Electrospinning Degradable Hydrogel Nanofibres for Tissue Engineering

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Statement of Purpose: Hydrogels have attracted significant attention as biomaterials due to their low protein adsorption, high water content, tunable mechanical and chemical properties as well as cell compatibility. [1] Considering that hydrogels are similar to soft tissue, they have been designed as matrices for tissue engineering. The main components of most natural extracellular matrix (ECM) are collegen and elastin nanofibers with diameters ranging from several nanometers to micrometers. This fibrous structure plays an important role in regulating cell behavior. [2] Herein, we aim to mimic this natual fiber morphology with a synthetic polymer by preparing nanofibrous hydrogels. Poly(oligoethylene glycol methacrylate) (POEGMA) is a hydrophilic and non-cytotoxic biomaterial; functionalization of oligomeric POEGMA precursors with hydrazide and aldehyde functional groups also imparts properties of degradability and injectability. [3] Using poly(ethylene oxide) (PEO) as an aid, electrospinning is proposed for use to make continuous hydrogel nanofibers to mimic natural ECM properties.

Methods: 1. POEGMA hydrogel preparation
Poly(oligoethylene glycol methacrylate) (POEGMA) polymers were prepared by chain transfer polymerization to limit the molecular weight and functionalized with hydrazide and aldehyde groups. [3] Hydrazide and aldehyde functionalized POEGMA can crosslink *in situ* to form a hydrazone cross-linked hydrogel (Figure 1).

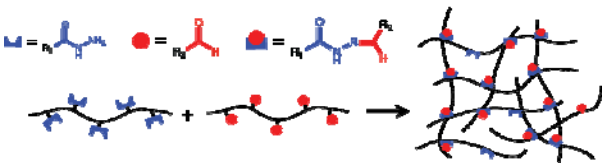

Figure 1. Scheme of hydrogel preparation

2. Electrospinning
Hydrazide and aldehyde polymer solutions (15 wt% in deionized water) were loaded into separate barrels of a double-barrel syringe (Figure 2). Each polymer was mixed with PEO solutions with different concentration, resulting in weight ratios of POEGMA to PEO from 3:1 to 15:1. Fibers were electrospun using a voltage of 8.5 kV, 10 cm distance between the needle and collector, and an 18-gauge needle.

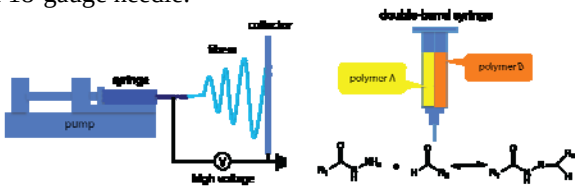

Figure 2. Scheme of electrospinning setup

Results: Nanofibers of diameter 200-300 nm could be produced. When half of the nanofibrous hydrogel scaffold was exposed to water (Fig. 3, bottom), a clear increase in nanofiber diameter was noted relative to the still-dry nanofibers (Fig. 3, top) due to swelling of the hydrogel; in addition, the fibers persisted over at least one week while PEO fibers dissolve within minutes, further confirming the hydrogel nanostructure within the fibers. The presence of POEGMA in the nanofibers was confirmed based on the ester peak at ~1700 cm^{-1} visible by FTIR-ATR as well as confocal microscopy of the nanofiber mat in which fluorescein isothiocyanate (FITC) was used to label hydrazide group (green) and rhodamine was used to label aldehyde group (red) (Figure 4); both fluorescent signals are observed throughout the nanofiber mat, confirming co-localization of the reactive precursor polymers as is required for gelation. Fiber morphologies ranging from smooth nanofibers (low humidity and higher PEO contents) to bead-in-nanofiber matrices (higher humidities and/or lower PEO contents) could be achieved by changing electrospinning conditions. The nanofibers are degradable at physiological conditions and show no significant cytotoxicity to model cells (3T3 fibroblasts).

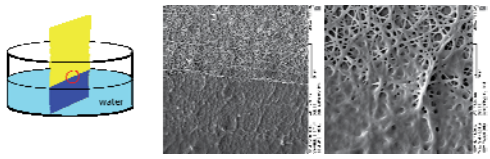

Figure 3. SEM images of the nanofibrous scaffold

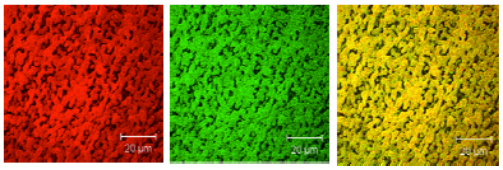

Figure 4. Confocal microscopy of cross-linked nanofibers

Conclusions: Nanofibrous hydrogels could be fabricated via electrospinning. The production of cross-linked nanofibers was confirmed through SEM, FTIR, and confocal microscopy. Hydrogel fibers were stable in water for at least one week. The scaffold morphology can be facilely controlled from fibers to beads by changing the humidity and PEO concentration. We anticipate these matrices have potential as cell-encapsulating matrices.

References:
[1] Ahmed EM. J. Adv. Res. 2013; 18: 1-17.
[2] He CL, et al. J. Mater. Chem. B. 2014; in press.
[3] Smeets NM, et al. Chem. Commun. 2014; 50: 3306-3309.