NOT TO BE MISSED

Clinical and Basic Research Papers – July 2005 Selections

Ego Seeman, Clinical Editor
Gordon J. Strewler, Editor

Bone Modeling and Remodeling


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-κB 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


Dendritic cell-specific transmembrane protein (DC-STAMP) is a G protein-coupled receptor that is induced by receptor activator of NF-κB 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

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


Other Studies of Potential Interests


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