Strategic design of electrospun fiber scaffolds to deliver multiple growth factors for bone regeneration

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Statement of Purpose: The design of scaffolds that can deliver multiple growth factors is a promising strategy to promote bone tissue regeneration. Here, we report the development of fibrous scaffolds by core-shell electrospinning to deliver dual growth factors (FGF2 and FGF18) that are released at different rates. Specifically, FGF2 was loaded in the core region of fibers for rapid release while FGF18 was incorporated into mesoporous nanocarriers (MN) for a long-term delivery.

Methods: Co-axial electrospinning solutions were made of PCL and PEO as the outer and inner layer, respectively. While FGF2 was loaded directly within the PEO part, the FGF18 was pre-loaded within bioactive mesoporous nanocarriers which made of 85Si/15Ca glass composition. The morphology of the scaffolds was observed by SEM and TEM. The mechanical properties of the scaffolds, including tensile strength, elastic modulus and elongation were examined. The apatite forming ability of the scaffolds was examined in SBF, as the in vitro bone-bioactivity index. The release of growth factors was monitored for up to 60 days. The cell proliferation was analyzed by CCK method, and the osteogenic differentiation of cells was assessed in terms of alkaline phosphatase activity and Alizarin Red S staining. The in vivo bone forming ability of the scaffolds was examined in rat calvarium defect model.

Results: The bioactive nanocarriers used had a diameter of ~105 nm and mesopore size of ~7 nm. Within the mesopores, the growth factors were effectively loaded. The SEM morphologies revealed the generation of well-structured core-shell hollow fibers (Fig. 1). Due to the incorporation of nanocarriers, the mechanical strength and elastic modulus of the scaffolds were enhanced; however, the elongation was reduced. Furthermore, the nanocarrier-added scaffolds showed higher bone bioactivity. Importantly, the release of growth factors was shown to be sequential, i.e., earlier release of FGF2 than FGF18 where the release was prolonged up to a couple of months. The growth factors-releasing scaffolds promoted cell proliferation and osteogenic differentiation through the rapid release of FGF2 and slow release of FGF18, respectively. The in vivo findings at 6 weeks implantation in calvarium defect showed that FGF2/FGF18 releasing fiber scaffolds had higher bone volume and bone surface density than those without growth factors (Table 1).

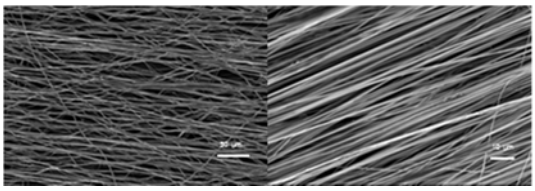

Fig. 1. SEM image of the electrospun core-shell fibers employed to deliver FGF2/FGF18 in a sequential manner.

	Control	*5% MN scaffold*	
		w/o	+F2, F18
Bone volume	14±4.23	21±3.28	34±6.58
Bone density	2±0.60	3±0.80	4±0.69

Table 1. Quantitative assessments of bone volume and density using μCT of the 3D-reconstructed images.

Conclusions: The currently-developed core-shell fibrous scaffolds promoted in vitro cellular functions and in vivo bone regeneration. This was possible by the delivery of two different growth factors in a sequential manner, i.e., FGF2 rapidly and FGF18 slowly. The developed scaffolds are thus considered to be a potential therapeutic platform for bone regeneration.

References: El-Fiqi A. RSC Adv. 2014;4:4444-4452.