective shortening followed by distraction osteogenesis for limb reconstruction: a comparison with simple lengthening. *J Orthop Res.* 2000;18:629-36.
- 195.**
Park SH, Silva M. Effect of intermittent pneumatic soft-tissue compression on fracture-healing in an animal model. *J Bone Joint Surg Am.* 2003;85:1446-53.
- 196.**
Yamane K, Okano T, Kishimoto H, Hagino H. Effect of ED-71 on modeling of bone in distraction osteogenesis. *Bone.* 1999;24:187-93.
- 197.**
Takahashi M, Yukata K, Matsui Y, Abbaspour A, Takata S, Yasui N. Bisphosphonate modulates morphological and mechanical properties in distraction osteogenesis through inhibition of bone resorption. *Bone.* 2006;39:573-81.
- 198.**
Rauch F, Lauzier D, Travers R, Glorieux F, Hamdy R. Effects of locally applied transforming growth factor-beta1 on distraction osteogenesis in a rabbit limb-lengthening model. *Bone.* 2000;26:619-24.
- 199.**
Rauch F, Lauzier D, Croteau S, Travers R, Glorieux FH, Hamdy R. Temporal and spatial expression of bone morphogenetic protein-2, -4, and -7 during distraction osteogenesis in rabbits. *Bone.* 2000;27:453-9.
- 200.**
Hamdy RC, Amako M, Beckman L, Kawaguchi M, Rauch F, Lauzier D, Steffen T. Effects of osteogenic protein-1 on distraction osteogenesis in rabbits. *Bone.* 2003;33:248-55.
- 201.**

- Little DG, Smith NC, Williams PR, Briody JN, Bilston LE, Smith EJ, Gardiner EM, Cowell CT. Zoledronic acid prevents osteopenia and increases bone strength in a rabbit model of distraction osteogenesis. *J Bone Miner Res.* 2003;18:1300-7.
- 202.**
Smith EJ, McEvoy A, Little DG, Baldock PA, Eisman JA, Gardiner EM. Transient retention of endochondral cartilaginous matrix with bisphosphonate treatment in a long-term rabbit model of distraction osteogenesis. *J Bone Miner Res.* 2004;19:1698-705.
- 203.**
Shirley D, Marsh D, Jordan G, McQuaid S, Li G. Systemic recruitment of osteoblastic cells in fracture healing. *J Orthop Res.* 2005;23:1013-21.
- 204.**
Street JT, McGrath M, O'Regan K, Wakai A, McGuinness A, Redmond HP. Thromboprophylaxis using a low molecular weight heparin delays fracture repair. *Clin Orthop Relat Res.* 2000;381:278-89.
- 205.**
Park SH, O'Connor K, McKellop H, Sarmiento A. The influence of active shear or compressive motion on fracture-healing. *J Bone Joint Surg Am.* 1998;80:868-78.
- 206.**
Walsh WR, Morberg P, Yu Y, Yang JL, Haggard W, Sheath PC, Svehla M, Bruce WJ. Response of a calcium sulfate bone graft substitute in a confined cancellous defect. *Clin Orthop Relat Res.* 2003;406:228-36.
- 207.**
Mousavi M, David R, Schwendenwein I, Schaden E, Marlovits S, Kolonja A, Schwanzer E, Heinz T, Vécsei V. Influence of controlled reaming on fat intravasation after femoral osteotomy in sheep. *Clin Orthop Relat Res.* 2002;394:263-70.
- 208.**
Bertone A, Lipson D, Kamei J, Litsky A, Weisbrode S. Effective bone hemostasis and healing using radiofrequency and conductive fluid. *Clin Orthop Relat Res.* 2006;446:278-85.
- 209.**
Hill PF, Clasper JC, Parker SJ, Watkins PE. Early intramedullary nailing in an animal model of a heavily contaminated fracture of the tibia. *J Orthop Res.* 2002;20:648-53.
- 210.**
den Boer FC, Wippermann BW, Blokhuis TJ, Patka P, Bakker FC, Haarman HJ. Healing of segmental bone defects with granular porous hydroxyapatite augmented with recombinant human osteogenic protein-1 or autologous bone marrow. *J Orthop Res.* 2003;21:521-8.
