A novel antagonist of the canonical Wnt-signalling pathway, SOSTDC1, is expressed in an experimental model of myeloma and suppresses bone formation

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Introduction

Patients with multiple myeloma (MM) commonly present with devastating bone disease mediated by increased bone resorption and suppressed bone formation. We have previously shown that blocking activity of the Wnt antagonist DKK1 protects osteoblastogenesis and inhibits development of bone lesions in experimental models of MM. In the 5T murine models of MM, tumour cells home to the bone marrow. Injection of 5T2MM cells into the mouse calvariae. mice were injected with SOSTDC1 (15µg/kg.day) via the tail vein. Bone volume (BV) was measured using µCT. Data obtained using BMP2 not significantly lower than control (p<0.0024), as well as reduced bone formation rate (mineral apposition rate x mineralising surface) (Figure 5). Representative images of bone cross-sections were recorded for qualitative assessment of bone formation (Figure 6). Statistical analysis was performed using Student’s unpaired t test. SOSTDC1 suppressed Wnt- and BMP-induced phosphorylated β-catenin levels in cultured mouse OB (Figure 6). Data obtained using BMP2/7 not significantly different from control. OB number and OB perimeter were significantly reduced in SOSTDC1-treated mice compared to control (Figure 5).

Discussion

Our in vivo data suggest that SOSTDC1 is a significant inhibitor of OB activity. Taken together with the in vitro studies, which demonstrate that rhSOSTDC1 inhibits both Wnt- and BMP-induced OB differentiation (outlined in Figure 7), they suggest that blocking myeloma-derived Wnt signalling in MM patients with myeloma bone disease.

References


Conflict of interest – none declared by authors.