Acta Biomaterialia 8 (2012) 2578–2586

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Enhancement of bone regeneration through facile surface functionalization of solid freeform fabrication-based three-dimensional scaffolds using mussel adhesive proteins

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ARTICLE INFO

Article history:
Received 22 December 2011
Received in revised form 3 March 2012
Accepted 27 March 2012
Available online 2 April 2012

Keywords:
Mussel adhesive protein
3-D scaffold
Surface functionalization
Stem cells
Bone regeneration

ABSTRACT

Solid freeform fabrication (SFF) is recognized as a promising tool for creating tissue engineering scaffolds due to advantages such as superior interconnectivity and highly porous structure. Despite structural support for SFF-based three-dimensional (3-D) scaffolds that can lead to tissue regeneration, lack of cell recognition motifs and/or biochemical factors has been considered a limitation. Previously, recombinant mussel adhesive proteins (MAPs) were successfully demonstrated to be functional cell adhesion materials on various surfaces due to their peculiar adhesive properties. Herein, MAPs were applied as surface functionalization materials to SFF-based 3-D polycaprolactone/poly(lactic-*co*-glycolic acid) scaffolds. We successfully coated MAPs onto scaffold surfaces by simply dipping the scaffolds into the MAP solution, which was confirmed through X-ray photoelectron spectroscopy and scanning electron microscopy analyses. Through in vitro study using human adipose tissue-derived stem cells (hADSCs), significant enhancement of cellular activities such as attachment, proliferation, and osteogenic differentiation was observed on MAP-coated 3-D scaffolds, especially on which fused arginine–glycine–aspartic acid peptides were efficiently exposed. In addition, we found that in vivo hADSC implantation with MAP-coated scaffolds enhanced bone regeneration in a rat calvarial defect model. These results collectively demonstrate that facile surface functionalization of 3-D scaffolds using MAP would be a promising strategy for successful tissue engineering applications.

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1. Introduction

Tissue engineering approaches, including cells, scaffolds, and biochemical factors, have been used in an attempt to promote tissue regeneration. Tissue engineering scaffolds play a critical role in terms of providing biochemical and mechanical support for desired cell behaviors [1–3]. Biodegradable synthetic polymers are widely used as biomaterials for fabricating artificial tissue engineering scaffolds, which are created using diverse methods, such as solvent casting/particulate leaching, gas foaming, emulsion freeze-drying, phase separation, and fiber bonding using synthetic polymers [4–9]. However, controlling interconnectivity and scaffold geometry is quite difficult when using these methods and practical tissue engineering applications are limited due to toxic organic solvents that can remain during the fabrication process [10].

Alternatively, the solid freeform fabrication (SFF) method, which is able to construct a fully interconnected and well-defined porous structure, has recently emerged [11–13]. In addition, highly permissive transportation of oxygen and nutrients throughout the scaffolds is considered another advantage. Previously, we developed the multihead deposition system (MHDS), one form of SFF technology [14]. MHDS has high mechanical strength and biocompatibility because of its organic solvent-free environment during the fabrication process [15]. Indeed, several studies reported that

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http://dx.doi.org/10.1016/j.actbio.2012.03.041