- 211.**
Klein P, Opitz M, Schell H, Taylor WR, Heller MO, Kassi JP, Kandziora F, Duda GN. Comparison of unreamed nailing and external fixation of tibial diastases—mechanical conditions during healing and biological outcome. *J Orthop Res.* 2004;22:1072-8.
- 212.**
Viateau V, Guillemain G, Bousson V, Oudina K, Hannouche D, Sedel L, Logeart-Avramoglou D, Petite H. Long-bone critical-size defects treated with tissue-engineered grafts: a study on sheep. *J Orthop Res.* 2007;25:741-9.
- 213.**
Wolinsky PR, Banit D, Parker RE, Shyr Y, Snapper JR, Rutherford EJ, Johnson KD. Reamed intramedullary femoral nailing after induction of an “ARDS-like” state in sheep: effect on clinically applicable markers of pulmonary function. *J Orthop Trauma.* 1998;12:169-76.
- 214.**
Trumble T, Allan CH, Miyano J, Clark JM, Ott S, Jones DE, Fernicola P, Magnusson M, Tencer A. A preliminary study of joint surface changes after an intraarticular fracture: a sheep model of a tibia fracture with weight bearing after internal fixation. *J Orthop Trauma.* 2001;15:326-32.
- 215.**
Panagiotopoulos E, Fortis AP, Lambiris E, Kostopoulos V. Rigid or sliding plate. A mechanical evaluation of osteotomy fixation in sheep. *Clin Orthop Relat Res.* 1999;358:244-9.
- 216.**
Lucarelli E, Fini M, Beccheroni A, Giavaresi G, Di Bella C, Aldini NN, Guzzardella G, Martini L, Cenacchi A, Di Maggio N, Sangiorgi L, Fornasari PM, Mercuri M, Giardino R, Donati D. Stromal stem cells and platelet-rich plasma improve bone allograft integration. *Clin Orthop Relat Res.* 2005;435:62-8.
- 217.**
Seligson D, Mehta S, Mishra AK, FitzGerald TJ, Castleman DW, James AH, Voor MJ, Been J, Nawab A. In vivo study of stainless steel and Ti-13Nb-13Zr bone plates in a sheep model. *Clin Orthop Relat Res.* 1997;343:213-23.
- 218.**
Kirker-Head CA, Gerhart TN, Armstrong R, Schelling SH, Carmel LA. Healing bone using recombinant human bone morphogenetic protein 2 and copolymer. *Clin Orthop Relat Res.* 1998;349:205-17.
- 219.**

- Regauer M, Jurgens P, Budenhofer U, Hartstock M, Bocker W, Burklein D, Mutschler W, Sader R, Schieker M. Quantitative scanning acoustic microscopy compared to microradiography for assessment of new bone formation. *Bone*. 2006;38:564-70.
- 220.**
Augat P, Margevicius K, Simon J, Wolf S, Suger G, Claes L. Local tissue properties in bone healing: influence of size and stability of the osteotomy gap. *J Orthop Res*. 1998;16:475-81.
- 221.**
Augat P, Burger J, Schorlemmer S, Henke T, Peraus M, Claes L. Shear movement at the fracture site delays healing in a diaphyseal fracture model. *J Orthop Res*. 2003;21:1011-7.
- 222.**
Moore DC, Leblanc CW, Muller R, Crisco JJ 3rd, Ehrlich MG. Physiologic weight-bearing increases new vessel formation during distraction osteogenesis: a micro-tomographic imaging study. *J Orthop Res*. 2003;21:489-96.
- 223.**
Hente R, Fuchtmeier B, Schlegel U, Ernstberger A, Perren SM. The influence of cyclic compression and distraction on the healing of experimental tibial fractures. *J Orthop Res*. 2004;22:709-15.
- 224.**
Lienau J, Schell H, Epari DR, Schutze N, Jakob F, Duda GN, Bail HJ. CYR61 (CCN1) protein expression during fracture healing in an ovine tibial model and its relation to the mechanical fixation stability. *J Orthop Res*. 2006;24:254-62.
