P044

Osteomodulin Impacts Positively The Bone Remodeling Process In Osteoarthritis

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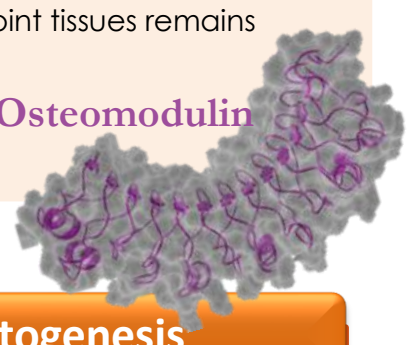
INTRODUCTION Osteomodulin **(OMD)** is an extracellular matrix protein from the Small Leucine Rich Proteoglycan (SLRP) family highly specific to bone. The SLRPs are known to perform various functions such as regulating the extracellular matrix assembly, growth and of cell differentiation. Therefore SLRPs have a crucial role in the regulation of bone homeostasis and development. OMD is thought to play the role of a **cytokines reservoir** by binding them in the matrix. It would be involved in the **mineralization** process and its expression and protein level are downregulated in osteoblasts from osteoarthritic (OA) patients associated with **bone sclerosis**. Its roles in other joint tissues remains unknown to date, except that *in vitro* it is able to stimulate the production of **aggrecan** by articular chondrocytes.



PURPOSE This study aimed to investigate the biological activities of OMD on **osteoblasts** and **osteoclasts** *in vitro*.

RESULTS

OMD enhances bone mineralization

Primary osteoblasts coming from the sclerotic and non-sclerotic zone of OA cortical bone were isolated for *in vitro* culture. It was previously showed that sclerotic osteoblasts present an impaired mineralization. However, when treated with OMD, their **mineralization was partially recovered** (Fig 1).

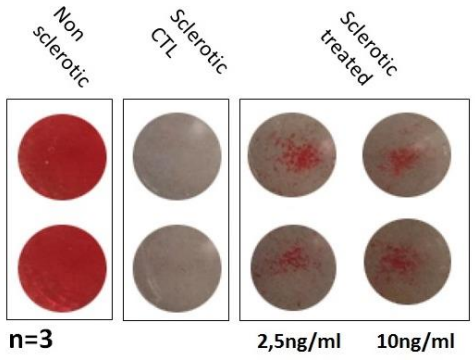


Figure 1. Alizarin Red staining at 17-d on non-sclerotic cortical osteoblasts as mineralization positive control and sclerotic cortical osteoblasts treated with 2,5 and 10 ng/ml of OMD.

The **Alkaline phosphatase (ALP) activity** of **non-sclerotic** cortical osteoblasts was **enhanced** with OMD treatment. However, OMD had no effect on the ALP activity of osteoblasts isolated from trabecular bone showing its effect could be bone type dependent(Fig 2).

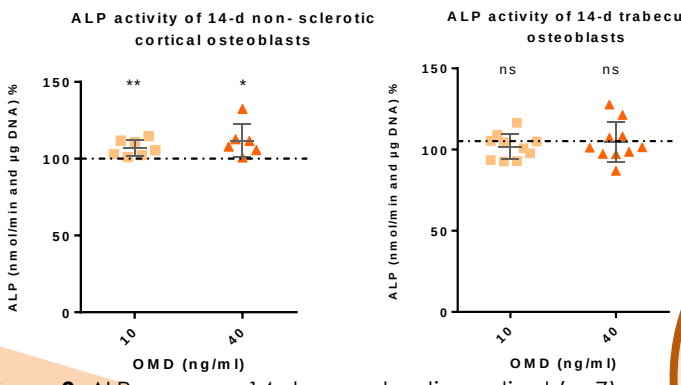


Figure 2. ALP assay on 14-d non-sclerotic cortical (n=7) or trabecular (n=10) osteoblasts. Values of treated osteoblasts were normalized via the control values as a percentage.

