

## Integrins and Cadherins could be important regulators of osteogenic differentiation and bone formation in dental stem cells

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Regenerative medicine aims to translate the regeneration of tissues and organs into clinical application. Numerous studies have reported beneficial effects of Adult stem cells therapy in the treatment of disease and disabilities. New sources of mesenchymal stem cells (MSCs) are emerging in adult organisms, and dental tissues, that are easily accessible, have been identified as a source of postnatal MSCs capable of self-renewal and multipotency. Dental Follicle Stem Cells (DFSCs) isolated from tooth buds of healthy paediatric patients showed  $\geq 95\%$  expression of stemness makers (CD73, CD90, CD146, CD44, CD105, and HLA-I) [1]. Moreover DFSCs differentiated into osteoblast-like cells, produced mineralized matrix nodules and expressed typical osteoblastic markers. Cell interactions with extracellular matrix (ECM) and neighbor cells are critical for tissue morphogenesis and architecture, and are mediated by two classes of adhesion molecules, respectively Integrins and Cadherins, which also act intracellularly by modulating crucial pathways of proliferation and differentiation. Thus, in this study, DFSCs were characterized for the expression of adhesion molecules Cadherins and Integrins. In basal conditions DFSCs expressed higher levels of N-Cadherin and Cadherin-11 in comparison to E-Cadherin and P-Cadherin, which were low expressed. The examined Cadherins showed different behaviours during DFSCs osteogenic differentiation: N-cadherin expression was high during the first steps, while decreased at the later times; Cadherin-11 progressively increased; E-Cadherin and P-Cadherin did not change a Cadherin profile reflecting the osteoblastic commitment of the cells. DFSCs expressed the Integrin subunits alpha V, beta 3, alpha 5, and beta 1 in basal undifferentiated conditions but their expression increased time-dependently under osteogenic treatment. In addition we found that the subunits alpha V and beta 3 associated and formed the functional integrin, which localized at the focal adhesion in response to osteogenic trigger; similarly, alpha 5 and beta 1 subunits were found to associate and localize at the cell borders mostly in differentiated cells. Finally we found that osteogenic differentiation of DFSCs was prompted out by seeding the cells on ECM protein coated surfaces. Functional tissue engineering for bone regeneration requires the appropriate combination of MSCs with biocompatible scaffolds, thus acting on cell surface and ECM molecules could optimize osteogenic differentiation of MSCs and contribute to the successful regeneration of damaged bone tissue.

### References

[1] Mori et al. (2012) Osteogenic differentiation of dental follicle stem cells. *Int J Med Sci.* 9(6):480-487.

### Keywords

Stem cells, mesenchymal stem cells, bone regeneration, Integrin, Cadherin.