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Calcium Metabolism Regulated by RANKL/OPG Balance in the Gut

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Summary

Calcium is stored primarily in bone and released to blood with bone remodeling by regulating various hormones. Bone turnover is thus inextricably associated with calcium metabolism. The bone remodeling is maintained by a balance between bone formation by osteoblast and bone resorption by osteoclast. The osteoclast differentiation is regulated by receptor activator of NFκB ligand (RANKL) and its receptor, RANK. Osteoprotegerin (OPG) is a soluble decoy receptor of RANKL and serves as an endogenous inhibitor of RANKL-RANK signaling, resulting in the suppression of osteoclast activation. OPG itself may be involved in calcium metabolism. Circulating OPG is increased in chronic kidney disease patients. Parathyroid hormone (PTH) inhibits OPG expression in primary cultures of human osteoblast cells; on the other hand, estrogen stimulates OPG expression. Here we show that enteroendocrine cell, which is specialized cells of gastrointestinal tract with endocrine function, express OPG. The ischemia-induced acute nephritis in BALB/c mice simultaneously increased circulating OPG and stimulated OPG mRNA expression in the intestinal epithelium. Administration of estrogen to BALB/c mice decreased the expression of OPG mRNA in intestinal epithelium although PTH did not change OPG expression. There data suggests that OPG secreted from enteroendocrine cells contributes to the amount of circulating OPG in acute nephritis and estrogen treated mice.