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The chitinases role in osteoclasts activity

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The integrity of skeletal mass require continuous bone renewal by a combination of modeling and remodeling, mediated by osteoclasts (OCs) and osteoblasts (OBLs). Osteolysis mediated by OCs is a hallmark of different bone diseases [1]. In multiple myeloma (MM), osteolytic bone disease is a manifestation that leads to progressive skeleton destruction and is the most severe cause of morbidity. Our hypothesis was that a family genes called Chitinases could play a role in bone loss mediated by OCs. These genes exert important biological functions in the monocyte lineage and chronic inflammatory diseases [2]. In this respect, we evaluated the chitinases expression in OCs differentiation and in MM cell lines under Bortezomib (BO) treatment. Our results showed an increasing of CHI3L1 and CHIT1 during the osteoclastogenesis. As well, the confocal immunofluorescence (IF) and immunohistochemistry (IHC) analysis demonstrated the presence of CHI3L1 and CHIT1 uniformly distributed into the OCs. The OCs treatments with chitosan, a natural ligand for chitinases, and the silencing with small interfering RNA (siRNA) of CHI3L1 and CHIT1, resulted in a significant reduction in bone resorption. Based on this results, the OCs treatments with BO during the osteoclastogenesis, had reduced the digestive activity and the chitinases mRNA and protein expression levels. Moreover, the IF evaluation of mature OCs showed that BO was able to induce CHI3L1 translocations into the nucleus, while CHIT1 remained into the cytoplasm. Since MM cell lines showed high levels of CHIT1 activity, we analyzed bone resorption ability of U266. Silencing chitinases proteins in U266 cell line with siRNA, resulted in pits number reduction on dentine disks. Overall, all these results have demonstrate crucial role of chitinases in promoting bone resorption. In the light of all this, the chitinases are new potential candidate markers for therapeutic targeting in bone loss.

References

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Key words

Osteoclast, chitinase, multiple myeloma.