The osteogenic differentiation of bone chip-derived mesenchymal stem cells is controlled via specific receptor signaling

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Mesenchymal stem cells (MSCs) are an attractive cell source for Regenerative Dentistry in particular due to their ability to differentiate towards osteoblasts, among other lineages. Tooth and jaw bone loss are frequent sequelae of traumatic and pathological conditions in both the young and the elderly and must be met by appropriate prosthetic replacements. For successful osseointegration of the dental implant a sufficient bone level is necessary. Besides the utilization of bone autografts or synthetic biomaterials, medical research is more and more focused on the utilization of MSCs. Compared to cells obtained from liposuction material, ectomesenchymal stem cells derived from the head area *e.g.* out of dental follicles or particulate, non-vascularized bone chips show a higher differentiation potential towards osteoblasts. This implies that due to their different origin, ectomesenchymal stem cells are stronger committed towards hard tissues and are therefore interesting candidate cells for bone regeneration.[1,2]

Parathyroid hormone-related protein (PTHrP) is known to be involved in tooth eruption. It acts as a signaling molecule that stimulates local bone resorption.[3] Recently, PTHrP was found to affect the MSC differentiation process. The differential expression level of specific PTHrP isoforms might be considered as a molecular signature associated with the respective differentiation state during osteogenesis.[4] Moreover, we could show that in addition to the role of purinergic 2 (P2) receptors in cellular processes such as proliferation, migration and apoptosis, they are also involved in stem cell differentiation. Several P2 receptor subtypes play a role in key steps during osteogenic lineage commitment. Further development of MSCs into progenitor cells, pre-osteoblasts and osteoblasts seemed to be triggered via the alteration of their P2 receptor expression patterns.[5]

Human mesenchymal stem cells were isolated from bone chip material harvested during oral surgery intervention. Their stem cell character was demonstrated by plastic-adherence and expression of the surface markers CD73, CD90, and CD105 following differentiation along the osteogenic lineage.[6] The mineralization process was monitored by Alizarin Red S staining of extracellular matrix components. Among the examined P2 receptor subtypes, down-regulation of P2Y14 appeared to be involved in the onset of this differentiation process. Today several artificial P2 receptor ligands are present in the market. The administration of a stimulating P2Y14 receptor ligand had a direct influence on the osteogenic differentiation potential. More precisely, the application of the potent and selective P2Y14 agonist MRS 2690 led to a dose-dependent reduction of the extracellular mineralization.

Taken together, bone chip-derived mesenchymal stem cells are promising candidate cells for bone replacement. Here we show that they are capable of differentiating into osteoblasts. The application of an artificial receptor agonist confirmed the functional role of P2Y14 during osteogenesis. Therefore, it is of major interest to develop selective and potent antagonists directed against this recently discovered member of the purinergic receptor family. Controlling the P2Y14 receptor signaling might improve future bone tissue engineering approaches in regenerative dentistry.

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