BoneKEy-Osteovision. 2004 December;1(12):1-2
http://www.bonekey-ibms.org/cgi/content/full/ibmske;1/12/1
DOI: 10.1138/20040140

NOT TO BE MISSED

Clinical and Basic Research Papers – November 2004 Selections

Ego Seeman, Clinical Editor
Gordon J. Strewler, Editor

Bone Modeling and Remodeling

Han Y, Cowin SC, Schaffler MB, Weinbaum S. Mechanotransduction and strain amplification in osteocyte cell processes. *Proc Natl Acad Sci U S A.* 2004 Nov 23;101(47):16689-94.

> *Bone is no moon rock or hard place illuminated by projected light; it has its own fire, like the New York telegraph exchange. You can see it, if you look hard enough. Han and colleagues do so and report that small tissue-level strains can be amplified through the lacunar-canalicular system, inducing strains in the actin filament bundles to induce chemical signaling. The authors propose a strain-amplification model as an alternative to the current fluid-shear hypothesis for excitation of osteocytes. —ES*

Paschalis EP, Shane E, Lyritis G, Skarantavos G, Mendelsohn R, Boskey AL. Bone fragility and collagen cross-links. *J Bone Miner Res.* 2004 Dec;19(12):2000-4.

> *Bone is a fancy piece of skin impregnated with mineral and rolled into a tube or sponge so that it can serve as a lever, spring, or both. We think about mineral, but not much about collagen and its decay with age. These investigators are putting a stop to this. They used Fourier transform infrared imaging to determine the ratio of nonreducible to reducible crosslinks in 2- to 4-μm-thick sections from human biopsy specimens. (See also Riggs BL*, et al*. J Bone Miner Res. 2004 Dec;19[12]:1945-54 [below].) —ES*

Riggs BL, Melton III LJ, Robb RA, Camp JJ, Atkinson EJ, Peterson JM, Rouleau PA, McCollough CH, Bouxsein ML, Khosla S. Population-based study of age and sex differences in bone volumetric density, size, geometry, and structure at different skeletal sites. *J Bone Miner Res.* 2004 Dec;19(12):1945-54.

> *A move away from the two-dimensional world "seen" by bone densitometry to three dimensions is a good thing, if we are remotely interested in structure. Larry Riggs and his colleagues make this move and report sex-specific differences across age that raise many new questions regarding the pathogenesis of bone fragility at the vertebrae and proximal femur in both sexes. —ES*

Vega RB, Matsuda K, Oh J, Barbosa AC, Yang X, Meadows E, McAnally J, Pomajzl C, Shelton JM, Richardson JA, Karsenty G, Olson EN. Histone deacetylase 4 controls chondrocyte hypertrophy during skeletogenesis. *Cell.* 2004 Nov 12;119(4):555-66.

> *Histone deacetylase 4 (HDAC4) is part of the class 2 family of transcriptional coregulators. Other members of the family regulate the hypertrophy of cardiomyocytes, but* HDAC4 *is expressed in hypertrophic cartilage and represses expression of* runx2*, and possibly* runx1 *and* runx3*. Removal of* HDAC4 *causes premature hypertrophy and ossification. Overexpression of HDAC4 in cartilage eliminates hypertrophic cartilage and endochondral bone formation, similarly to removal of runx2. Surprisingly, this suggests that most of the skeletal effects of runx2 deficiency occur in cartilage, not in bone. —GJS*

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Physiology and Metabolism

Armas LA, Hollis BW, Heaney RP. Vitamin D2 is much less effective than vitamin D3 in humans. *J Clin Endocrinol Metab.* 2004 Nov;89(11):5387-91.

> *We recently learned that we can't measure vitamin D in patients (Binkley N,* et al*. J Clin Endocrinol Metab. 2004 Jul;89[7]:3152-7); now we learn why we can't replace it. This paper reports that vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) are equally absorbed; however, vitamin D3 has a much longer half-life, thus the dose of vitamin D2 required to achieve an effect is three to nine times higher than the dose of vitamin D3. This may be why clinicians treating vitamin D deficiency have difficulty normalizing vitamin D levels with high doses of vitamin D2. —GJS*

Gao Y, Qian WP, Dark K, Toraldo G, Lin AS, Guldberg RE, Flavell RA, Weitzmann MN, Pacifici R. Estrogen prevents bone loss through transforming growth factor beta signaling in T cells. *Proc Natl Acad Sci U S A.* 2004 Nov 23;101(47):16618-23.
Commentary in Teitelbaum SL. Postmenopausal osteoporosis, T cells, and immune dysfunction. *Proc Natl Acad Sci U S A.* Nov 2004;101(48):16711-2.

> *The Pacifici laboratory has implicated T lymphocytes in estrogen-deficient bone loss and now reports a role of transforming growth factor β (TGF-β). Ovariectomy reduces bone marrow levels of TGF–β, and overexpression of TGF-β prevents loss of bone after ovariectomy. Bone sparing by estrogen treatment of ovariectomized mice can be prevented by a dominant negative TGF–β receptor that is targeted to T cells. Estrogen prevents bone loss through TGF-β-dependent suppression of interferon-γ, which would otherwise activate T cells to produce tumor necrosis factor α, and induce the generation of osteoclasts. —GJS*

Reviews, Perspectives, and Editorials

Allen MR, Hock JM, Burr DB. Periosteum: biology, regulation, and response to osteoporosis therapies. *Bone.* 2004 Nov;35(5):1003-12.

Other Studies of Potential Interest

Bostrom K, Zebboudj AF, Yao Y, Lin TS, Torres A. Matrix GLA protein stimulates VEGF expression through increased transforming growth factor-β1 activity in endothelial cells. *J Biol Chem.* 2004 Dec 17;279(51):52904-13.

Wang K, Yamamoto H, Chin JR, Werb Z, Vu TH. Epidermal Growth Factor Receptor-deficient Mice Have Delayed Primary Endochondral Ossification Because of Defective Osteoclast Recruitment. *J Biol Chem.* 2004 Dec 17;279(51):53848-56.

Zheng W, Xie Y, Li G, Kong J, Feng JQ, Li YC. Critical role of calbindin-d28k in calcium homeostasis revealed by mice lacking both vitamin d receptor and calbindin-d28k. *J Biol Chem.* 2004 Dec 10;279(50):52406-13.