

NOT TO BE MISSED

Clinical and Basic Research Papers – July 2005 Selections

Ego Seeman, Clinical Editor
Gordon J. Strewler, Editor

Bone Modeling and Remodeling

✦ Idris AI, van't Hof RJ, Greig IR, Ridge SA, Baker D, Ross RA, Ralston SH. Regulation of bone mass, bone loss and osteoclast activity by cannabinoid receptors. *Nat Med.* 2005 Jul;11(7):774-9. [[Abstract](#)]

This paper reports that mice in which the cannabinoid receptor CB1 is inactivated have increased adult bone mass and are protected against ovariectomy (OVX)-induced bone loss. Pharmacologic cannabinoid receptor antagonists also block bone loss after OVX. In vitro, cannabinoid receptor antagonists inhibit osteoclastogenesis in response to receptor activator of NF- κ B ligand (RANKL) and agonists have the opposite effect. Cannabinoids have central effects on appetite, known as the marijuana munchies. The results thus parallel findings in the leptin system, and à la leptin, central effects of cannabinoids on bone mass could also be present. —GJS

✦ Yagi M, Miyamoto T, Sawatani Y, Iwamoto K, Hosogane N, Fujita N, Morita K, Ninomiya K, Suzuki T, Miyamoto K, Oike Y, Takeya M, Toyama Y, Suda T. DC-STAMP is essential for cell-cell fusion in osteoclasts and foreign body giant cells. *J Exp Med.* 2005 Aug 1;202(3):345-51. [[Abstract](#)]

✦ Vignery A. Macrophage fusion: the making of osteoclasts and giant cells. *J Exp Med.* 2005 Aug 1;202(3):337-40. [[Abstract](#)]

Dendritic cell-specific transmembrane protein (DC-STAMP) is a G protein-coupled receptor that is induced by receptor activator of NF- κ B ligand on the surface of osteoclast precursors. Mice in which the DCSTAMP gene has been removed have no multinucleate osteoclasts, and DC-STAMP is essential for the fusion of macrophages into osteoclasts or foreign body giant cells. Mice with only mononuclear osteoclasts have relatively mild osteopetrosis, indicating that such cells have residual bone-resorbing activity. The ligand for DC-STAMP is unknown; one possibility is the chemokine CCL2/MCP1, which was recently shown to participate in macrophage fusion. —GJS

Pathophysiology

✦ Sabbagh Y, Carpenter TO, Demay MB. Hypophosphatemia leads to rickets by impairing caspase-mediated apoptosis of hypertrophic chondrocytes. *Proc Natl Acad Sci U S A.* 2005 Jul 5;102(27):9637-42. [[Abstract](#)] [[Full Text](#)]

Hypophosphatemia is associated with rickets in diverse circumstances. This paper showed that hypophosphatemia impairs the apoptosis of hypertrophic chondrocytes. By comparing three models of hypophosphatemia (vitamin D receptor(-/-), Hyp, and the feeding of a low phosphate/high calcium diet), the authors inferred that only hypophosphatemia (not hyperparathyroidism, hypocalcemia, or an altered fibroblast growth factor 23 level) is correlated with impaired chondrocyte apoptosis. Caspase 3 activity is impaired in hypophosphatemia, and caspase inhibitors also produce a rachitic phenotype. —GJS

- ◆ Sipkins DA, Wei X, Wu JW, Runnels JM, Cote D, Means TK, Luster AD, Scadden DT, Lin CP. In vivo imaging of specialized bone marrow endothelial microdomains for tumour engraftment. *Nature*. 2005 Jun 16;435(7044):969-73. [[Abstract](#)]

Confocal imaging techniques were used to observe fluorescently labeled tumor cells in vivo in the bone vascular microenvironment of mouse calvaria. Tumor cells expressed the chemokine receptor CXCR-4 and homed to a niche defined by the presence of E-selectin and the CXCR-4 ligand stromal-derived factor 1 (SDF-1). Homing of Nalm-6 cells (an acute lymphoblastic leukemia cell line) was slightly reduced in E-selectin(-/-) mice, but markedly reduced by a variety of strategies to block interactions of SDF-1 and CXCR-4. The new technology is a powerful tool to define cellular niches in bone at high temporal and spatial resolution. —GJS

