



Workshop Abstract

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Prostaglandins in cross talk in bone

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Prostaglandins (PGs), particularly prostaglandin E₂ (PGE₂), are potent multifunctional regulators of many cellular functions in bone. PGE₂ has been shown to stimulate bone resorption and formation, but can also have inhibitory effects. Most of the hormones, cytokines and growth factors that influence bone cell function also affect PG production in the osteoblasts, and some affect production in cells of the osteoclast lineage. A number of potential amplification loops have been identified. Bone morphogenetic protein-2 (BMP-2), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF) and Interleukins-1 and 6 have been shown to activate the inducible cyclooxygenase (COX-2) and increase PG production and may also be stimulated by PGs themselves. PGs are local regulators, but it is not clear whether they act largely by paracrine or intracrine pathways. The intracellular location of the synthetic enzymes and some receptors support the latter possibility. PGE₂ can affect osteoclast production and function directly, independent of any effects on osteoblasts. An inhibitory effect on osteoclast function could be important in mediating the effect of high calcium concentration, which also induces COX-2, on osteoclast activity. Studies using transgenic mice with deletions of COX-2 or specific PGE₂ receptors as well as studies using selective PG receptor agonists have helped to analyze the multiple and complex effects of prostaglandins on bone cells, but much remains to be learned concerning their specific roles in human physiology and pathology.