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2007 Amgen/ANZBMS Outstanding Abstract Award Recipient

Winner: Dr Natalie Sims

Abstract:

Oncostatin M is an essential stimulus of bone formation and osteoclastogenesis

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Murine oncostatin M (OsM) signals through gp130 and a specific OsMR expressed by osteoblasts. OsM is reported to increase osteoclastogenesis by stimulating RANKL production by osteoblasts, but the effects of OsM on bone formation are not defined.

To determine whether OsM is essential in vivo, we studied OsMR deficient mice. Male and female OsMR null mice demonstrated a 75% increase in trabecular bone volume in distal tibia and lumbar vertebrae. Femoral trabecular BMD was also elevated by 40% in males and females. This was associated with a significant reduction in osteoclast surface and reduced resorption. Bone formation was also reduced, with significant reductions in osteoid thickness, osteoblast surface and bone formation rate. In contrast, marrow adipocyte number was elevated 4 fold.

Consistent with this phenotype, OsM treatment dose-dependently increased alkaline phosphatase activity and mineralization by Kusa4b10 stromal cells compared to untreated controls, while adipocyte formation was more than halved. Real time PCR analysis demonstrated a 20-fold increase in expression of the transcription factor C/EBPd within 1 hour of OsM administration. C/EBPd synergises with runx2 to enhance osteocalcin transcription; consistent with this we observed a dose-dependent increase in activity of a 6xOSE-luciferase reporter construct. Furthermore, local injection of OsM over the calvariae of young wild type mice significantly increased calvarial thickness and bone formation rate indicating an anabolic effect in vivo.

This reveals an inhibitory role for OsM in adipocyte differentiation and a critical role in stimulating bone formation in vivo.