OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Involvement of cannabinoids in bone mass control and ovariectomy-induced bone loss

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Bone remodeling is a complex process that is regulated by an interplay between circulating hormones and locally produced factors that act in a concerted manner to regulate osteoblast and osteoclast activity. There has been recently increasing interest in the role that the nervous system and neurotransmitters play in the regulation of bone remodeling. Reflecting this fact, the endocannabinoid pathway has recently been implicated as are important regulator of bone turnover and bone mass. The type 2 cannabinoid receptor (CB2) has been reported to regulate bone mass, but conflicting results have been reported with regard to its effects on bone resorption and osteoclast function. In this study [1], the authors investigated the role that CB2 plays in regulating bone mass and osteoclast function using a combination of pharmacological and genetic approaches.

CB2 antagonists inhibited osteoclast formation and activity in vitro, whereas CB2-selective agonists stimulated osteoclast formation. Osteoclasts generated from CB2 knockout mice were resistant to the inhibitory effects of selective antagonists in vitro, consistent with a CB2-mediated effect. There was no significant difference in peak bone mass between CB2 knockout mice and wild-type littermates, but after ovariectomy, bone was lost to a greater extent in wild type compared with CB2 knockout mice in which osteoclast activity and bone resorption was low. Furthermore, CB2 antagonists protected against bone loss in wild-type mice, but the effect was lost in CB2 knockout mice.

It is concluded that CB2 stimulates osteoclast formation and bone resorption in vitro and that under conditions of increased bone turnover, such as after ovariectomy, CB2 promotes bone loss. These observations indicate that CB2 contributes to ovariectomy-induced bone loss and demonstrate that cannabinoid receptor antagonists may be of value in the treatment of bone diseases characterized by increased osteoclast activity.

1. Idris AI et al. *Endocrinology.* 2008;149:5619–5626.

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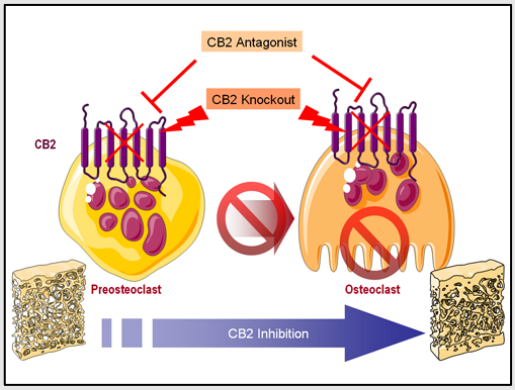
Osteoclast formation and activity is controlled by hormones and mediators. Bone-resorbing cells express the type 2 cannabinoid receptor called CB2 which is a membrane receptor coupled to G proteins able to bind endocannabinoids. CB2 antagonists inhibit osteoclast formation and activity whereas CB2 agonists stimulate osteoclast formation. A similar inhibition of osteoclast formation and activity is observed in CB2 knockout mice. Bone was lost to a greater extent after ovariectomy in wild type compared with CB2 knockout mice.

These observations indicate that CB2 contributes to ovariectomy-induced bone loss and demonstrate that cannabinoid receptor antagonists may be of value in the treatment of bone diseases with high resorption.



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