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NOT TO BE MISSED

Clinical and Basic Research Papers – February 2011

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Clinical Studies and Drug Effects

Kukuljan S, Nowson CA, Sanders KM, Nicholson GC, Seibel MJ, Salmon J, Daly RM. Independent and combined effects of calcium-vitamin D3 and exercise on bone structure and strength in older men: an 18-month factorial design randomized controlled trial. *J Clin Endocrinol Metab*. 2011 Jan 5. [Epub ahead of print] [Abstract]

> *This study assessed whether calcium-vitamin D3 fortified milk could enhance the effects of exercise on bone strength, structure, and BMD in men, in an 18-month factorial design randomized controlled trial. 180 men aged 50-79 years were randomized to the 4 arms: exercise+fortified milk; exercise-only; fortified milk-only; and controls. Exercise led to an average 2.1% net gain in femoral neck section modulus, an ~1.9% gain in aBMD, and a 2.2% gain in lumbar spine trabecular BMD. There were no main effects of the fortified milk at any skeletal site. Moreover, there were no combined effects or interactions between exercise/fortified milk at any skeletal site.*
> —DK

Nagahama K, Kanayama M, Togawa D, Hashimoto T, Minami A. Does alendronate disturb the healing process of posterior lumbar interbody fusion? A prospective randomized trial. *J Neurosurg Spine*. 2011 Jan 28. [Epub ahead of print] [Abstract]

> *Spine surgeons have been concerned that bisphosphonates interfere with spinal fusion; studies in this regard were often based on very high doses of bisphosphonates. This randomized controlled trial allocated 20 patients with osteoporosis requiring single-level posterior lumbar interbody fusion to receive alendronate 35 mg/week or vitamin D. 95% of alendronate-treated patients had a solid fusion at 1 year compared to 65% of controls. No vertebral fractures were observed in the alendronate group, whereas 24% of patients in the control group showed subsequent vertebral fractures.*
> —DGL

Padhi D, Jang G, Stouch B, Fang L, Posvar E. Single-dose, placebo-controlled, randomized study of AMG 785, a sclerostin monoclonal antibody. *J Bone Miner Res*. 2011 Jan;26(1):19-26. [Abstract]

> *Finding a drug that increases bone formation and reduces bone resorption at the cellular and tissue levels is an unmet need. The initial findings with this sclerostin antibody (AMG 785) are encouraging. 72 healthy subjects received AMG 785 or placebo (3:1) subcutaneously (0.1, 0.3, 1, 3, 5, or 10 mg/kg) or intravenously (1 or 5 mg/kg). Dose-related increases in P1NP, BAP, and osteocalcin were observed, with a*

dose-related decrease in sCTx and increases in BMD (5.3% at the spine, 2.8% at the total hip compared with placebo), on day 85. Six subjects in the higher-dose groups developed anti-AMG 785 antibodies, 2 of which were neutralizing. —ES

Poole KE, Treece GM, Ridgway GR, Mayhew PM, Borggrefe J, Gee AH. Targeted regeneration of bone in the osteoporotic human femur. *PLoS One*. 2011 Jan 14;6(1):e16190. [Abstract]

In this interesting work, CT-based high-resolution cortical thickness mapping of the hip in EUROFORS subjects shows discrete areas of cortical thickening with teriparatide. The distribution of effects suggests a possible synergistic effect of habitual load and PTH in the human proximal femur, since peak effects are seen at sites that are highly stressed by walking. —SF

Yates CJ, Bartlett MJ, Ebeling PR. An atypical subtrochanteric femoral fracture from pycnodysostosis - a lesson from nature. *J Bone Miner Res*. 2010 Dec 7. [Epub ahead of print] [Abstract]

It is a case report, but the very typical features of an atypical femoral fracture, including cortical thickening, seen here – in the absence of bisphosphonates – further support the hypothesis that susceptibility to atypical fractures in bisphosphonate users might be carried by gene mutations (cathepsin K in this case) causing alterations in bone turnover and/or strength. —SF

Cancer and Bone

Barker HE, Chang J, Cox TR, Lang G, Bird D, Nicolau M, Evans HR, Gartland A, Erler JT. LOXL2-mediated matrix remodeling in metastasis and mammary gland involution. *Cancer Res*. 2011 Jan 19. [Epub ahead of print] [Abstract]

