

## LEPTIN, OSTEOPROTEGERIN AND RANKL IN CONDITIONED MEDIUM DURING LONG-LASTING CULTURE OF MARROW MESENCHYMAL CELLS IN PATIENTS AFTER ALLOGENEIC HEMOPOIETIC STEM CELL TRANSPLANTATION

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We have recently documented an increase in serum leptin levels after allogeneic stem cell transplantation (allo-SCT). In physiological conditions, leptin seems to have a predominant peripheral anabolic effect on bone. Currently, it is unknown which role can have the increased leptin production and the osteoprotegerin (OPG)/RANKL system in bone remodelling after allo-SCT. Thirty-six patients (14F) were enrolled and compared to 36 controls. By using enriched mesenchymal stem cells, deriving from bone marrow biopsies, in the colony-forming-unit fibroblast (CFU-F) assay, the osteogenic stromal lineage was evaluated. Leptin, OPG and RANKL levels were measured in bone marrow plasma and in conditioned medium of long-lasting cultures (1 and 3 mos) of mesenchymal cells. Lumbar and femoral BMD values as well as number of CFU-F colonies were significantly lower in patients than in controls ( $p < 0.01$ ). There were no significant differences in leptin levels between patients and controls. OPG was lower in patients than in controls in all determinations ( $p < 0.005$ ). In both groups, the average OPG levels resulted higher after 1 (5-6 folds) and 3 months (>10 folds) of culture when compared to marrow plasma levels ( $p < 0.01$ ). RANKL resulted similar among patients and controls, being lower in conditioned medium than in marrow plasma ( $p < 0.01$ ). The OPG/RANKL ratio was significantly lower in patients than in controls ( $p < 0.05$ ). Number of CFU-F colonies correlated with lumbar and femoral BMD ( $p < 0.05$ ). No correlation was found between leptin, OPG or RANKL levels and the number of CFU-F. In conclusion, these results let hypothesize an independent reduction of functional capacity of osteoblasts, beside the previously described deficit in their repopulation capacity. Further studies are needed to clarify a possible role of leptin in post-transplant bone remodelling.