Biomaterials and Biomechanics in Bioengineering, *Vol. 1, No. 3 (2014) 151-162*
(Formerly, Biomaterials and Biomedical Engineering)
DOI: http://dx.doi.org/10.12989/bme.2014.1.3.151

Delivery of growth factor-associated genes to mesenchymal stem cells for cartilage and bone tissue regeneration

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(Received September 29, 2014, Revised September 30, 2014, Accepted September 30, 2014)

Abstract. Genetically-modified mesenchymal stem cells (GM-MSCs) have emerged as promising therapeutic tools for orthopedic degenerative diseases. GM-MSCs have been widely reported that they are able to increase bone and cartilage tissue regeneration not only by secreting transgene products such as growth factors in a long-term manner, also by inducing MSCs into tissue-specific cells. For example, MSCs modified with BMP-2 gene increased secretion of BMP-2 protein resulting in enhancement of bone regeneration, while MSCs with TGF-b gene did cartilage regeneration. In this review, we introduce several growth factors for gene delivery to MSCs and strategies for bone and cartilage tissue regeneration using GM-MSCs. Furthermore, we describe strategies for strengthening GM-MSCs to more intensively induce tissue regeneration by co-delivery system of multiple genes.

Keywords: growth factor; transcription factor; genetically-modified mesenchymal stem cells; cartilage; bone; tissue regeneration

1. Introduction

Critical-sized bone defects and articular cartilage injuries induced by various reasons including trauma, surgery, and diseases do not self-repair, which are a major challenge in the orthopedic field. The gold standard of clinical therapeutic strategies to enhance bone and cartilage regeneration is the use of tissue transplantation, since they possess the essential components such as progenitor cells as well as osteo/chondro inductive growth factors and extracellular matrix (ECM) (O'Driscoll 1998, Bauer and Muschler 2000, Kneser *et al.* 2006, Oryan *et al.* 2014). Autogenic, allogenic, and xenogenic tissue grafts have been applied to the treatment of bone and cartilage disease (Oryan *et al.* 2014). However, autogenic tissue grafts may lead to limited quantity and morbidity of the donor site, while allo- and xenogenic tissue grafts may give rise to serious

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 ISSN: 2288-3738 (Print), 2288-3746 (Online)

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