Lysyl oxidase-related enzyme LOXL2 expression is correlated with metastasis and decreased survival in patients with aggressive breast cancer. In immunocompromised or immunocompetent orthotopic and transgenic breast cancer models, targeting LOXL2 is highly effective against spontaneous lung, liver and bone metastases. —PC

Goldstein RH, Reagan MR, Anderson K, Kaplan DL, Rosenblatt M. Human bone marrow-derived MSCs can home to orthotopic breast cancer tumors and promote bone metastasis. *Cancer Res*. 2010 Dec 15;70(24):10044-50. [Abstract]

Human bone marrow-derived mesenchymal stem cells (hBMSCs) from a tissue-engineered bone subcutaneous implant home to orthotopic human breast tumors, enhancing their growth and increasing the frequency of skeletal metastases. IL-17B produced by hBMSCs promotes this metastatic process. —PC

Liu S, Ginestier C, Ou SJ, Clouthier SG, Patel SH, Monville F, Korkaya H, Heath A, Dutcher J, Kleer CG, Jung Y, Dontu G, Taichman R, Wicha MS. Breast cancer stem cells are regulated by mesenchymal stem cells through cytokine networks. *Cancer Res*. 2011 Jan 15;71(2):614-24. [Abstract]

The interaction between BMSCs and SUM159 breast cancer cells leads to the production of cytokines (IL-6 and CXCL-7) that regulate the in vitro expansion of breast cancer stem cells. In NOD/SCID mice, BMSCs traffic from the bone marrow to primary breast tumor sites in the mammary fat pad where they increase the breast cancer stem cell population. —PC

Molyneux SD, Di Grappa MA, Beristain AG, McKee TD, Wai DH, Paderova J, Kashyap M, Hu P, Maiuri T, Narala SR, Stambolic V, Squire J, Penninger J, Sanchez O, Triche TJ, Wood GA, Kirschner LS, Khokha R. Prkar1a is an osteosarcoma tumor suppressor that defines a molecular subclass in mice. *J Clin Invest*. 2010 Sep 1;120(9):3310-25. [Abstract]

> *cAMP-dependent protein kinase type I, α regulatory subunit (Prkar1a) is a bone tumor suppressor gene, the loss of which induces osteosarcoma development in mice and RANKL overexpression in these tumors. In addition, RANKL was overexpressed in human osteosarcomas expressing low PRKAR1A levels.* —PC

Saini S, Majid S, Yamamura S, Tabatabai ZL, Suh SO, Shahryari V, Chen Y, Deng G, Tanaka Y, Dahiya R. Regulatory role of miR-203 in prostate cancer progression and metastasis. *Clin Cancer Res*. 2010 Dec 15. [Epub ahead of print] [Abstract]

> *The authors identified miR-203 as being progressively lost in advanced metastatic prostate cancer. To assess the biological significance of miR-203, miR-203 was reintroduced in metastatic PC3 human prostate cancer cells. Re-expression of miR-203 suppressed metastasis-relevant traits in vitro (inhibition of cancer cell migration and invasion, reduction of proliferation), induced mesenchymal-to-epithelial transition (MET), and suppressed prostate cancer metastasis in vivo.* —PC

Genetics

Briggs TA, Rice GI, Daly S, Urquhart J, Gornall H, Bader-Meunier B, Baskar K, Baskar S, Baudouin V, Beresford MW, Black GC, Dearman RJ, de Zegher F, Foster ES, Francès C, Hayman AR, Hilton E, Job-Deslandre C, Kulkarni ML, Le Merrer M, Linglart A, Lovell SC, Maurer K, Musset L, Navarro V, Picard C, Puel A, Rieux-Laucat F, Roifman CM, Scholl-Bürgi S, Smith N, Szynkiewicz M, Wiedeman A, Wouters C, Zeef LA, Casanova JL, Elkon KB, Janckila A, Lebon P, Crow YJ. Tartrate-resistant acid phosphatase deficiency causes a bone dysplasia with autoimmunity and a type I interferon expression signature. *Nat Genet*. 2011 Feb;43(2):127-31. [Abstract]

