NC STATE

Wilson College of Textiles

Textile Engineering, Chemistry and Science

A Fiber-Reinforced Composite Vascular Graft that Mediates the Macrophage Response

Fan ZHANG[1], Martin W. KING[1,2]

[1] Wilson College of Textiles, North Carolina State University, Raleigh (USA), [2] College of Textiles, Donghua University, Shanghai (China)

INTRODUCTION

- Tissue-engineered vascular grafts (TEVGs) have been studied in recent decades as a promising alternative to synthetic vascular prostheses to treat cardiovascular and peripheral vascular disease.
- Yet only a few studies have proceeded to a clinical trial and no TEVG has been commercialized for coronary and peripheral artery bypass surgery [1].
- Recent studies have uncovered that the host innate immune response regulates vascular cell recruitment and tissue regeneration [2].
- The main player, macrophages, can be modulated to a pro-inflammatory M1 phenotype that clears tissue debris and contaminations and accelerates vascular sprouting. They can also be signaled to a pro-regenerative M2 phenotype to promote vascular stabilization and maturation, which is crucial to the regeneration of the vascular tissue and the ultimate success of a TEVG after implantation.

REFERENCES

[1] King MW et al Springer Briefs Materials 2020; 21-29

[2] Hibino N et al J Thorac Cardiovasc Surg 2010;139:431.

[3] Zhang F et al Biofabrication 2019 ;11: 035020

[4] Zhang F et al Mater Sci Eng C 2021;118: 111418.

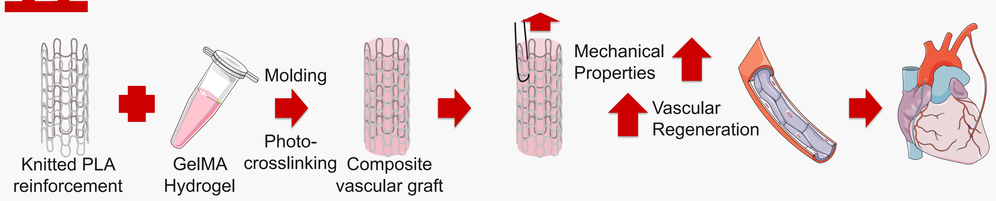
[5] Loessner D et al Nat Protoc 2016;11:727.

[6] Cha, BH et al Adv Healthc Mater, 2017; 6(21):1700289.

OBJECTIVE

In the present study, we engineered a fiber-reinforced hydrogel composite vascular graft that promoted an M2 macrophage phenotype after 7 days of *in vitro* cell culture, rendering the potential for a successful and fast-repairing TEVG for the application of vascular bypass or replacement surgery.

MATERIAL & METHODS



RESULTS

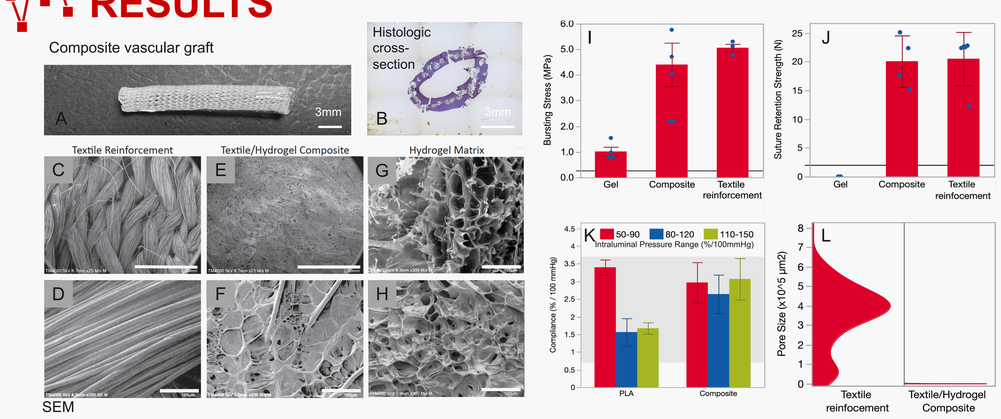


Figure 1 Morphology and Mechanical properties of the composite vascular graft. (A) Gross photo and (B) cross-section with H&E staining of the composite vascular graft. (C&D) SEM of the textile reinforcement, (E&F) composite and (G&H) hydrogel matrix. (I) Bursting strength and (J) suture retention strength were both significantly improved due to the incorporation of the textile reinforcement. Black lines refer to the minimum requirement for a vascular graft [3]. (K) The radial dynamic compliance was comparable to the human saphenous vein (range marked in grey [4]). (L) Pore size was significantly reduced due to the addition of the hydrogel matrix, which prevents blood leakage through the graft wall.

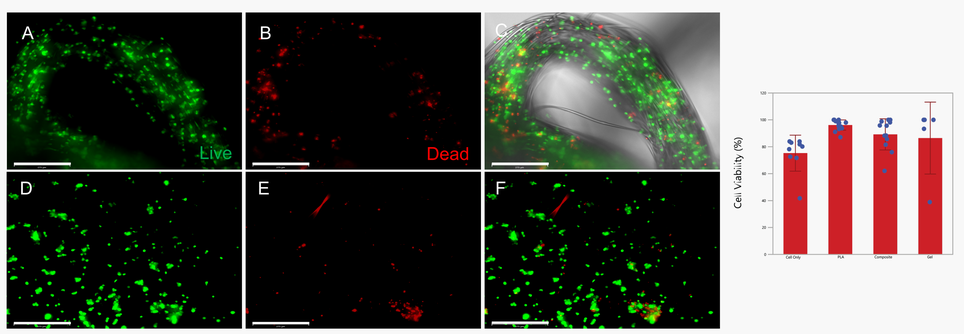


Figure 2 Cell viability of the THP-1 induced macrophages on (A-C) PLA fiber reinforced scaffold and the (D-F) composite scaffold. Live cells were stained in green and dead cell stained in red. Scale bar=275 µm. Cell viability was calculated by comparing the live cells to the total number of cells. There was no significant difference among the cells on the PLA reinforcement, GelMA matrix, composite scaffold, and the cell only control.

