

# OSTEOSCOOP

News on current events in osteoporosis and rheumatology

## Transmigration of mature multinucleated osteoclasts

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Osteoclasts (OCs) are large multinucleated cells of hematopoietic origin formed by the differentiation and fusion of mononuclear monocyte–macrophage lineage precursors after stimulation by RANKL and macrophage colony-stimulating factor (M-CSF). OC access to the bone surface requires precursor recruitment from the circulation into bone and a capacity to migrate to find their way to suitable stromal sites for their development into bone-resorptive mature multinucleated OCs (MMOCs). Mononucleated osteoclasts precursors (pre-OCs) have the capacity to transmigrate through endothelial cells. MMOCs also exhibit several features usually involved in cell invasion such as expression of the proto-oncogene *c-src*. Disruption of *c-src* leads to osteopetrosis in mice, resulting in the excessive accumulation of bone matrix caused by defective OC functions. Matrix metalloproteinases (MMPs), which play a major role in tumor cell invasion and metastasis, are also involved in OC function by promoting their recruitment and the degradation of the mineralized bone matrix. Finally, OCs exhibit podosomes, highly dynamic actin-rich structures involved in adhesion, migration, and matrix degradation, and sealing zones insuring attachment to bone surface.

As the functions of MMOCs are associated with molecules (*c-src*, MMPs) and actin structures (podosomes) that are all involved in cell invasion, Saltel et al. [1] studied whether MMOCs possess invasive properties. They observed that multinucleated osteoclasts specifically transmigrate through confluent layers of various cell types present in the bone microenvironment in vitro. This efficient process required *c-src* and MMPs but was independent of podosomes. Moreover, conditioned medium from bone metastatic breast cancer cells stimulates osteoclast transmigration.

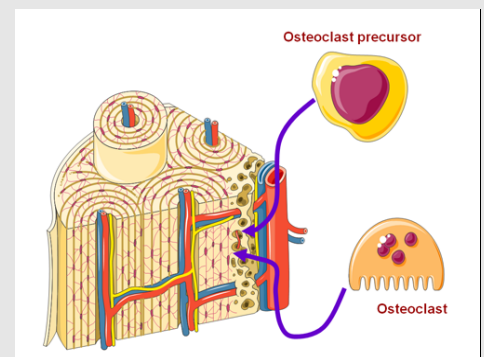
These data show for the first time that MMOCs can transmigrate through multilayers of several cell types, a new property of OCs that may contribute to bone loss in osteopenic disorders such as osteoporosis and the establishment of breast cancer metastatic osteolytic lesions.

1. Saltel F et al. *J Bone Miner Res.* 2006;21:1913-1923.

### Transmigration of mature multinucleated osteoclasts

Monocytes/macrophages, which are osteoclast precursors, have the ability to cross vessel walls and tissue structures to reach their site of action. This property is called transmigration.

This ability to transmigrate is shared by mature multinucleated osteoclasts which are responsive to stimuli of cell invasion. Osteoclasts can transmigrate through multilayers of several cell types, a newly discovered property that may contribute to bone loss in osteopenic disorders such as osteoporosis and the establishment of breast cancer metastatic osteolytic lesions.



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