Lausch E, Janecke A, Bros M, Trojandt S, Alanay Y, De Laet C, Hübner CA, Meinecke P, Nishimura G, Matsuo M, Hirano Y, Tenoutasse S, Kiss A, Machado Rosa RF, Unger SL, Renella R, Bonafé L, Spranger J, Unger S, Zabel B, Superti-Furga A. Genetic deficiency of tartrate-resistant acid phosphatase associated with skeletal dysplasia, cerebral calcifications and autoimmunity. *Nat Genet*. 2011 Feb;43(2):132-7. [Abstract]

> *The genetic disorder spondyloenchondrodysplasia (SPENCD) is characterized by vertebral and metaphyseal dysplasia, spasticity with cerebral calcifications, and a strong predisposition to autoimmune diseases. These two groups independently identified biallelic mutations in ACP5, encoding tartrate-resistant acid phosphatase (TRAP), on chromosome 19p13 with loss-of-function of TRAP in all the SPENCD patients studied. Lack of TRAP activity results in hyperphosphorylation and gain-of-function of osteopontin (OPN). Extracellular phospho-OPN causes the skeletal defects and may also cause the cerebral calcifications with neurologic symptoms. Intracellular phospho-OPN causes enhanced TLR9 signaling, which increases IFN-α production by dendritic cells. Elevated IFN-α leads to systemic autoimmunity by increasing antigen presentation. These findings reveal a novel link between TRAP activity, OPN and IFN-α signaling in the genesis of common autoimmune disorders.* —TM

Evangelou E, Valdes AM, Kerkhof HJ, et al. Meta-analysis of genome-wide association studies confirms a susceptibility locus for knee osteoarthritis on chromosome 7q22. *Ann Rheum Dis*.

2011 Feb;70(2):349-55. [Abstract]

Panoutsopoulou K, Southam L, Elliott KS, et al. Insights into the genetic architecture of osteoarthritis from stage 1 of the arcOGEN study. *Ann Rheum Dis*. 2010 Dec 21. [Epub ahead of print] [Abstract]

> *The etiology of osteoarthritis (OA) is multifactorial, with a strong heritable component. These 2 papers reported genome-wide association studies (GWAS) of OA. In the first paper, a meta-analysis of 4 studies was performed in 2,371 Caucasian cases of knee OA and 35,909 controls. Replication of the top hits was attempted with data from 10 additional replication datasets, including East Asian cases and controls. One genome-wide significant locus was identified on chromosome 7q22, which contains six genes: PRKAR2B, HPB1, COG5, GPR22, DUS4L, and BCAP29. COG5 (component of oligomeric golgi complex 5) was previously reported in a subsample of this meta-analysis. Expression of all 6 genes was confirmed in primary cells derived from joint tissues.*
>
> *In the second paper, the authors performed a GWAS for knee and hip OA in 3,177 cases and 4,894 population-based controls from the UK. Replication of promising signals was carried out both in silico and de novo in independent samples of European descent. However, none of the association signals reached genome-wide significance levels. The authors believe they need even larger sample sizes and homogenous phenotypes to succeed.* —DK

Kim SJ, Bieganski T, Sohn YB, Kozlowski K, Semënov M, Okamoto N, Kim CH, Ko AR, Ahn GH, Choi YL, Park SW, Ki CS, Kim OH, Nishimura G, Unger S, Superti-Furga A, Jin DK. Identification of signal peptide domain SOST mutations in autosomal dominant craniodiaphyseal dysplasia. *Hum Genet*. 2011 Jan 9. [Epub ahead of print] [Abstract]

> *Many mutations causing monogenic bone disorders remain to be identified. This work broadens the spectrum of diseases associated with SOST mutations, in addition to sclerosteosis and Van Buchem disease, by identifying 2 mutations that prevent the secretion of sclerostin, resulting in the most severe form of osteosclerosis in 2 affected individuals.* —SF

Bone Modeling, Remodeling, and Repair

Aspenberg P, Agholme F, Magnusson P, Fahlgren A. Targeting RANKL for reduction of bone loss around unstable implants: OPG-Fc compared to alendronate in a model for mechanically induced loosening. *Bone*. 2011 Feb 1;48(2):225-30. [Abstract]

> *In a rat model of unstable titanium plate osseointegration, OPG-Fc and high-dose alendronate, but not low-dose, inhibited bone resorption and/or osteoclastogenesis. This experiment provides the rationale to test RANKL inhibitors to prevent and/or treat prosthesis loosening.* —SF

