Gene Cell Tissue. 2019 July; 6(3):e95441. doi: 10.5812/gct.95441.

Published online 2019 July 27. **Letter**

Preconditioning Can Improve Osteogenic Potential of Mesenchymal Stem Cells in Hypothyroidism

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Received 2019 June 16; **Revised** 2019 July 01; **Accepted** 2019 July 03.

Keywords: Hypothyroidism, Mesenchymal Stem Cells, Osteogenic Differentiation, Conditioned Media, Preconditioning

Dear Editor,

Thyroid hormones (TH) have a critical role in bone growth and metabolism (1) through direct or indirect action of TH on osteoblast and osteoclast cells (2). In patients with hypothyroidism, there is a reduction in bone turnover and increased fracture risk (3). Moreover, bone marrow mesenchymal stem cells (BMSC) have receptors for thyroid hormones (TRα, TRβ) and so they are T3-responsive cells (4). It has been shown that the osteogenic differentiation of MSCs is influenced by T3 in a dose-dependent manner. In this study, the 10 pM of T3 was the more effective dose on MSCs differentiation (5).

In addition, administration of TR-specific agonist GC-1 could improve the skeletal development in hypothyroid rats (1). Boeloni et al. reported a decrease in osteogenic potential of hypothyroid rat MSCs. The number of the mineralized nodules and expression of some estrogenic markers was reduced in hypothyroid MSCs (6).

Another study has demonstrated that thyroidectomy and the absence of hormonal induction could suppress *in vitro* osteogenic differentiation of mesenchymal stem cells. Alkaline phosphatase activity was low and expression of osteogenic markers, such as osteocalcin and osteopontin, was not detected in thyroidectomized rat's MSCs (7).

It seems cell therapy for bone defects in hypothyroidism is difficult. Due to the limitation of osteogenic capacity of autogenic MSCs, another approach should be considered. On the other hand, normalizing hormonal levels using levothyroxine has problems, such as increased fracture risk within the first years of medication (3).

Normal allogeneic or xenogeneic stem cells can be used; however, an immunological reaction should be expected because of the different genetic content (8).

Preconditioning is a key strategy for improving MSCs properties *in vitro* and *in vivo*. The MSCs could be pretreated with various agents, such as trophic factors, cytokines, and physical factors before transplantation (9).

Laser has positive effects on MSCs. It has been reported that light emitting diodes (LED) increased proliferation and osteogenic differentiation of MSCs (10).

Some evidence has demonstrated that nanomaterials could enhance stem cell proliferation and differentiation (11). *In vitro* incubation with hydroxyapatite nanoparticles increases the expression of oseteogenic markers (ALP, osteocalcin, osteopontin, and Runx2) in hMSCs (12).

Application of MSCs conditioned media can improve osteogenic differentiation of MSCs. Conditioned media is cumulative of the wide range of growth factors and cytokines is secreted by MSCs. Many factors, such as insulin-like growth factor-1 (IGF-1), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), basic fibroblast growth factor (bFGF), interleukin 6 (IL-6), and bone morphogenetic proteins (BMPs) have been detected in the MSCs secretome (13). Some of these factors cooperate in bone regeneration (14).

Therefore, for cell therapy by autologous transplantation, preconditioning of hypothyroid stem cells with conditioned media, laser irradiation or nanomaterials before implantation may improve the osteogenic differentiation yield of stem cells and lead to further bone regeneration. Further studies and evaluation are required *in vitro* for a better understanding of the mechanism of this beneficial effect.

In conclusion, the lower osteogenic potential of the hypothyroid MSCs may improve with preconditioning by normal MSCs conditioned media or other factors before autologous transplantation.

Footnotes

Conflict of Interests: It is not declared by the author.

Funding/Support: It is not declared by the author.

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