

Oral Abstract

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Calcitonin attenuates the anabolic effect of PTH *in vivo* and rapidly upregulates sclerostin expression

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There is increasing evidence for a role of osteoclasts in the anabolic action of PTH. To determine whether osteoclast activity contributes to PTH anabolic action, 3-week-old rats were treated with daily subcutaneous hPTH(1-34) (30ug/kg) and co-treated with 0.5ug/kg salmon calcitonin (sCT). Co-treatment with sCT significantly attenuated the anabolic effect of PTH as detected by pQCT and histomorphometry.

Candidate gene targets modified by sCT co-administration with PTH were examined by qRT-PCR of metaphyseal bone from 3 week old female rats treated with a single injection of vehicle, 0.5ug/kg sCT, 30ug/kg hPTH(1-34) or co-administered sCT and hPTH(1-34). Several genes whose expression was affected by PTH were not modified by sCT co-treatment, including RANKL, IL-6 and ephrinB2. The osteocyte-derived bone formation inhibitor, sclerostin was inhibited 1.5 fold by PTH 1 hour post injection. This reduction was significantly diminished by sCT co-administration at all time points. Furthermore, sCT alone increased sclerostin mRNA at least 2.5-fold at 1.5, 4 and 6 hrs. This increase was confirmed by immunohistochemistry. The number of sclerostin positive osteocytes in tibial cortical bone was significantly increased 4 hrs following sCT administration (vehicle: 26% ±4%; sCT: 43% ±3%, p<0.01). Also at 4 hrs, qRT-PCR analysis revealed that sCT reduced mRNA for other osteocytic gene products including MEPE (-1.4 ±0.06 fold) and DMP-1 (-1.9 ±0.06 fold).

This data indicates that calcitonin can promote sclerostin production, and influence production of other genes characteristic of the osteocyte. Calcitonin might modify the anabolic effect of PTH through this pathway.