Li W, Zara JN, Siu RK, Lee M, Aghaloo T, Zhang X, Wu BM, Gertzman AA, Ting K, Soo C. Nell-1 enhances bone regeneration in a rat critical-sized femoral segmental defect model. *Plast Reconstr Surg*. 2011 Feb;127(2):580-7. [Abstract]

> *Nell-1 appears to be a novel growth factor with potent osteoinductive capacity, also inhibiting adipogenic differentiation. This study shows that Nell-1 protein in a demineralized bone matrix (DBM) carrier formed more bone than DBM alone in a critical defect model. It was not clear how mechanically competent the bone was. The*

authors state Nell-1 is downstream of Runx2. —DGL

Tatli U, Ustun Y, Kurkcu M, Erdogan O, Gurbuz CC, Ozgur H, Polat S. Effects of zoledronic acid on healing of mandibular fractures: an experimental study in rabbits. *J Oral Maxillofac Surg*. 2011 Jan 20. [Epub ahead of print] [Abstract]

Given the concern regarding ONJ, it seems reasonable to also examine the effects of bisphosphonates on mandibular fracture healing. Diaphyseal fracture healing has been shown to be improved by zoledronic acid treatment. This group examined mandibular fracture healing in rabbits given a single dose of 0.1 mg/kg zoledronic acid. Biomechanical testing data showed that this treatment resulted in a significant increase in healed bone strength. This result was supported by radiologic, histologic, and histomorphometric findings. —DGL

Molecular and Cell Biology

Glass GE, Chan JK, Freidin A, Feldmann M, Horwood NJ, Nanchahal J. TNF-alpha promotes fracture repair by augmenting the recruitment and differentiation of muscle-derived stromal cells. *Proc Natl Acad Sci U S A*. 2011 Jan 25;108(4):1585-90. [Abstract] [Full Text]

Using an in vivo murine model, the authors show that muscle-derived stromal cells (MDSCs) harvested after 3 days of exposure to an adjacent fracture differentiate into osteoblasts and form bone nodules in vitro. The osteogenic potential of these cells exceeds that of adipose and skin-derived stromal cells and is equivalent to bone marrow stromal cells in their contribution to accelerated healing. The main factor responsible for this is TNF-α. At low concentrations, TNF-α promotes MDSC migration with an ensuing osteogenic differentiation; it is, however, inhibitory at high concentrations. —DK

Hiramatsu K, Sasagawa S, Outani H, Nakagawa K, Yoshikawa H, Tsumaki N. Generation of hyaline cartilaginous tissue from mouse adult dermal fibroblast culture by defined factors. *J Clin Invest*. 2011 Jan 10. [Epub ahead of print] [Abstract]

The authors show that retroviral expression of two reprogramming factors (c-Myc and Klf4) and one chondrogenic factor (SOX9) induces polygonal chondrogenic cells directly from adult dermal fibroblast cultures. Induced chondrogenic cells expressed marker genes for chondrocytes and produced homogeneous hyaline cartilage-like tissue without type I collagen expression when subcutaneously injected into nude mice. Hyaline cartilage-like tissue remained for at least 16 weeks without tumor formation. This approach could lead to the preparation of patient-specific hyaline cartilage directly from skin, without generating induced pluripotent stem (iPS) cells. —TM

Ishii M, Kikuta J, Shimazu Y, Meier-Schellersheim M, Germain RN. Chemorepulsion by blood S1P regulates osteoclast precursor mobilization and bone remodeling in vivo. *J Exp Med*. 2010 Dec 20;207(13):2793-8. [Abstract]

The authors previously demonstrated that sphingosine-1-phosphate (S1P) controls the migration of osteoclast precursors (OPs) between the blood and bone via the S1P receptor 1 (S1PR1) that directs positive chemotaxis toward S1P. Here they show that OPs also express S1PR2, which mediates chemorepulsion under high S1P concentrations. S1PR2-deficient mice exhibit decreased bone resorption with moderate osteopetrosis, suggesting that S1PR2 contributes to chemorepulsion away from the blood where S1P levels are high. Inhibition of S1PR2 by the antagonist

JTE013 changed the migratory behavior of OPs, and relieved osteoporosis by reducing the number of osteoclasts on the bone surface. The reciprocal regulatory axis of S1P-dependent OP chemotaxis by S1PR1 and S1PR2 may become a therapeutic target in diseases with enhanced bone resorption. —TM