OMD inhibits the osteoclastogenesis

The **direct binding of RANKL** by OMD was investigated through Solid phase binding assay. By this way, we successfully demonstrated that OMD bound RANKL in a **dose dependent** manner (Fig 3).

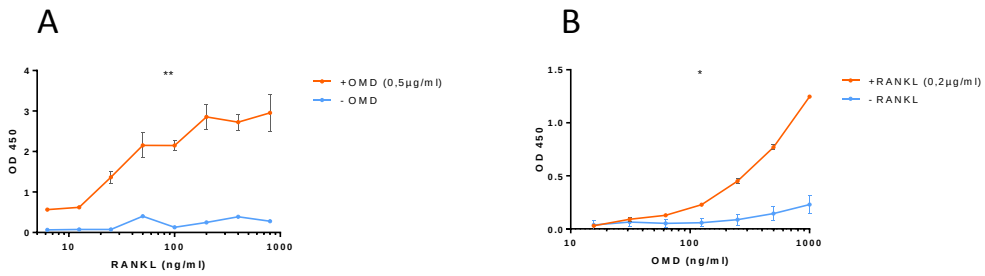


Figure 3. A) Solid phase binding assay with varying concentration of RANKL and fixed concentration of OMD at 0,5 µg/ml. B) Solid phase binding assay with varying concentration of OMD and fixed concentration of RANKL at 0,2 µg/ml.

The biological consequence of this binding was tested on primary murine osteoclasts culture. Pre-mix of RANKL/M-CSF with OMD induced a **decrease of the osteoclasts differentiation** (Fig 4).

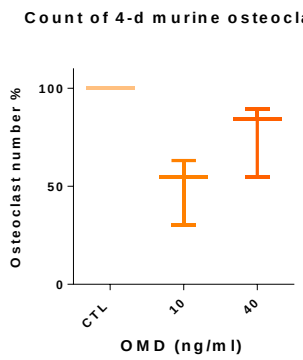


Figure 4. Primary osteoclasts culture from 3 mice. The cells were differentiated during 4 days with RANKL and M-CSF and treated with 10 or 40 ng/ml of OMD. Number of cells from the treated conditions were normalized via the control condition as a percentage.

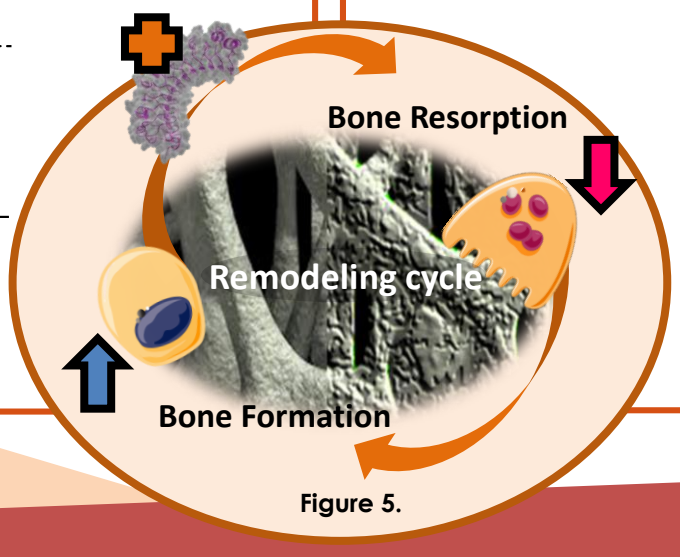


Figure 5.

CONCLUSION

OMD is a major proteoglycan in the **bone extracellular matrix turnover**. It improves the **mineralization** and inhibits the **osteoclast differentiation** through the **capture of RANKL** (Fig 5). Its decrease in OA subchondral bone could trigger the sclerosis by initiating or enhancing the imbalance of the bone matrix **remodeling**. These findings pinpoint OMD has a relevant bone sclerosis **OA biomarker**.

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