Biomimetic Matrices Delivering Growth Factors

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Abstract

Current research focuses on developing potent bone substitutes or biomimetic 3D matrices/scaffolds for restoring the function and structure of tissue, not only by osteoconduction but also to deliver growth factors (GF) to synergistically instruct the body's own mechanism for regeneration. A dose of 1 µg bone morphogenetic protein -2 (BMP-2), was physisorbed on nanodiamond particles (nDP) modified poly(LLA-co-CL) scaffolds and compared to BMP-2 physisorption on unmodified scaffolds. Release kinetics of BMP-2 was quantified for up to 70 days using mass spectrometry (MS) and their osteogenic potential was evaluated. Unmodified poly(LLA-co-CL) scaffolds were also functionalised by physisorption of a cocktail of GFs using human demineralised dentin matrix (DDM) and compared to control scaffolds. Release kinetics up to 21 days was studied and their efficacy on the osteogenic differentiation of human bone marrow mesenchymal stem cells (hBMSC) up to 21 days was evaluated. MS revealed a sustained release of low levels of BMP-2 from nanodiamond modified scaffolds (nDP-PHY) for up to 70 days compared to unmodified scaffolds plus BMP-2 (PHY). nDP-PHY and PHY scaffolds promoted bone regeneration in a rat mandible critical-sized defect after 4 weeks, however nDP-PHY scaffolds demonstrated osteogenic potential in vivo as well as in hBMSC cultures. When delivering cocktail of GFs, 390 proteins were identified by MS to be released from the DDM modified scaffolds, and the proteins involved in bone regeneration showed comparable release trends. Cells grown in DDM modified scaffolds showed the highest expression of inflammatory markers while also expressing higher mRNA expression of osteogenic markers. Poly(LLA-co-CL) scaffolds were successfully rendered biomimetic by physisorbing BMP-2 alone or a cocktail of GFs. In addition, nDP provide copolymer scaffolds with a platform for strongly binding a GFs, yet maintaining its bioactivity.