Biomaterials 33 (2012) 8802–8811

Contents lists available at SciVerse ScienceDirect

Biomaterials

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

Angiogenic and osteogenic potential of platelet-rich plasma and adipose-derived stem cell laden alginate microspheres

Yi Man [a,b,c,1], Ping Wang [a,b,c,1], Yongwen Guo [a,d,1], Lin Xiang [a,b], Yang Yang [a,b], Yili Qu [a], Ping Gong [a,b,*], Li Deng [c,**]

[a] State Key Laboratory of Oral Diseases, Sichuan University, Chengdu 610041, China
[b] Dental Implant Center, West China School of Stomatology, Sichuan University, Chengdu 610041, China
[c] Laboratory of Stem Cell and Tissue Engineering, Regenerative Medicine Research Center, West China Hospital, Sichuan University, No. 1, Keyuan Fourth Road, Chengdu 610041, China
[d] Department of Orthodontics, West China School of Stomatology, Sichuan University, Chengdu 610041, China

ARTICLE INFO

Article history:
Received 16 July 2012
Accepted 23 August 2012
Available online 12 September 2012

Keywords:
Adipose-derived stem cells
Alginate microspheres
Angiogenesis
Bone tissue engineering
Mineralization
Platelet-rich plasma

ABSTRACT

Improving vascularization of tissue-engineered bone can advance cell performance *in vivo* and further promote bone regeneration. How to achieve a functional vascular network within the construct is one of the biggest challenges so far. We hypothesized that a mixture of platelet-rich plasma (PRP) and adipose-derived stem cells (ADSCs) could endue the alginate microspheres with osteogenic and angiogenic potential. *In vitro* and *in vivo* studies were performed to investigate the potential of the PRP-ADSC-laden microspheres. Two intriguing observations were made in this study. First, we demonstrated that PRP sustained cell viability and meanwhile promoted cell migration from the interior of alginate microspheres to the surface. This phenomenon indicated that encapsulated cells have the potential to directly and actively participate into the regeneration process. Second, *in vivo*, a blood vessel network was found within the 10% PRP and 15% PRP-ADSC implants, which was associated with a significant increase in mineralization. It suggested that the PRP-ADSC-laden microspheres did enhance the vascularization and mineralization. In summary, this strategy not only provides a micro-invasive therapy for bone regeneration, but also could be incorporated with other matrices for extended application.

1. Introduction

In the field of orthopedics, oral and maxillofacial surgery, bone regeneration remains to be a clinical challenge, despite the introduction of various bone augmentation techniques and bone graft materials. In recent decades, development of bone tissue engineering brings great excitement through the combination of engineered scaffolds, cells, and biologically active molecules or microenvironment [1,2]. Extensive experimental and clinical researches have been done in the field, and considerable progress has been achieved [3–5]. However, its clinical success was mainly impeded by the poor vascularization in tissue-engineered constructs. The lack of vascular networks throughout constructs leads to insufficient oxygen and nutrients supply, and in no doubt compromises the survival rate of implanted cells and their final performance. To ensure the viability of seeded cells, a distance of less than 200 μm is required between cells and a blood vessel [6]. However, from the perspective of clinical application, 200 μm is such a short distance for any bone defect that the inner pre-seeded cells' viability is hardly to be maintained, not to expect these cells to participate in the regeneration process. Thus, a scaffold, seeded with appropriate pluripotent cells, providing a favorable micro-environment and nutrient for cells' prolonged viability, and with angiogenic and osteogenic potential, could be an inspiring strategy for bone tissue engineering.

Recently, adipose-derived stem cells (ADSCs) have been proposed by some researchers as a promising alternative for bone marrow stem cells (BMSCs) in bone tissue engineering [7]. With comparable multilineage capability to BMSCs, ADSCs are much more easily harvested in high yield using simpler, less expensive and less invasive procedures with a lower incidence of donor site morbidity. As an autologous cell-based therapy, ADSCs transplant have been successfully used in both soft tissue and bone regeneration [8–10]. A recent research showed that ADSCs, originating from pericytes, could contribute to vascularization both *in vitro* and

* Corresponding author. Dental Implant Center, West China School of Stomatology, Sichuan University, No. 14, 3rd Section, Renmin South Road, Chengdu 610041, China. Tel.: +86 13088090513.
** Corresponding author. Tel.: +86 18980601811.
E-mail addresses: dentistping@gmail.com (P. Gong), dengli2000@21cn.com (L. Deng).
[1] These authors contributed equally to this work.

0142-9612/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.biomaterials.2012.08.054