The increased expression of receptor activator of nuclear-?B ligand (RANKL) of multiple myeloma bone marrow stromal cells is inhibited by the bisphosphonate ibandronate

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The receptor activator of nuclear factor-kappaB ligand (RANKL) and interleukin-1beta are osteoclast activating factors which are abnormally expressed in bone marrow stromal cells and plasma cells of multiple myeloma patients. In this work we analyzed RANKL expression in human bone marrow mesenchymal stromal cells and the effect of the bisphosphonate ibandronate on RANKL expression after IL-1beta activation of ERK pathway. Mesenchymal stromal cells were obtained from bone marrow iliac aspirates from multiple myeloma patients at stages II/III and non-osteoporotics control donors; these cells were maintained under long-term culture conditions. Cells were cultured in the presence or the absence of 5 ng/ml IL-1beta and/or 5 ?M ibandronate, during selected periods. mRNA for RANKL and protein levels were assayed by RT-PCR and Western blot, respectively. Human bone marrow stromal cell line HS-5 was used for assessing IL 1beta- and ibandronate-ERK phosphorylation responses. Multiple myeloma mes