

## Oral Abstract

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### OCIL (osteoclast inhibitory lectin) deficiency causes osteopenia

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OCIL (or clrb) is a member of the Natural Killer cell C-type lectins which have a described role mostly in autoimmune cell function. OCIL was originally identified as an osteoblast-derived inhibitor of osteoclast formation *in vitro*. To determine the physiological function(s) of OCIL, we generated *ocil*<sup>-/-</sup> mice. These mice appeared healthy and were fertile, with no apparent immune function defect, and phenotypic abnormalities were limited to bone. Histomorphometric analysis revealed a significantly lower tibial trabecular bone volume and trabecular number in the 10- and 16-week old male *ocil*<sup>-/-</sup> mice compared to *wt*. Furthermore, *ocil*<sup>-/-</sup> mice showed reduced bone formation rate in the 10-week old females and 16-week old males associated with a 54% reduction in mineralizing surface in 10-week old females and a 33% reduction in mineral apposition rate in the 16-week old males. Static markers of bone formation (such as osteoblast number/surface, osteoid volume/surface/ thickness) showed no significant changes in male or female *ocil*<sup>-/-</sup> mice. Examination of bone resorption markers in the long bones of *ocil*<sup>-/-</sup> mice indicated a transient increase in osteoclast number per unit bone perimeter. Enhanced osteoclast formation was also observed when either bone marrow or splenic cultures were generated *in vitro* from *ocil*<sup>-/-</sup> mice relative to wild type control cultures. Loss of *ocil* therefore resulted in osteopenia in adult mice primarily as a result of increased osteoclast formation. The enhanced osteoclastic activity led to elevated serum calcium levels which resulted in the suppression of circulating parathyroid hormone in 10-week old *ocil*<sup>-/-</sup> mice compared to *wt* control mice. Collectively our data suggest that OCIL is a physiological negative regulator of osteoclastogenesis, and may further the links between immune-cell function and bone physiology.