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LIGHT/TNFSF14 affects basal bone remodeling

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LIGHT (TNFSF14), expressed by different cells of the immune system, binds two trans-membrane receptors: HVEM and LTβR. It is over-expressed in erosive rheumatoid arthritis and lytic myeloma-bone disease and controversial data have been published on its role in osteoclast (OC) formation in vitro. Here, we investigated the role of LIGHT on in vitro murine osteoclastogenesis model and bone phenotype in LIGHT-/- mice. Firstly, we showed that murine macrophages stimulated with LIGHT alone did not differentiate into OCs. Interestingly, the presence of LIGHT and sub-optimal RANKL concentration displayed synergic effects on OC formation through the early and sustained activation of Akt, NFκB and JNK pathways. Secondly, by microCT we found that the femurs of LIGHT-KO mice exhibited a 30% ($p<0.01$) decrease in trabecular BV/TV due to a significant reduction in trabecular thickness and number as well as the increase in trabecular spaces respect to wild-type (WT) mice. Furthermore, a five fold increase of OC number/bone surface was found in femora from KO mice compared to WT ($p<0.008$). To investigate the possible molecular mechanism/s responsible for this bone phenotype in LIGHT-/- mice we studied OPG levels in whole bone marrow (BM) extracts from the femurs of these mice and demonstrated a significant reduction in OPG mRNA transcript respect to WT. Further investigations showed that BM CD8+ T cells and B cell subpopulations from KO mice expressed lower levels of OPG compared to those from WT mice. Consistently, LIGHT treatment in a dose dependent manner increase OPG expression in BM CD8+ T cells and B-cells. In conclusion, our results identified LIGHT as a new important regulator of bone remodeling and highlighted a new modulator of OPG expression.

Keywords

LIGHT/TNFSF14; osteoclasts; bone remodeling.