- 225.**
Mayr E, Laule A, Suger G, Ruter A, Claes L. Radiographic results of callus distraction aided by pulsed low-intensity ultrasound. *J Orthop Trauma*. 2001;15:407-14.
- 226.**
Lawes TJ, Scott JC, Goodship AE. Increased insertion torque delays pin-bone interface loosening in external fixation with tapered bone screws. *J Orthop Trauma*. 2004;18:617-22.
- 227.**
Wolf S, Augat P, Eckert-Hubner K, Laule A, Krischak GD, Claes LE. Effects of high-frequency, low-magnitude mechanical stimulus on bone healing. *Clin Orthop Relat Res*. 2001;385:192-8.
- 228.**
Claes L, Ruter A, Mayr E. Low-intensity ultrasound enhances maturation of callus after segmental transport. *Clin Orthop Relat Res*. 2005;430:189-94.
- 229.**
Bishop NE, van Rhijn M, Tami I, Corveleijn R, Schneider E, Ito K. Shear does not necessarily inhibit bone healing. *Clin Orthop Relat Res*. 2006;443:307-14.
- 230.**
Reichel H, Lebek S, Alter C, Hein W. Biomechanical and densitometric bone properties after callus distraction in sheep. *Clin Orthop Relat Res*. 1998;357:237-46.
- 231.**
Hantes ME, Mavrodontidis AN, Zalavras CG, Karantanas AH, Karachalios T, Malizos KN. Low-intensity transosseous ultrasound accelerates osteotomy healing in a sheep fracture model. *J Bone Joint Surg Am*. 2004;86:2275-82.
- 232.**
Seebeck P, Bail HJ, Exner C, Schell H, Michel R, Amthauer H, Bragulla H, Duda GN. Do serological tissue turnover markers represent callus formation during fracture healing? *Bone*. 2005;37:669-77.
- 233.**
Malizos KN, Papachristos AA, Protopappas VC, Fotiadis DI. Transosseous application of low-intensity ultrasound for the enhancement and monitoring of fracture healing process in a sheep osteotomy model. *Bone*. 2006;38:530-9.
- 234.**
Schell H, Lienau J, Epari DR, Seebeck P, Exner C, Muchow S, Bragulla H, Haas NP, Duda GN. Osteoclastic activity begins early and increases over the course of bone healing. *Bone*. 2006;38:547-54.
- 235.**
Epari DR, Schell HS, Bail HJ, Duda GN. Instability prolongs the chondral phase during bone healing in sheep. *Bone*. 2006;38:864-70.
- 236.**
Krawczyk A, Kuroпка P, Kuryszko J, Wall A, Dragan S, Kulej M. Experimental studies on the effect of osteotomy technique on the bone regeneration in distraction osteogenesis. *Bone*. 2007;40:781-91.
- 237.**
Keijser LC, Schreuder HW, Boons HW, Keulers BJ, Buma P, Huiskes R, Veth RP. Bone grafting of cryosurgically treated bone defects: experiments in goats. *Clin Orthop Relat Res*. 2002;396:215-22.
- 238.**
Anderson ML, Dhert WJ, de Bruijn JD, Dalmeijer RA, Leenders H, van Blitterswijk CA, Verbout AJ. Critical size defect in the goat's os ilium. A model to evaluate bone grafts and substitutes. *Clin Orthop Relat Res*. 1999;364:231-9.

- 239.**
Lamerigts NM, Buma P, Aspenberg P, Schreurs BW, Slooff TJ. Role of growth factors in the incorporation of unloaded bone allografts in the goat. *Clin Orthop Relat Res.* 1999;368:260-70.
- 240.**
Gravel CA, Le TT, Chapman MW. Effect of neoadjuvant chemotherapy on distraction osteogenesis in the goat model. *Clin Orthop Relat Res.* 2003;412:213-24.
- 241.**
Bolder SB, Schreurs BW, Verdonschot N, Veth RP, Buma P. Wire mesh allows more revascularization than a strut in impaction bone grafting: an animal study in goats. *Clin Orthop Relat Res.* 2004;423:280-6.