Li JY, Tawfeek H, Bedi B, Yang X, Adams J, Gao KY, Zayzafoon M, Weitzmann MN, Pacifici R. Ovariectomy disregulates osteoblast and osteoclast formation through the T-cell receptor CD40 ligand. *Proc Natl Acad Sci U S A*. 2011 Jan 11;108(2):768-73. [Abstract] [Full Text]

CD40 ligand (CD40L)-CD40 interactions between T cells and antigen-presenting cells are a key co-stimulatory pathway for adaptive immune and inflammatory processes and a target for the development of biologic treatment of inflammatory disorders. Considering the role of T cells in osteoclast activation and bone loss, including in response to estrogen deprivation, it comes as no surprise that CD40L knockout mice and mice treated with CD40L neutralizing antibody were protected against ovariectomy-induced bone loss. Even more interestingly, an interaction between T cell-expressed CD40L and "stromal cells" controlled the expansion of stromal cells as well as osteoblast proliferation and differentiation, including their production of osteoclastogenic factors. —SF

Siqueira MF, Flowers S, Bhattacharya R, Faibish D, Behl Y, Kotton DN, Gerstenfeld L, Moran E, Graves DT. FOXO1 modulates osteoblast differentiation. *Bone*. 2011 Jan 28. [Epub ahead of print] [Abstract]

Forkhead box (FoxOs) activate antioxidant scavenger proteins; FOXO1 is known to inhibit proliferation in a variety of cells. Studies suggested that FoxO activation in response to oxidative stress plays a major role in the adverse effects of aging on both osteoblast and osteoclast number. In this study, investigators examined the functional role of FOXO1 in a culture system in which pre-osteoblastic MC3T3-E1 cells undergo terminal differentiation in vitro. FOXO1 knockdown by RNAi reduced the number of mineralized nodules formed. However, FOXO1 overexpression in MC3T3-E1 cells reduced proliferation. These findings indicate that FOXO1 plays an important role in promoting osteoblast differentiation and suppressing proliferation in differentiating cells and confirm observations that oxidative stress seems to be one of the determinants of osteoporosis. —DK

Public Health

Song X, Shi N, Badamgarav E, Kallich J, Varker H, Lenhart G, Curtis JR. Cost burden of second fracture in the US Health System. *Bone*. 2011 Jan 4. [Epub ahead of print] [Abstract]

Pike C, Birnbaum HG, Schiller M, Swallow E, Burge RT, Edgell ET. Economic burden of privately insured non-vertebral fracture patients with osteoporosis over a 2-year period in the US. *Osteoporos Int*. 2011 Jan;22(1):47-56. [Abstract]

Morin S, Lix LM, Azimaee M, Metge C, Caetano P, Leslie WD. Mortality rates after incident non-traumatic fractures in older men and women. *Osteoporos Int*. 2010 Dec 16. [Epub ahead of print] [Abstract]

A second fracture in the year after a first is common and costly; three recent papers make this and other points. The notion of vertebral fractures as "the" osteoporosis fracture is flawed. Recognition of the burden of disease produced by nonvertebral fractures raises many issues, one being the few studies addressing anti-nonvertebral fracture efficacy of drugs. Song et al. report the 1-year medical costs associated with

second fracture(s) in patients with an initial hip, clinical vertebral or non-hip non-vertebral fracture. For privately insured patients, the 1-year second fracture rate was 8.0%, 5.1%, and 4.0%, and 1-year incremental costs were $47,351, $43,238, and $23,852, respectively; for Medicare patients, corresponding rates and costs were 8.8%, 9.2%, and 8.2%, and $18,645, $19,702, and $19,697. The nationally projected annual cost of second fracture was $834 million for patients with commercial insurance and $1.13 billion for Medicare patients.

In the paper by Pike et al., during the 2 years following an incident fracture, patients with a non-vertebral fracture (hip, femur, pelvis, lower leg, upper arm, forearm, rib, and multiple sites) were compared to controls with osteoporosis but without a fracture (N = 3,781). Comorbidity rates and resource use remained higher among non-vertebral fracture patients during the second year following a non-vertebral fracture. Patients with fractures of the pelvis, hip, and femur had the highest excess costs in the second year ($5,121, $3,930, and $3,828, respectively). Although hip fractures had the highest excess costs over both years, non-hip non-vertebral fracture patients made up a larger proportion of the sample and were more costly than controls.

