3D ELASTOMERIC SCAFFOLDS FOR CARDIAC REGENERATION

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Introduction

Heart failure (HF) is the last stage of cardiovascular diseases, including myocardial infarction (MI). It is one of the most important causes of premature death in the 21st century. MI occurs as a result of a reduction in blood supply to a part of the myocardium. The replacement of diseased myocardium *via* tissue engineering is one of the most promising regenerative therapies to re-establish the blood supply to the affected area[1]. This approach aims to increase the patient´s life expectancy by addressing both the death of cardiomyocyte cells and the malfunction of the muscular heart tissue, in order to avoid heart failure. Here we propose a tissue engineering strategy consisting of three main platforms: (1) Synthesis of novel elastomeric multiblock copolymers. (2) Control of the scaffold production by optimizing electrospinning parameters in order to achieve coiled/curly fiber morphologies that mimic the contractility of the heart tissue; this is expected to provide better biomechanical support for the cells and cardiac muscle regeneration [2,3]. (3) Vary the surface chemistry of the scaffolds in a controlled manner by biologically active compounds.

Materials and Methods

Series of 3D scaffolds utilizing synthesized elastomeric multiblock copolymers of poly(butylene succinate) (PBS) either with dimer linoleic diol (DLA-OH) or dihydroxy poly(isobutylene)(PIB), were produced *via* electrospinning. In order to obtain the coiled/curly fiber morphology, different electrospinning parameters were tested including: voltage, distances between needle and collector, flow rates of solution feeding, copolymer concentrations, solvents mixtures and addition of salts or poly(ethylene glycol) (PEG) to increase the conductivity and viscosity of the solutions. The morphology of the obtained scaffolds was analysed by laser scanning microscopy.

Chemical structures of the synthesized multiblock copolymers were confirmed by ^{1}H NMR and ATR FT-IR spectroscopy. The thermal properties were studied by differential scanning calorimetry (DSC). The wettability of the elastomeric scaffolds was assessed by contact angle measurement and the mechanical properties were measured in tensile tests. Direct cytocompatibility and cell adhesion studies were carried out using murine fibroblasts (L929) on the 3D scaffolds in static conditions.

Results and Discussion

Analysis of chemical structure with ^{1}H NMR and ATR FT-IR spectroscopy confirmed the presence of specific bonds and groups characteristic of the presence of DLA and PIB units in the soft segments of the copolymers. DSC analysis indicated that all of the synthesized copolymers were elastomeric at physiological temperature, which is expected to affect the mechanical properties, degradation profile, and biocompatibility, depending on the amount and nature of the soft segments. Electrospinning process was successfully optimized to produce scaffolds with different morphologies, with an increasing presence of coiled/curly fibers with the addition of PEG or salts to the solutions (FIG. 1).

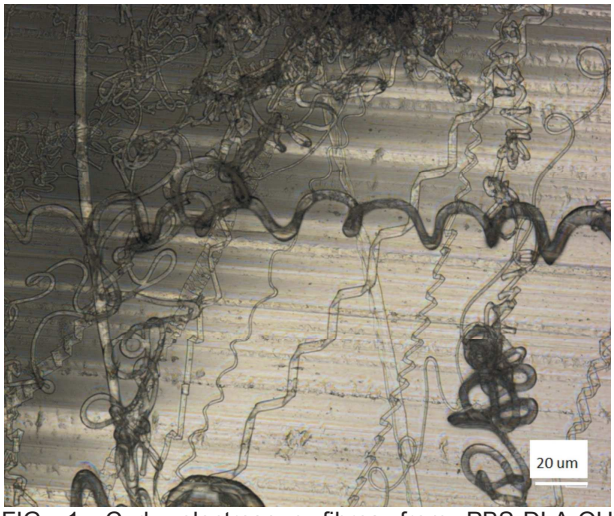

FIG. 1. Curly electrospun fibres from PBS-DLA-OH copolymer containing 50-wt% of soft segments.

The elasticity combined with the curly fiber morphology will result in improved biomechanical match of the scaffold to the heart tissue, improving biointegration. Mechanical tests and cell adhesion studies are being performed to study the effect of fiber morphology and elasticity. Preliminary cytotoxicity experiments indicate that the novel copolymers are non-toxic.

Conclusions

Novel multiblock copolymers, with different hard to soft segment ratios and soft segments building blocks, were successfully synthesized. The ^{1}H NMR, ATR FT-IR spectra and DSC measurements were consistent with the structure and thermal properties expected. The electrospinning process was optimized in order to obtain coiled/curly fiber morphologies. Ongoing studies are characterizing the mechanical and degradation properties, as well as cytocompatibility and cell adhesion. Mechanical and biological properties are expected to be different depending on the compositions and morphologies of the electrospun scaffolds. The future goal of the work is to demonstrate the suitability of the developed materials for cardiac tissue engineering.

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