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PTH combination with anti-IL17 prevents bone loss by disruption of PTHR1/LRP-6 interaction

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R ecent studies have shown that combinations of anabolic and anti-resorptive agents have the potential to improve bone density more than either of the agent alone. In this study, we determined the combining effect of anti-IL17 antibody and PTH (1-34) in mitigation of ovariectomy induced bone loss. Ovariectomized BALB/c female mice were treated with neutralizing anti-IL17 and anti-RANKL antibodies and their combination with iPTH. After one-month time period, treatment was started for four weeks in Ovx mice. Groups in experiments were sham operated (ovary intact) mice, ovariectomized (Ovx) mice, Ovx mice +iPTH (40 μ g/kg/day), Ovx+ anti-RANKL (300 μ g/mice) twice a week, Ovx+anti-17A (100 ng/mice) twice a week, Ovx + iPTH (40 μ g/kg/day)+anti-IL-17A (100 ng/mice) twice a week IN Ovx mice. Combination of iPTH and anti-IL17 has synergistic effect in the restoration of skeletal and immune parameters compared to mono-therapies. Immunofluorescence analysis shows decreased expression of PTHR1 in iPTH+anti-IL17 treated bone sections. Our studies show that IL-17 up-regulates N-cadherin which disrupts PTHR1/LRP-6 interaction thereby inhibiting wnt signaling and promoting bone loss. Our study recommends the use of iPTH and anti-IL17 combination therapy for post-menopausal osteoporosis.

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