Reviews, Perspectives, and Editorials

- ◆ Boland R, Buitrago C, Boland AR. Modulation of tyrosine phosphorylation signalling pathways by 1 α ,25(OH)₂-vitamin D₃. *Trends Endocrinol Metab*. 2005 Aug;16(6):280-7. [[Abstract](#)]
- ◆ Clowes JA, Khosla S, Eastell R. Potential Role of Pancreatic and Enteric Hormones in Regulating Bone Turnover. *J Bone Miner Res*. 2005 Sep;20(9):1497-1506. [[Info](#)]
- ◆ Cozzolino M, Brancaccio D, Gallieni M, Slatopolsky E. Pathogenesis of vascular calcification in chronic kidney disease. *Kidney Int*. 2005 Aug;68(2):429-36. [[Abstract](#)]
- ◆ Hodsman AB, Bauer DC, Dempster DW, Dian L, Hanley DA, Harris ST, Kendler DL, McClung MR, Miller PD, Olszynski WP, Orwoll E, Yuen CK. Parathyroid hormone and teriparatide for the treatment of osteoporosis: a review of the evidence and suggested guidelines for its use. *Endocr Rev*. 2005 Aug;26(5):688-703. [[Abstract](#)] [[Full Text](#)]
- ◆ Jentsch TJ, Maritzen T, Zdebik AA. Chloride channel diseases resulting from impaired transepithelial transport or vesicular function. *J Clin Invest*. 2005 Aug;115(8):2039-46. [[Abstract](#)] [[Full Text](#)]
- ◆ Marx SJ, Simonds WF. Hereditary hormone excess: genes, molecular pathways, and syndromes. *Endocr Rev*. 2005 Aug;26(5):615-61. [[Abstract](#)] [[Full Text](#)]
- ◆ Mathieu C, Badenhop K. Vitamin D and type 1 diabetes mellitus: state of the art. *Trends Endocrinol Metab*. 2005 Aug;16(6):261-6. [[Abstract](#)]
- ◆ Nagpal S, Na S, Rathnachalam R. Noncalcemic actions of vitamin D receptor ligands. *Endocr Rev*. 2005 Aug;26(5):662-87. [[Abstract](#)] [[Full Text](#)]
- ◆ Schwartz GG. Vitamin D and the epidemiology of prostate cancer. *Semin Dial*. 2005 Jul-Aug;18(4):276-89. [[Abstract](#)]

Other Studies of Potential Interests

- ◆ Arlot M, Meunier PJ, Boivin G, Haddock L, Tamayo J, Correa-Rotter R, Jasqui S, Donley DW, Dalsky GP, Martin JS, Eriksen EF. Differential Effects of Teriparatide and Alendronate on Bone Remodeling in Postmenopausal Women Assessed by Histomorphometric Parameters. *J Bone Miner Res*. 2005 Jul;20(7):1244-53. [[Abstract](#)]
- ◆ Aya K, Alhawagri M, Hagen-Stapleton A, Kitaura H, Kanagawa O, Veis Novack D. NF-kappaB-inducing kinase controls lymphocyte and osteoclast activities in inflammatory arthritis. *J Clin Invest*. 2005 Jul 1;115(7):1848-54. [[Abstract](#)] [[Full Text](#)]