- 242.**
Leung KS, Cheung WH, Yeung HY, Lee KM, Fung KP. Effect of weightbearing on bone formation during distraction osteogenesis. *Clin Orthop Relat Res.* 2004;419:251-7.
- 243.**
Yeung HY, Lee SK, Fung KP, Leung KS. Expression of basic fibroblast growth factor during distraction osteogenesis. *Clin Orthop Relat Res.* 2001;385:219-29.
- 244.**
Welch RD, Jones AL, Bucholz RW, Reinert CM, Tjia JS, Pierce WA, Wozney JM, Li XJ. Effect of recombinant human bone morphogenetic protein-2 on fracture healing in a goat tibial fracture model. *J Bone Miner Res.* 1998;13:1483-90.
- 245.**
Starr AJ, Welch RD, Eastridge BJ, Pierce W, Zhang H. The effect of hemorrhagic shock in a caprine tibial fracture model. *J Orthop Trauma.* 2002;16:250-6.
- 246.**
den Boer FC, Bramer JA, Blokhuis TJ, Van Soest EJ, Jenner JM, Patka P, Bakker FC, Burger EH, Haarman HJ. Effect of recombinant human osteogenic protein-1 on the healing of a freshly closed diaphyseal fracture. *Bone.* 2002;31:158-64.
- 247.**
Salkeld SL, Patron LP, Barrack RL, Cook SD. The effect of osteogenic protein-1 on the healing of segmental bone defects treated with autograft or allograft bone. *J Bone Joint Surg Am.* 2001;83:803-16.
- 248.**
Arinzech TL, Peter SJ, Archambault MP, van den Bos C, Gordon S, Kraus K, Smith A, Kadiyala S. Allogeneic mesenchymal stem cells regenerate bone in a critical-sized canine segmental defect. *J Bone Joint Surg Am.* 2003;85:1927-35.
- 249.**
Boyan BD, Caplan AI, Heckman JD, Lennon DP, Ehler W, Schwartz Z. Osteochondral progenitor cells in acute and chronic canine nonunions. *J Orthop Res.* 1999;17:246-55.
- 250.**
Kanamiya T, Naito M, Ikari N, Hara M. The effect of surgical dissections on blood flow to the tibial tubercle. *J Orthop Res.* 2001;19:113-6.
- 251.**
Theyse LF, Oosterlaken-Dijksterhuis MA, van Doorn J, Dhert WJ, Hazewinkel HA. Growth hormone stimulates bone healing in a critical-sized bone defect model. *Clin Orthop Relat Res.* 2006;446:259-67.
- 252.**
Bruder SP, Kraus KH, Goldberg VM, Kadiyala S. The effect of implants loaded with autologous mesenchymal stem cells on the healing of canine segmental bone defects. *J Bone Joint Surg Am.* 1998;80:985-96.
- 253.**
Sumner DR, Turner TM, Urban RM, Viridi AS, Inoue N. Additive enhancement of implant fixation following combined treatment with rhTGF-beta2 and rhBMP-2 in a canine model. *J Bone Joint Surg Am.* 2006;88:806-17.
- 254.**
Cullinane DM, Lietman SA, Inoue N, Deitz LW, Chao EY. The effect of recombinant human osteogenic protein-1 (bone morphogenetic protein-7) impregnation on allografts in a canine intercalary bone defect. *J Orthop Res.* 2002;20:1240-5.
- 255.**
Sumner DR, Turner TM, Urban RM, Turek T, Seeherman H, Wozney JM. Locally delivered rhBMP-2 enhances bone ingrowth and gap healing in a canine model. *J Orthop Res.* 2004;22:58-65.
- 256.**
Hupel TM, Aksenov SA, Schemitsch EH. Cortical bone blood flow in loose and tight fitting locked unreamed intramedullary nailing: a canine segmental tibia fracture model. *J Orthop Trauma.* 1998;12:127-35.
