

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Regulation of cancer cell migration and bone metastasis by RANKL

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Bone metastases are a frequent complication of many cancers that result in severe disease burden and pain. It is now acknowledged that the microenvironment of the local host tissue actively participates in the propensity of certain cancers to metastasize to specific organs, and that bone provides an especially fertile 'soil.' In the case of breast cancers, the local chemokine milieu is now emerging as an explanation for why these tumors preferentially metastasize to certain organs. However, as the inhibition of chemokine receptors *in vivo* only partially blocks metastatic behavior, other factors must exist that regulate the preferential metastasis of breast cancer cells.

Jones et al. performed an elegant study [1] showing that the cytokine RANKL (receptor activator of NF- κ B ligand) triggers migration of human epithelial cancer cells and melanoma cells that express the receptor RANK. RANK is expressed on cancer cell lines and breast cancer cells in patients. In a mouse model of melanoma metastasis, *in vivo* neutralization of RANKL by osteoprotegerin results in complete protection from paralysis and a marked reduction in tumor burden in bones but not in other organs.

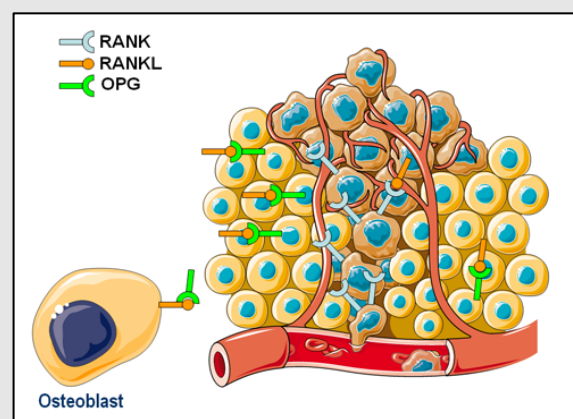
These data show that local differentiation factors such as RANKL have an important role in cell migration and the tissue-specific metastatic behaviour of cancer cells. They establish that RANKL can act as a tissue-specific factor for migration of cancer cells and that RANKL is a prominent 'soil' factor for bone-specific metastases of epithelial tumours. Therefore, inhibition of RANKL–RANK interactions may offer a promising therapeutic target for interfering with tumour metastasis and progression in bones.

1. Jones DH et al. *Nature*.2006;440: 692-696.

Regulation of cancer cell migration by RANKL

RANKL, secreted by osteoblasts, can act as a bone-specific factor for migration of cancer cells and is therefore is a prominent 'soil' factor for bone-specific metastases of epithelial tumors.

Inhibition of RANKL–RANK interactions, with osteoprotegenin for example, may offer a promising therapeutic target for interfering with tumor metastasis and progression in bones



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