Finally, in the study by Morin et al., 21,067 incident fractures in men were followed by 10,724 (50.1%) deaths, and 49,197 incident fractures in women were followed by 22,018 deaths (44.8%). 76% percent of the fractures were at sites other than the hip and vertebrae. The risk of death was increased in both sexes for hip, vertebral, humerus, wrist (in men only), and other fracture sites. Post-fracture mortality was higher in men than women. —ES

Reviews, Perspectives and Editorials

Marie PJ, Kassem M. Extrinsic mechanisms involved in age-related defective bone formation. *J Clin Endocrinol Metab*. 2011 Jan 5. [Epub ahead of print] [Abstract]

Roth SM. Genetic variation and skeletal muscle traits: implications for sarcopenia. In: Lynch GS, ed. *Sarcopenia – Age-Related Muscle Wasting and Weakness Mechanisms and Treatments*. Dordrecht, Netherlands: Springer; 2011.

Other Studies of Potential Interest

Cao X, Wu X, Frassica D, Yu B, Pang L, Xian L, Wan M, Lei W, Armour M, Tryggestad E, Wong J, Wen CY, Lu WW, Frassica FJ. Irradiation induces bone injury by damaging bone marrow microenvironment for stem cells. *Proc Natl Acad Sci U S A*. 2011 Jan 25;108(4):1609-14. [Abstract] [Full Text]

Das S, Samant RS, Shevde LA. Hedgehog signaling induced by breast cancer cells promotes osteoclastogenesis and osteolysis. *J Biol Chem*. 2010 Dec 18. [Epub ahead of print] [Abstract]

Francesca R, Giulia B, Livio L, Marco T, Silvia M, Luciano DP, Stefania P, Dario S, Mariantonietta S, Nicola C, Silverio P, Bruno N, Vincenzo DM, Sabatino M; Endocannabinoid Research Group (ERG), Italy. The endovanilloid/endocannabinoid system: A new potential target for osteoporosis therapy. *Bone*. 2011 Jan 13. [Epub ahead of print] [Abstract]

Gupta M, Cheung CL, Hsu YH, Demissie S, Cupples LA, Kiel DP, Karasik D. Identification of homogenous genetic architecture of multiple genetically correlated traits by block clustering of genome-wide associations. *J Bone Miner Res*. 2011 Jan 4. [Epub ahead of print] [Abstract]

Hirai T, Chagin AS, Kobayashi T, Mackem S, Kronenberg HM. Parathyroid hormone/parathyroid hormone-related protein receptor signaling is required for maintenance of the growth plate in postnatal life. *Proc Natl Acad Sci U S A*. 2011 Jan 4;108(1):191-6. [Abstract] [Full Text]

Histing T, Marciniak K, Scheuer C, Garcia P, Holstein JH, Klein M, Matthys R, Pohlemann T, Menger MD. Sildenafil accelerates fracture healing in mice. *J Orthop Res*. 2011 Jan 18. [Epub ahead of print] [Abstract]

Kaplan RC, Petersen AK, Chen MH, Teumer A, Glazer NL, Döring A, Lam CS, Friedrich N, Newman A, Müller M, Yang Q, Homuth G, Cappola A, Klopp N, Smith H, Ernst F, Psaty BM, Wichmann HE, Sawyer DB, Biffar R, Rotter JI, Gieger C, Sullivan LS, Völzke H, Rice K, Spyroglou A, Kroemer HK, Ida Chen YD, Manolopoulou J, Nauck M, Strickler HD, Goodarzi MO, Reincke M, Pollak MN, Bidlingmaier M, Vasan RS, Wallaschofski H. A genome-wide association study identifies novel loci associated with circulating IGF-I and IGFBP-3. *Hum Mol Genet*. 2011 Jan 13. [Epub ahead of print] [Abstract]

Kawakatsu M, Kanno S, Gui T, Gai Z, Itoh S, Tanishima H, Oikawa K, Muragaki Y. Loss of Smad3 gives rise to poor soft callus formation and accelerates early fracture healing. *Exp Mol Pathol*. 2011 Feb;90(1):107-15. [Abstract]

