Bioactive Hybrid Nanomatrix Developed by Electrospun Polycaprolactone and Biomimetic Self-Assembled Peptide Amphiphiles

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Statement of Purpose

Electrospinning has been extensively used to produce fibrous scaffolds for various biomedical applications. This technology produces nanofibrous scaffolds using both synthetic and natural polymers in a controlled manner to mimic the structure of the extracellular matrix (ECM). However, the current limitation of electrospinning is its inability to produce bioactive surfaces to control cellular behaviors. To address this issue, we have developed a novel strategy to produce a bioactive hybrid nanomatrix by combining electrospun polycaprolactone (PCL) with self-assembled, ECM mimicking peptide amphiphiles (PAs). It is hypothesized that these PAs, with inscribed cell adhesive ligands, can be self-assembled onto the surface of the electrospun PCL nanofibers and thus endow the PCL nanofibers with bioactivity. PAs are amphiphilic molecules consisting of a hydrophobic alkyl tail attached to a functional hydrophilic peptide sequence.[1,2] The functional peptide region of the PAs designed in this study consists of an matrix metalloproteinase – 2 (MMP-2) enzyme degradable site[2] coupled to either an RGDS cell adhesive ligand (PA-RGDS) or to no ligand (PA). The self-assembly of PAs onto electrospun PCL has been characterized with TEM, and the initial attachment of human mesenchymal stem cells (hMSCs) on uncoated electrospun PCL (PCL), electrospun PCL coated with PA without a ligand (PCL-PA), and electrospun PCL coated with PA-RGDS (PCL-PA-RGDS) was evaluated.

Materials and Methods

All PAs were synthesized by solid-phase synthesis using Fmoc chemistry and their self-assembly into nanofibers evaluated using TEM. Electrospun PCL scaffolds were fabricated by dissolving 22.5 wt% PCL (Mn = 80000) in a solvent system of 1:1 chloroform: methanol, and applying a voltage of +21 kV at a distance of 28 cm between the needle and the collector. The self-assembled coating of PAs onto PCL nanofibers was characterized using TEM. Initial attachment of hMSCs was evaluated using the PicoGreen assay.

Results

Electrospun PCL scaffolds have been successfully fabricated with typical fiber diameters ranging from 200 nm – 400 nm (*Fig. 1).* This distribution falls within the range of collagen fiber bundles found in native tissue.[3]

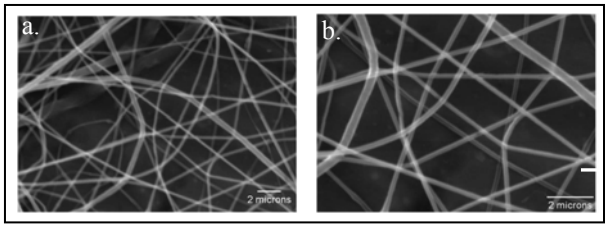

Fig. 1. SEM images of electrospun PCL at (a) 7400X and (b) 14800X. Scale bar = 2 µm.

PAs were successfully synthesized and self-assembled into nanofibers with diameters of 8 nm onto electrospun PCL scaffolds by solvent evaporation. Self-assembly was confirmed by TEM (*Fig. 2)*. *Fig. 2b* shows the same PCL fiber as *Fig. 2a* tilted by 42° to demonstrate PA coating all around the PCL fiber.

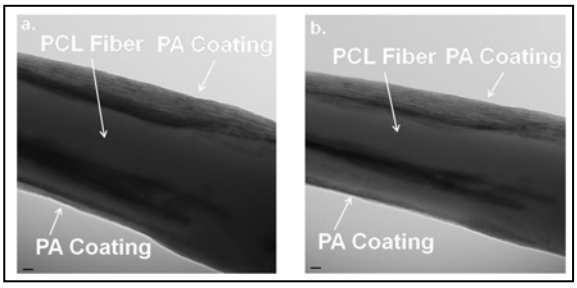

Fig. 2. TEM images show successful self-assembly of PA coated onto electrospun PCL at (a) 0° and (b) 42° tilt. Scale bar = 20 nm.

Fig. 3 shows that the initial attachment on PCL-PA-RGDS was significantly greater than on PCL-PA and PCL, indicating that hMSCs can recognize the RGDS ligand inscribed into the PA.

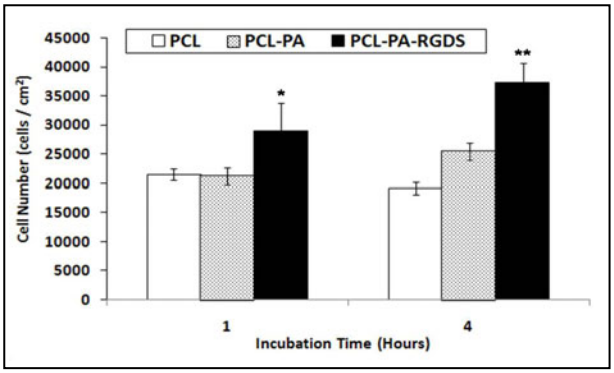

Fig. 3. Initial attachment of hMSCs. PCL-PA-RGDS shows significantly greater cell attachment than PCL-PA and PCL (*,**: $p<0.05$, *n=4*).

Conclusion

This study shows a novel strategy to endow electrospun scaffolds with bioactivity using self-assembled ECM mimicking PAs. This natural tissue mimicking hybrid scaffold can be adapted for a variety of tissue regeneration applications.

References

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