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Intercellular communication in bone metastasis

Bone is the most frequent site for metastasis of breast and prostate cancers, often resulting in pathologic changes in bone metabolism and severe pain. Our understanding of the biological mechanisms involved is limited, although the most popular view is that the tumour cells initiate the release of factors from bone, which in turn, stimulates tumour cells to proliferate and cause further bone degradation. The application of this hypothesis, often called the vicious cycle model, has led to the development of many therapeutic strategies aimed at disrupting the role that osteoclasts play in this process. Unfortunately, the vicious cycle does not fully account for many clinical features observed in patients. Although the model is predictive in osteolytic disease, it does not guide us in our understanding of the progression of the osteoblastic metastases common to many prostate cancers. Significantly, the model does not directly address the severe pain that is experienced by patients with either bone phenotype. To complement the successes of the vicious cycle, other models need to be developed to allow us to move forward in our understanding of this complex disease. We have developed an intercellular communication hypothesis that may be applied to this problem. Many chemical factors released by tumour cells are known to interfere with the fine balance that exists between bone resorption and formation in normal bone. The suggestion that bone metastasis pathology may be the result of a communication problem represents a novel perspective in our understanding of bone metastasis, and this concept may lead to practical targets for therapeutic intervention in bone metastasis and chronic bone cancer pain.