Komrakova M, Werner C, Wicke M, Sehmisch S, Tezval M, Rohrberg M, Brandsch T, Stuermer KM, Stuermer EK. Influence of intermittent administration of human parathyroid hormone (hPTH 1-34) on muscle tissue and bone healing in orchiectomized rats or controls. *J Endocrinol*. 2011 Jan 13. [Epub ahead of print] [Abstract]

Martineau AR, Timms PM, Bothamley GH, Hanifa Y, Islam K, Claxton AP, Packe GE, Moore-Gillon JC, Darmalingam M, Davidson RN, Milburn HJ, Baker LV, Barker RD, Woodward NJ, Venton TR, Barnes KE, Mullett CJ, Coussens AK, Rutterford CM, Mein CA, Davies GR, Wilkinson RJ, Nikolayevskyy V, Drobniewski FA, Eldridge SM, Griffiths CJ. High-dose vitamin D(3) during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial. *Lancet*. 2011 Jan 15;377(9761):242-50. [Abstract]

Palmer MT, Lee YK, Maynard CL, Oliver JR, Bikle DD, Jetten AM, Weaver CT. Lineage-specific effects of 1,25-dihydroxyvitamin D(3) on the development of effector CD4 T cells. *J Biol Chem*. 2011 Jan 14;286(2):997-1004. [Abstract] [Full Text]

Patsch JM, Kohler T, Berzlanovich A, Muschitz C, Bieglmayr C, Roschger P, Resch H, Pietschmann P. Trabecular bone microstructure and local gene expression in iliac crest biopsies of men with idiopathic osteoporosis. *J Bone Miner Res*. In press. [Abstract]

Sharma S, Gao X, Londono D, Devroy SE, Mauldin KN, Frankel JT, Brandon JM, Zhang D, Li QZ, Dobbs MB, Gurnett CA, Grant SF, Hakonarson H, Dormans JP, Herring JA, Gordon D, Wise CA. Genome-wide association studies of adolescent idiopathic scoliosis suggest candidate susceptibility genes. *Hum Mol Genet*. 2011 Jan 20. [Epub ahead of print] [Abstract]

Smietana MJ, Arruda EM, Faulkner JA, Brooks SV, Larkin LM. Reactive oxygen species on bone mineral density and mechanics in Cu,Zn superoxide dismutase (Sod1) knockout mice. *Biochem Biophys Res Commun*. 2010 Dec 3;403(1):149-53. [Abstract]

Tassani S, Ohman C, Baruffaldi F, Baleani M, Viceconti M. Volume to density relation in adult human bone tissue. *J Biomech*. 2011 Jan 4;44(1):103-8. [Abstract]

Vanleene M, Saldanha Z, Cloyd KL, Jell G, Bou-Gharios G, Bassett JH, Williams GR, Fisk NM,

Oyen ML, Stevens MM, Guillot PV, Shefelbine SJ. Transplantation of human fetal blood stem cells in the osteogenesis imperfecta mouse leads to improvement in multiscale tissue properties. *Blood*. 2011 Jan 20;117(3):1053-60. [Abstract]

Yarilina A, Xu K, Chen J, Ivashkiv LB. TNF activates calcium-nuclear factor of activated T cells (NFAT)c1 signaling pathways in human macrophages. *Proc Natl Acad Sci U S A*. 2011 Jan 25;108(4):1573-8. [Abstract] [Full Text]

Zhang H, Hu YQ, Zhang ZL. Age trends for hip geometry in Chinese men and women and the association with femoral neck fracture. *Osteoporos Int*. 2011 Jan 6. [Epub ahead of print] [Abstract]

Conflict of Interest: Dr. Clézardin reports receiving research support from Novartis (Basel, Switzerland) and honoraria for advisory work and speaking engagements from Novartis and Amgen. Dr. Ferrari reports that he receives research support from Amgen and Merck Sharp & Dohme, and is an advisory committee member and lectures occasionally at conference symposia for the Alliance for Better Bone Health (sanofi aventis/P&G), Amgen, Merck Sharp & Dohme, Eli Lilly, Servier, and Novartis. Dr. Little reports that he receives royalties, research funds and consultancy fees from Novartis Pharma, as well as research support from Stryker Biotech. Dr. Seeman reports that he is an advisory committee member for sanofi-aventis, Eli Lilly, Merck Sharp & Dohme, Novartis, and Servier, and that he lectures occasionally at conference symposia for those companies. Dr. Matsumoto and Dr. Karasik report no conflicts of interest.