- ◆ Babitt JL, Zhang Y, Samad TA, Xia Y, Tang J, Campagna JA, Schneyer AL, Woolf CJ, Lin HY. Repulsive Guidance Molecule (RGMa), a DRAGON Homologue, Is a Bone Morphogenetic Protein Co-receptor. *J Biol Chem*. 2005 Aug 19;280(33):29820-7. [[Abstract](#)] [[Full Text](#)]
- ◆ Barna M, Pandolfi PP, Niswander L. Gli3 and Plzf cooperate in proximal limb patterning at early stages of limb development. *Nature*. 2005 Jul 14;436(7048):277-81. [[Abstract](#)]
- ◆ Bundschu K, Knobloch KP, Ullrich M, Schinke T, Amling M, Engelhardt CM, Renne T, Walter U, Schuh K. Gene disruption of *spred-2* causes dwarfism. *J Biol Chem*. 2005 Aug 5;280(31):28572-80. [[Abstract](#)] [[Full Text](#)]
- ◆ Chen S, Rani S, Wu Y, Unterbrink A, Gu TT, Gluhak-Heinrich J, Chuang HH, Macdougall M. Differential regulation of dentin sialophosphoprotein expression by Runx2 during odontoblast cytodifferentiation. *J Biol Chem*. 2005 Aug 19;280(33):29717-27. [[Abstract](#)] [[Full Text](#)]
- ◆ Hwang SG, Yu SS, Poo H, Chun JS. c-Jun/activator protein-1 mediates interleukin-1 β -induced dedifferentiation but not cyclooxygenase-2 expression in articular chondrocytes. *J Biol Chem*. 2005 Aug 19;280(33):29780-7. [[Abstract](#)] [[Full Text](#)]
- ◆ Kang JS, Alliston T, Delston R, Derynck R. Repression of Runx2 function by TGF- β through recruitment of class II histone deacetylases by Smad3. *EMBO J*. 2005 Jul 20;24(14):2543-55. [[Abstract](#)]
- ◆ Keller H, Kneissel M. SOST is a target gene for PTH in bone. *Bone*. 2005 Aug;37(2):148-58. [[Abstract](#)]
- ◆ Lee FY, Kim DW, Karmin JA, Hong D, Chang SS, Fujisawa M, Takayanagi H, Bigliani LU, Blaine TA, Lee HJ. μ -calpain regulates receptor activator of NF- κ B ligand (RANKL)-supported osteoclastogenesis via NF- κ B activation in RAW 264.7 Cells. *J Biol Chem*. 2005 Aug 19;280(33):29929-36. [[Abstract](#)] [[Full Text](#)]
- ◆ Liu YZ, Dvornyk V, Lu Y, Shen H, Lappe JM, Recker RR, Deng HW. A novel pathophysiological mechanism for osteoporosis suggested by an in vivo gene expression study of circulating monocytes. *J Biol Chem*. 2005 Aug 12;280(32):29011-6. [[Abstract](#)] [[Full Text](#)]
- ◆ Ljusberg J, Wang Y, Lang P, Norgard M, Dodds R, Hultenby K, Ek-Rylander B, Andersson G. Proteolytic Excision of a Repressive Loop Domain in Tartrate-resistant Acid Phosphatase by Cathepsin K in Osteoclasts. *J Biol Chem*. 2005 Aug 5;280(31):28370-381. [[Abstract](#)] [[Full Text](#)]
- ◆ Mayhew PM, Thomas CD, Clement JG, Loveridge N, Beck TJ, Bonfield W, Burgoyne CJ, Reeve J. Relation between age, femoral neck cortical stability, and hip fracture risk. *Lancet*. 2005 Jul 12;366(9480):129-35. [[Abstract](#)]
- ◆ Migliorati CA, Schubert MM, Peterson DE, Seneda LM. Bisphosphonate-associated osteonecrosis of mandibular and maxillary bone. *Cancer*. 2005 Jul 1;104(1):83-93. [[Abstract](#)]
- ◆ Oliver BL, Cronin CG, Zhang-Benoit Y, Goldring MB, Tanzer ML. Divergent stress responses to IL-1 β , nitric oxide, and tunicamycin by chondrocytes. *J Cell Physiol*. 2005 Jul;204(1):45-50. [[Abstract](#)]
- ◆ Schaefer L, Babelova A, Kiss E, Hausser HJ, Baliova M, Krzyzankova M, Marsche G, Young MF, Mihalik D, Gotte M, Malle E, Schaefer RM, Grone HJ. The matrix component biglycan is proinflammatory and signals through Toll-like receptors 4 and 2 in macrophages. *J Clin Invest*. 2005 Aug 1;115(8):2223-33. [[Abstract](#)] [[Full Text](#)]
- ◆ Scheel O, Zdebik AA, Lourdel S, Jentsch TJ. Voltage-dependent electrogenic chloride/proton exchange by endosomal CLC proteins. *Nature*. 2005 Jul 21;436(7049):424-7. [[Abstract](#)]

✦ Wang Y, Xiao R, Yang F, Karim BO, Iacovelli AJ, Cai J, Lerner CP, Richtsmeier JT, Leszl JM, Hill CA, Yu K, Ornitz DM, Elisseeff J, Huso DL, Jabs EW. Abnormalities in cartilage and bone development in the Apert syndrome FGFR2+/S252W mouse. *Development*. 2005 Aug;132(15):3537-48. [[Abstract](#)]

✦ Wu X, Ahn EY, McKenna MA, Yeo H, McDonald JM. Fas binding to calmodulin regulates apoptosis in osteoclasts. *J Biol Chem*. 2005 Aug 19;280(33):29964-70. [[Abstract](#)] [[Full Text](#)]