- 257.**

- Moed BR, Kim EC, van Holsbeeck M, Schaffler MB, Subramanian S, Bouffard JA, Craig JG. Ultrasound for the early diagnosis of tibial fracture healing after static interlocked nailing without reaming: histologic correlation using a canine model. *J Orthop Trauma*. 1998;12:200-5.
- 258.**
Foux A, Yeadon AJ, Uthoff HK. Improved fracture healing with less rigid plates. A biomechanical study in dogs. *Clin Orthop Relat Res*. 1997;339:232-45.
- 259.**
An YH, Friedman RJ, Powers DL, Draughn RA, Latour RA Jr. Fixation of osteotomies using bioabsorbable screws in the canine femur. *Clin Orthop Relat Res*. 1998;355:300-11.
- 260.**
Nakamura T, Hara Y, Tagawa M, Tamura M, Yuge T, Fukuda H, Nigi H. Recombinant human basic fibroblast growth factor accelerates fracture healing by enhancing callus remodeling in experimental dog tibial fracture. *J Bone Miner Res*. 1998;13:942-9.
- 261.**
Sciadini MF, Dawson JM, Johnson KD. Bovine-derived bone protein as a bone graft substitute in a canine segmental defect model. *J Orthop Trauma*. 1997;11:496-508.
- 262.**
Edwards RB 3rd, Seeherman HJ, Bogdanske JJ, Devitt J, Vanderby R Jr, Markel MD. Percutaneous injection of recombinant human bone morphogenetic protein-2 in a calcium phosphate paste accelerates healing of a canine tibial osteotomy. *J Bone Joint Surg Am*. 2004;86:1425-38.
- 263.**
Sciadini MF, Dawson JM, Banit D, Juliao SF, Johnson KD, Lenington WJ, Schwartz HS. Growth factor modulation of distraction osteogenesis in a segmental defect model. *Clin Orthop Relat Res*. 2000;381:266-77.
- 264.**
Fink B, Neuen-Jacob E, Lehmann J, Francke A, Ruther W. Changes in canine peripheral nerves during experimental callus distraction. *Clin Orthop Relat Res*. 2000;376:252-67.
- 265.**
Fink B, Neuen-Jacob E, Lienert A, Francke A, Niggemeyer O, Ruther W. Changes in canine skeletal muscles during experimental tibial lengthening. *Clin Orthop Relat Res*. 2001;385:207-18.
- 266.**
Inoue N, Ohnishi I, Chen D, Deitz LW, Schwardt JD, Chao EY. Effect of pulsed electromagnetic fields (PEMF) on late-phase osteotomy gap healing in a canine tibial model. *J Orthop Res*. 2002;20:1106-14.
- 267.**
Matsuyama J, Ohnishi I, Kageyama T, Oshida H, Suwabe T, Nakamura K. Osteogenesis and angiogenesis in regenerating bone during transverse distraction: quantitative evaluation using a canine model. *Clin Orthop Relat Res*. 2005;433:243-50.
- 268.**
Ohashi S, Ohnishi I, Kageyama T, Fukuda S, Tsuchiya A, Imai K, Matsuyama J, Nakamura K. Effect of vascularity on canine distracted tibial callus consolidation. *Clin Orthop Relat Res*. 2005;438:253-9.
- 269.**
Ohashi S, Ohnishi I, Kageyama T, Imai K, Nakamura K. Distraction osteogenesis promotes angiogenesis in the surrounding muscles. *Clin Orthop Relat Res*. 2007;454:223-9.
- 270.**
Cochran GV, Wu DD, Lee BY, Bieber W, Otter MW. Streaming potentials in gap osteotomy callus and adjacent cortex. A pilot study. *Clin Orthop Relat Res*. 1997;337:291-301.
- 271.**
Larsson S, Kim W, Caja VL, Egger EL, Inoue N, Chao EY. Effect of early axial dynamization on tibial bone healing: a study in dogs. *Clin Orthop Relat Res*. 2001;388:240-51.
- 272.**
Lammens J, Liu Z, Aerssens J, Dequeker J, Fabry G. Distraction bone healing versus osteotomy healing: a comparative biochemical analysis. *J Bone Miner Res*. 1998;13:279-86.
