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Sighting receptor-activator of nuclear kappaB ligand in highly active aneurysmal bone cysts

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Introduction: Aneurysmal bone cysts (ABCs) are rare benign skeletal tumors which are typically associated with a growing mass, swelling, pain and bone destruction. The current treatment option of choice for symptomatic and active ABCs is intralesional curettage followed by bone grafting. However, incomplete resectability of the lesion is a major problem resulting in recurrence in up to 20% of cases. ABCs, especially affecting the spine, sacrum or pelvis make surgical treatment crucial. Though the mechanism of bone destruction is not certain, the very recent literaure hypothetised that ABC express both RANK and RANKL similary to GCTB and that targeted RANKL therapy will mitigate ABC tumour progression. The use of Denosumab, a monoclonal antibody specifically binding receptor-activator of nuclear kappaB ligand (RANKL), which inhibits bone resorption, might be a promising treatment alternative. Our objective was to verify the target of Denosumab.

Methods: Cellular expression of RANKL and RANK was observed in freshly harvested ABC samples (n=4) in confocal laser microscopy after IRB approval. Each patient diagnosis was confirmed by an orthopaedic pathologist in combination with interpretation of radiographic imaging, histology, and cytogenetic analysis as part of a multidisciplinary musculoskeletal oncology tumor board. Formalin fixed paraffin embeded 2.5µm slides were processed to immunofluorescencestaining with monoclonal Antobodies for RANKL and RANK, additional isotype controls were included in this study.

Results: In all four ABC samples localized expression of RANK and RANKL was determined in confocal laser microscopy. Higher immunopositivity for RANKL and RANK we found in areas of stromal spindel cells, interestingly nearly no staining could be detected in osteoclast like giant cells. Overall higher RANK presence differs differentyl from lower RANKL positivity in highly active ABCs.

Conclusion: The immunofluorescence experiments in our study support the hypothesis showing expression of RANK and RANKL in stromal spindle cells in highly active ABCsbut its causal mechanisms remain to be identified in detail. These findings contribute to the idea that the RANK-RANKL signalling axis is possibly involved in ABC tumor progression and therefore denosumab might be a treatment option for ABCs- respectively more data are needed to determine ultimately its safety and efficacy to ABCs.