INCORPORATION AND DELIVERY OF TWO GROWTH FACTORS USING BILAYER NANOFIBROUS SCAFFOLDS FOR GASTROINTESTINAL REGENERATION

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INTRODUCTION: With advances in tissue engineering, relatively simple human body tissues such as bone can be regenerated[1]. It is important now to investigate the regeneration of complex body tissues such as gastrointestinal (GI) tract. GI tract has a multilayered structure, with one layer having endothelial cells and two layers having smooth muscle cells. Growth factors (GFs) regulate cell activities and promote tissue regeneration. Vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) are critical for regenerating GI tract. Electrospinning is widely used for making nanofibrous scaffolds[2] and emulsion electrospinning is often used for incorporating GFs in scaffolds[3]. This study investigated dual incorporation and delivery of VEGF and PDGF for bilayer fibrous scaffolds.

MATERIALS AND METHODS: Emulsion preparation followed our established procedure[4] and poly(lactic-co-glycolic acid) polymers (PLGA 50/50, LA:GA=50:50; PLGA 75/25, LA:GA =75:25) were used to make respective fibrous layers in the bilayer scaffolds. Electrospun mono- or bilayer scaffolds consisting of aligned fibers were fabricated by using a high-speed rotating collector. The scaffolds formed were characterized using various techniques (SEM, TEM, etc.). In vitro release of GFs from scaffolds was studied via immersion experiments up to 21 days. Release profiles of VEGF and PDGF were established by using respective ELISA kit. Scaffold structural changes after immersion were observed using SEM.

RESULTS AND DISCUSSION: Using our technique, monolayer and bilayer PLGA scaffolds consisting of aligned fibers could be fabricated via emulsion electrospinning (Fig.1a). Fibers exhibited core-shell structures where GFs were incorporated in the aqueous core of fibers (Fig.1b). VEGF was incorporated in PLGA 50/50 fibers while PDGF was incorporated in PLGA 75/25 fibers. The loading efficiency of VEGF and PDGF was 52.3% and 45.1%, respectively. In vitro release profiles of the two GFs are shown in Fig.2a. They indicated that controlled and sustained release of VEGF and PDGF was achieved after 24 hours. Burst release was not severe. For the

first 24 hours, 1.45% PDGF and 8.48% VEGF were released, respectively. The small initial burst release may be associated with the diffusion of GFs on the surface of fibers. The subsequent controlled and sustained release was attributed to the diffusion of GFs and the erosion of polymers. Moreover, the release profiles of VEGF and PDGF showed a sequential release where the release of VEGF was faster than that of PDGF. The sequential release of VEGF and PDGF would be beneficial for vascularization in the gastrointestinal regeneration process because VEGF is a major contributor of angiogenesis and PDGF promotes the maturation of blood vessels. After 21-day immersion, the matrix of the electrospun scaffolds collapsed and small pores appeared on the surface of fibers, indicating the degradation of scaffolds (Fig.2b).

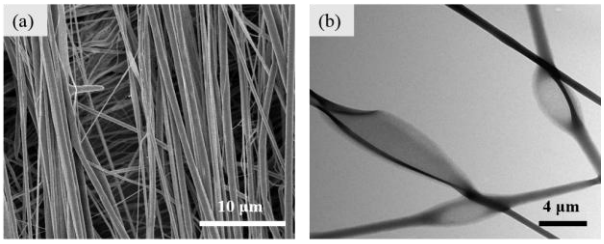

Fig. 1. (a) SEM image of a bilayer scaffold; (b) TEM image showing the core-shell structures of nanofibers produced by emulsion electrospinning.

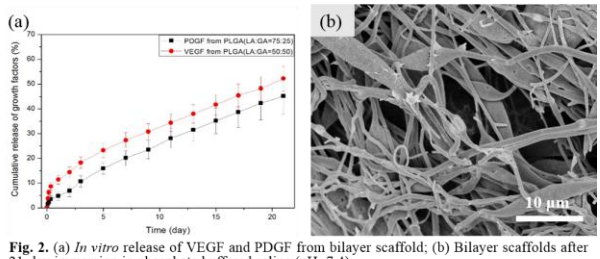

Fig. 2. (a) *In vitro* release of VEGF and PDGF from bilayer scaffold; (b) Bilayer scaffolds after 21-day immersion in phosphate buffered saline (pH=7.4).

CONCLUSION: This study demonstrates that bilayer scaffolds with aligned nanofibers could be made and that different growth factors could be incorporated in different fibrous components via emulsion electrospinning. Through careful scaffold design, growth factors could be released from different fibers sequentially. The VEGF and PDGF incorporated in bilayer scaffolds exhibited controlled and sustained release, which would be very useful for GI tract regeneration.

This is work was supported by Hong Kong Research Grants Council through a GRF Grant (HKU 717713E).

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