Hypoxia-mimicking porous calcium/ phosphate coated silk scaffolds with controllable cobalt ion release for bone tissue engineering

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Abstract

Low oxygen pressure (hypoxia) plays an important role in stimulating angiogenesis; there are, however, few studies to prepare hypoxia-mimicking tissue engineering scaffolds. Silk fibroin (SF) is a natural polymer with great permeability to oxygen and water, good mechanical properties, low immunogenicity and good cell adhesion and growth characteristics. Ionic cobalt (Co) is established as a chemical inducer of hypoxia-inducible factor (HIF)-1α, which induces hypoxia-like response. The aim of this study was to develop hypoxia-mimicking a nanocomposite scaffold based on silk/calcium phosphate (Ca/P)/Co by freeze-drying and investigate if the addition of Co (2+) ions would induce a cellular hypoxic response in such a tissue engineering scaffold system. The highly porous scaffold possessed appropriate chemical and physical structure as confirmed by FTIR, XRD and SEM analysis and the cellular effects of scaffold on the proliferation, differentiation, bone and endothelial related gene expression of mesenchymal stem cell (MSC) were systematically investigated. The results showed that low amounts of Co (<5%) incorporated into scaffolds had no significant cytotoxicity and that their incorporation significantly enhanced bone and endothelial related gene expression in MSCs, and also that the silk Ca/P/Co scaffolds support MSC attachment and proliferation. Our results indicate that incorporating cobalt ions into silk Ca/P scaffolds is a viable option for preparing hypoxia-mimicking tissue engineering scaffolds and significantly enhanced angiogenesis. The hypoxia-mimicking silk Ca/P/Co scaffolds have great potential for bone tissue engineering applications by combining enhanced angiogenesis with already existing osteogenic properties.

Key word: cobalt, silk, angiogenesis, osteogenesis, bone tissue engineering