

## Osteocytes signaling events induced by intermittent vs continuous Teriparatide treatment affect *in vitro* osteoblast differentiation and mineralization

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PTH(1-34), also known as Teriparatide, is an active anabolic drug used in the treatment of some forms of osteoporosis and occasionally exploited to speed fracture healing. The effect of such therapies are dependent on the type of administration, in fact it has been largely demonstrated that a short administration of Teriparatide (also called *intermittent*) increases the bone mass, meanwhile a long administration of the same agent (known as *continuous*) leads to an increased resorption.

The molecular reason why the type of administration is so critical for the fate of the bone remodeling is still largely unknown but it is probably due to the fact that it affects several signaling pathways and alters the biological activity of a cohort of cells: osteoblasts, lining cells, osteoclasts, and osteocytes. In the present work, we firstly focused the attention on molecular events induced by intermittent vs continuous Teriparatide treatment in a well-known osteocytes *in vitro* model, the MLO-Y4 cells. By the use of a gene array platform, we found many molecules upregulated or downregulated depending on the temporal administration modes, suggesting that the drug affects in diverse manner the osteocytes related signaling pathways. In particular, we paid attention to Wisp-2, a protein of the Wnt pathway that has been demonstrated to be able to interact and influence the differentiation of osteoblasts into osteocytes and their mineralization. Secondly, through the mineralization assay, we analyzed the functional effects, involving the differentiation of osteoblast IDG-SW3 cell line, upon the conditioning culture with MLO-Y4 medium, that were pre-treated with short and long time administration of Teriparatide. These findings, consistent with the crucial role performed by osteocytes on osteoblast differentiation, clarify the molecular events downstream the short treatment with Teriparatide, suggesting that the perturbation of certain signaling pathways, such as the Wnt pathway, is crucial for the positive regulation of bone formation.

### References

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### Keywords

Osteocyte, Osteoblast, Teriparatide, Wisp-2, mineralization, gene array