- 273.**
Schemitsch EH, Jain R, Turchin DC, Mullen JB, Byrick RJ, Anderson GI, Richards RR. Pulmonary effects of fixation of a fracture with a plate compared with intramedullary nailing. A canine model of fat embolism and fracture fixation. *J Bone Joint Surg Am*. 1997;79:984-96.
- 274.**
Radomsky ML, Aufdemorte TB, Swain LD, Fox WC, Spiro RC, Poser JW. Novel formulation of fibroblast growth factor-2 in a hyaluronan gel accelerates fracture healing in nonhuman primates. *J Orthop Res*. 1999;17:607-14.
- 275.**
Kropfl A, Davies J, Berger U, Hertz H, Schlag G. Intramedullary pressure and bone marrow fat extravasation in reamed and unreamed femoral nailing. *J Orthop Res*. 1999;17:261-8.
- 276.**

- Seeherman HJ, Bouxsein M, Kim H, Li R, Li XJ, Aioloa M, Wozney JM. Recombinant human bone morphogenetic protein-2 delivered in an injectable calcium phosphate paste accelerates osteotomy-site healing in a nonhuman primate model. *J Bone Joint Surg Am.* 2004;86:1961-72.
- 277.**
Seeherman H, Li R, Bouxsein M, Kim H, Li XJ, Smith-Adaline EA, Aioloa M, Wozney JM. rhBMP-2/calcium phosphate matrix accelerates osteotomy-site healing in a nonhuman primate model at multiple treatment times and concentrations. *J Bone Joint Surg Am.* 2006;88:144-60.
- 278.**
Manabe T, Mori S, Mashiba T, Kaji Y, Iwata K, Komatsubara S, Seki A, Sun YX, Yamamoto T. Human parathyroid hormone (1-34) accelerates natural fracture healing process in the femoral osteotomy model of cynomolgus monkeys. *Bone.* 2007;40:1475-82.
- 279.**
Raschke M, Kolbeck S, Bail H, Schmidmaier G, Flyvbjerg A, Lindner T, Dahne M, Roenne IA, Haas N. Homologous growth hormone accelerates healing of segmental bone defects. *Bone.* 2001;29:368-73.
- 280.**
Kolbeck S, Bail H, Schmidmaier G, Alquiza M, Raun K, Kappelgard A, Flyvbjerg A, Haas N, Raschke M. Homologous growth hormone accelerates bone healing—a biomechanical and histological study. *Bone.* 2003;33:628-37.
- 281.**
Bail HJ, Kolbeck S, Krummrey G, Weiler A, Windhagen HJ, Hennies K, Raun K, Raschke MJ. Ultrasound can predict regenerate stiffness in distraction osteogenesis. *Clin Orthop Relat Res.* 2002;404:362-7.
- 282.**
Raschke MJ, Bail H, Windhagen HJ, Kolbeck SF, Weiler A, Raun K, Kappelgard A, Skiaerbaek C, Haas NP. Recombinant growth hormone accelerates bone regenerate consolidation in distraction osteogenesis. *Bone.* 1999;24:81-8.
- 283.**
Bail HJ, Raschke MJ, Kolbeck S, Krummrey G, Windhagen HJ, Weiler A, Raun K, Mosekilde L, Haas NP. Recombinant species-specific growth hormone increases hard callus formation in distraction osteogenesis. *Bone.* 2002;30:117-24.
- 284.**
Seo EG, Norman AW. Three-fold induction of renal 25-hydroxyvitamin D3-24-hydroxylase activity and increased serum 24,25-dihydroxyvitamin D3 levels are correlated with the healing process after chick tibial fracture. *J Bone Miner Res.* 1997;12:598-606.
- 285.**
Kato A, Seo EG, Einhorn TA, Bishop JE, Norman AW. Studies on 24R,25-dihydroxyvitamin D3: evidence for a nonnuclear membrane receptor in the chick tibial fracture-healing callus. *Bone.* 1998;23:141-6.
- 286.**
Hutchison C, Pilote M, Roy S. The axolotl limb: a model for bone development, regeneration and fracture healing. *Bone.* 2007;40:45-56.