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2007 Amgen/ANZBMS Outstanding Abstract Award Recipient

Winner: Dr Colin Dunstan

Abstract:

Accelerated bone resorption, due to dietary calcium deficiency, promotes tumour growth in a murine model of breast cancer bone metastasis

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The skeleton is a major site of breast cancer metastases. High bone turnover increases risk of disease progression and death. However, there is no direct evidence that high bone turnover is causally associated with the establishment and progression of metastases. In this study, we investigate the effects of high bone turnover on tumour growth in a rodent model of bone metastasis.

Female nude mice commenced a diet containing normal (0.6%) ('Normal-Ca') or low (0.1%) ('Low-Ca') calcium content. Mice were concurrently treated with vehicle or recombinant osteoprotegerin (OPG; 1mg/kg/day sc; n = 16/group). Three days later (day 0), 50,000 MDA-MB-231-TXSA cells were implanted by intra-tibial injection and mice were followed until day 17.

PTH and TRAcP5b levels, indicating secondary hyperparathyroidism and high bone turnover, which was maintained until day 17. Treatment with OPG increased serum PTH but profoundly reduced bone resorption. On day 17, in mice receiving 'Low-Ca' alone, lytic lesion and tumour area and cancer cell proliferation increased by 43%, 24% and 24%, respectively compared to mice receiving 'normal Ca' ($p<0.01$). In contrast, OPG treatment completely inhibited lytic lesions, reduced tumour area, decreased cancer cell proliferation and increased cancer cell apoptosis.

We conclude that increased bone turnover, due to dietary calcium deficiency, promotes tumour growth in bone, independent of the action of PTH. These findings have clinical implications as breast cancer patients, much like the older population in general, frequently have a low dietary calcium intake and high bone turnover.