Galectin-1 is involved in osteoclast biology

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Osteolytic bone disease (OBD) is a frequent complication of multiple cancers, such as multiple myeloma. OBD is due to the disruption of balanced bone remodelling, with higher bone resorption due to increased osteoclast activation and osteoblast inhibition. Lectin-glycoprotein interactions have been implicated in osteoclast formation. In the current study, we set out to identify lectins that are involved in osteoclastogenesis and to study their role in this process. We anticipate that this research will lead to the identification of new targets for the treatment of OBD.

Gene Set Enrichment Analysis on publically available microarray data showed a lower expression of galectin-1 (gal-1) in mature osteoclasts compared to monocytic progenitor cells. Gal-1 is a β-galactoside binding protein implicated in myeloma and interestingly already implicated in trophoblast and myoblast fusion. We confirmed a decrease of gal-1 expression during osteoclast formation on the RNA and protein level on primary and cell line-derived osteoclast cultures. Gal-1 localization by confocal microscopy was found to be predominantly membranous in mature osteoclasts while it was ubiquitous in progenitor cells. siRNA-mediated silencing of gal-1 resulted in an increased osteoclastogenesis and larger osteoclasts. Treatment of osteoclast cultures by Anginex, an anti-angiogenic synthetic peptide that targets gal-1, resulted in a reduced osteoclast formation. We observed no difference in osteoclast number in primary cultures derived from gal-1-/- mice compared to wild-type controls. However, gal-1-/- osteoclasts showed a higher resorption activity, corroborated by a higher expression and secretion of tartrate resistant acid phosphatase in these cultures.

Taken together, our data implicate gal-1 in osteoclast biology. Analyses of bone parameters by μCT and immunohistomorphometry in gal-1$^{-/-}$ and wildtype mice are currently ongoing. In addition, gain-of-function studies and analysis of signalling pathways in osteoclasts will be performed. Finally, the role of gal-1 in OBD will be studied in the 5TGM.1 murine multiple myeloma model.