IJAE
Vol. 123, n. 1 (Supplement): 22, 2018
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Wisp2 overexpression induced by short Teriparatide treatment affects IDG-SW3 osteogenic differentiation

Jessika Bertacchini[1], Alberto Smargiassi[1], Marta Checchi[1], Maria Sara Magarò[1], Francesco Potì[2], Elena Tenedini[3], Giuliana Montosi[4], Jonathan Vinet[1], Delphine Maurel[5], Carla Palumbo[1]

[1] University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neuronal Sciences, Modena
[2] University of Parma, Department of Medicine and Surgery, Parma
[3] University of Modena and Reggio Emilia, Department of Medical and Surgical Sciences, Modena
[4] University of Modena and Reggio Emilia, Department of Internal Medicine II, Modena
[5] University of Bordeaux, BIOTIS, INSERM, Bordeaux

The Osteocyte, recognized as a major orchestrator of osteoblast and osteoclast activity, is the most important key player during bone remodeling processes. Imbalances occurring during bone remodeling, caused by hormone perturbations or by mechanical loading alterations, can induce bone pathologies such as osteoporosis or sarcopenia. The active fraction of parathormone [PTH (1-34)], a drug named Teriparatide, has long been chosen as election treatment for osteoporosis. The effect of such therapy is dependent on the temporal manner of administration, in fact it has been largely demonstrated that a short administration of Teriparatide increases bone formation but a long administration of the same agent leads to an increased bone resorption. The molecular reasons why the type of administration regimen is so critical for the outcame of bone mass recovery are numerous and not yet well known. The short administration of PTH (1-34) was demonstrated to induce osteoblast hyperplasia and to increase osteoblast survival, in parallel augmenting their ability to differentiate and to induce the preosseus matrix mineralization. On the contrary, the long term treatment with PTH (1-34), leads to the increment of osteoclast number and to the increase of their activity during bone resorption. Based on these considerations, our study attempts to analyze diverse signaling pathways directly activated in osteocytes (using the well-known in vitro model, the MLO-Y4 osteocyte) by Teriparatide treatment. In particular, by the use of a gene array platform, we found many molecules upregulated or downregulated in osteocytes, depending on the temporal administration modes, suggesting that the drug affects differently the osteocyte-related signaling pathways. Further, we paid attention to Wisp2, a well-established marker of canonical WNT activation. In particular we found that in MLO-Y4 cell line, a short Teriparatide treatment is able to induce β-Catenin nuclear translocation and a subsequent transcription of its target genes including Wisp2. Moreover, we found that Wisp 2 was secreted in MLO-Y4 medium and is responsible of increased matrix mineralization during osteoblast differentiation process.In conclusion, these data support the importance of osteocytes in controlling the action of the other bone cells and suggest that the perturbation of certain signaling cascades, such as the Wnt pathway, is crucial for the positive regulation of bone formation.

This work was supported by grant from "FAR Int 2017 UNIMORE"

References

[1] Cavani et al. (2017) PTH(1-34) effects on repairing experimentally drilled holes in rat femur: novel aspects - qualitative vs. quantitative improvement of osteogenesis. J Anat. 230:75-84
[2] Hammarstedt et al. (2013) WISP2 regulates preadipocyte commitment and PPARγ activation by BMP4. Proc Natl Acad Sci U S A. 110:2563-8.

Key words

PTH(1-34), Bone remodelling, Wisp2, Wnt, osteocyte.