**The anti-angiogenic peptide Anginex blocks osteoclastogenesis**

Muller J, Binsfeld M, Dubois S, Carmeliet G, Beguin Y, Heusschen R, Caers J

Osteolytic bone disease (OBD) is a hallmark of multiple myeloma (MM), a hematological malignancy characterized by the accumulation of malignant monoclonal plasma cells in the bone marrow. An uncoupling of bone remodeling, with an increased rate of bone resorption by osteoclasts and a decreased rate of bone formation, causes rapid bone loss and as a result bone pain, pathological fractures and hypercalcemia. Multinuclear osteoclasts form following the fusion of monocytic progenitor cells and several glycans have been implicated in this process. In the current project we set out to identify glycan receptors, i.e. lectins, that play a role in osteoclastogenesis and that can be targeted for the treatment of OBD.

We performed a gene set enrichment analysis (GSEA) on microarray data and found that galectin-1 (gal-1) expression was significantly higher in monocytes compared to osteoclasts. Galectins are a family of -galactoside binding proteins that can act both extra- and intra-cellularly. Interestingly, gal-1 has been implicated in myoblast- and throphoblast-fusion and has recently been shown to affect MM development. We further confirmed a loss of gal-1 expression during osteoclast differentiation by real-time PCR and Western blot on primary and cell line-derived osteoclast cultures. Confocal microscopy imaging revealed changes in gal-1 localization and suggest a role for this lectin in monocyte fusion. Treatment of osteoclast cultures with an anti-angiogenic peptide that targets gal-1, i.e. Anginex, hampers osteoclastogenesis without influencing the survival of monocytes. Conversely, siRNA-mediated knockdown of gal-1 resulted in increased osteoclastogenesis with larger individual osteoclasts.

Our findings support a role for gal-1 in osteoclast differentiation. Additional experiments to further dissect the contribution of gal-1 to this process and ultimately to osteolysis are currently ongoing.