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Inhibition of RANK/RANKL interactions prevent ovariectomy-induced growth of disseminated breast cancer cells in bone

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Dormant disseminated tumour cells can be detected in the bone marrow of breast cancer patients several years after resection of the primary tumour. The majority of these patients will remain asymptomatic, however, approximately 15% will go on to develop overt bone metastases and this condition is currently incurable. The reason why these dormant cells are stimulated to proliferate and form bone tumours in some patients and not others remains to be elucidated. We have recently shown that in an *in vivo* model, increasing bone turnover by ovariectomy stimulated proliferation of disseminated tumour cells, resulting in formation of bone metastasis. This awakening of MDA-MB-231 tumour cells in bone from a dormant to a proliferative state was prevented following administration of the antiresorptive drug zoledronic acid and therefore appeared to be driven by osteoclast mediated mechanisms. In agreement with this hypothesis we have also shown that disruption of RANK-RANKL interactions following administration of OPG-Fc inhibits growth of these dormant tumour cells *in vivo*. Our pre-clinical data support early intervention with anti-resorptive therapy in a low-oestrogen environment to prevent development of bone metastases.

Biography

Ottewell is a lecturer in the Academic Unit of Clinical Oncology, University of Sheffield UK. She was awarded a PhD from the Department of Gastroenterology at The University of Liverpool in 2005. Ottewell first arrived in Sheffield in 2005 when she took up a position as a post-doctoral scientist working on breast cancer. During her time here Dr Ottewell has carried out international collaborative work spending time at INSERM (University of Lyon), France and at TUFTS University in Boston, USA. Her multi-award winning research focuses on advanced breast cancer with particular emphasis on looking at how and why breast cancer cells spread from the primary site to the skeleton. Ottewell has been awarded a total of 10 prizes for her research including the prestigious Breast Cancer Campaign Research Team of the year award in 2008 and the International Bone and Mineral Society Gregory Mundy Research Fellowship in 2011.

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