Porous hydroxyapatite and biphasic calcium phosphate ceramics promote ectopic osteoblast differentiation from mesenchymal stem cells

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Abstract. Because calcium phosphate (Ca–P) ceramics have been used as bone substitutes, it is necessary to investigate what effects the ceramics have on osteoblast maturation. We prepared three types of Ca–P ceramics with different Ca–P ratios, i.e. hydroxyapatite (HA), beta-tricalcium phosphate (β-TCP), and biphasic calcium phosphate (BCP) ceramics with dense-smooth and porous structures. Comprehensive gene expression microarray analysis of mouse osteoblast-like cells cultured on these ceramics revealed that porous Ca–P ceramics considerably affected the gene expression profiles, having a higher potential for osteoblast maturation. In the *in vivo* study that followed, porous Ca–P ceramics were implanted into rat skeletal muscle. Sixteen weeks after the implantation, more alkaline-phosphatase-positive cells were observed in the pores of hydroxyapatite and BCP, and the expression of the osteocalcin gene (an osteoblast-specific marker) in tissue grown in pores was also higher in hydroxyapatite and BCP than in β-TCP. In the pores of any Ca–P ceramics, 16 weeks after the implantation, we detected the expressions of marker genes of the early differentiation stage of chondrocytes and the complete differentiation stage of adipocytes, which originate from mesenchymal stem cells, as well as osteoblasts. These marker gene expressions were not observed in the muscle tissue surrounding the implanted Ca–P ceramics. These observations indicate that porous hydroxyapatite and BCP had a greater potential for promoting the differentiation of mesenchymal stem cells into osteoblasts than β-TCP.

Keywords: calcium phosphate ceramics, porous structure, osteogenesis, gene expression

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