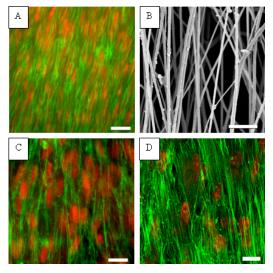
## **Tissue Engineered Nanofibrous Vascular Graft**

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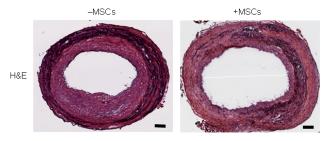
Blood vessel replacement is a common treatment for vascular diseases such as atherosclerosis and aneurysm. Tissue-engineered vascular graft (TEVG) is a potential solution for small diameter vascular graft. Here we developed a new approach to construct TEVGs by using bone marrow mesenchymal stem cells (MSCs) and nanofibrous scaffolds. Poly(lactic acid) was fabricated into nanofibrous sheets by electrospinning technique, and the nanofibers were aligned by mechanical stretching. MSCs were seeded onto nanofibrous scaffolds, and rolled into small-diameter TEVG after 2 days. The cells were aligned in the circumferential direction of the TEVG, which simulated cell alignment in the vascular wall. Cells in the scaffolds were viable and well-organized, as characterized by fluorescence microscopy.



**Figure 1 :** Characterization of biomimetic cellscaffold interactions. **a)**. *En face* staining of smooth muscle cells in a native rat common carotid artery after endothelial cell denudation. The samples were

stained for actin filaments by using FITC conjugated phalloidin (green), and counterstained for nuclei using propidium iodide (red). **b**). SEM of aligned nanofibers made form PLLA. **c**). Human SMCs seeded on aligned nanofiber surface, with same staining as in **a**). **d**). MSCs seeded on aligned nanofiber surface, with same staining as in **a**. Scale bar =  $20 \mu m$ .

To determine the performance of TEVG in vivo, carotid bypass surgery was performed in rat model. The TEVGS showed patency within 2-month experimental period. Significant matrix remodeling was observed in the wall of TEVGs, including the production of collagen and elastin. Endothelial cell monolayer formed in the lumen of TEVGs, and layers of smooth muscle cells were observed under endothelial monolayer. This study demonstrates the potential of using stem cells and nanofibrous scaffolds for the construction of small diameter TEVGs, and may lead to clinical applications for cardiovascular repair.



**Figure 2 :** Cell organization and ECM remodeling after 60 days for acellular (-MSC) and cellular (+MSC) small-diameter nanofibrous vascular grafts. Images are representatives from at least three independent samples. Scale bar =  $100 \mu m$ .

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