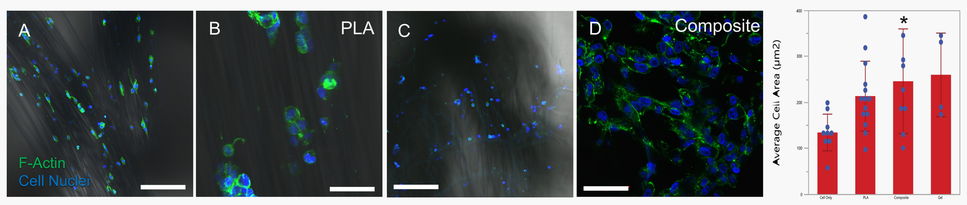


Figure 3 THP-1 cell morphology. (C & D) The composite conduit showed a higher cell density and induced an elongated cell morphology, which suggests a polarization to the pro-regenerative macrophage phenotype compared to cells on (A & B) the PLA reinforcement control. Scale bar: A & C=200µm, B & D=50µm.

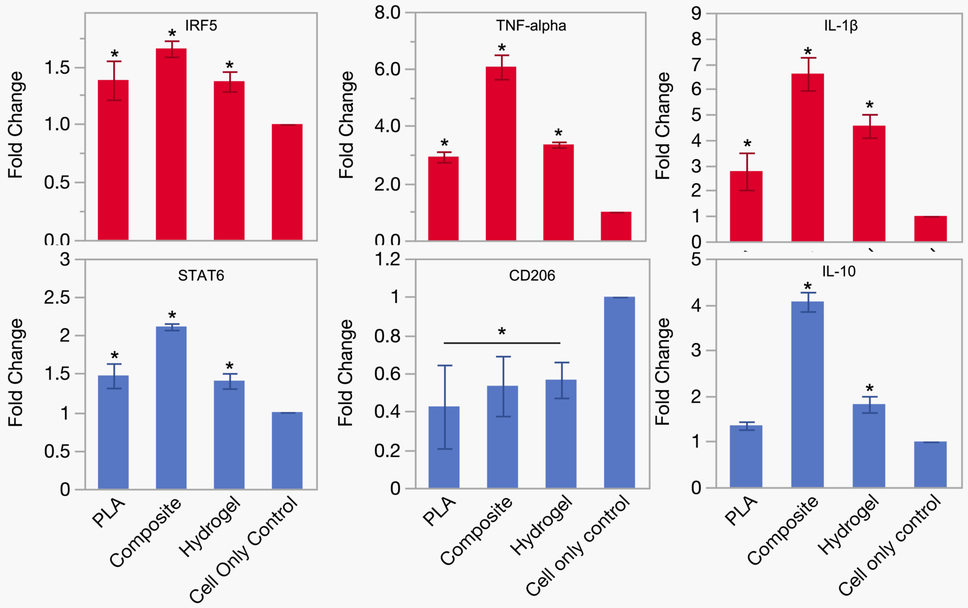


Figure 4 Gene expression of the THP-1-induced macrophages. The composite scaffold enhanced the macrophage responses compared to the tissue culture plate. The M1-related genes IRF5, TNF-alpha and IL-1beta, and M2-related genes STAT6 and IL-10 were all upregulated, indicating a mix of M1 and M2 phenotype induced by the composite graft.

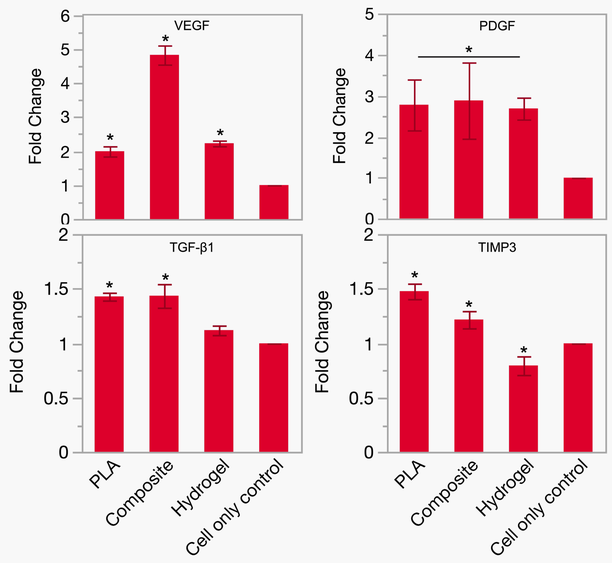


Figure 5 Expression of vascular-development-related genes in the THP-1-induced macrophages. The composite graft enhanced gene expression related to vascular development.

CONCLUSIONS

In this study, we engineered a fiber-reinforced composite conduit as a scaffold for a tissue engineered vascular graft. It was designed to modulate early inflammatory response and enhance vascular regeneration. Both M1 and M2 related genes expression were upregulated in macrophages, indicating a mixture of M1 and M2 macrophages. Vascular-development related genes were also upregulated in macrophages, which might enhance vascular regeneration in the vascular graft.

Contact: Fan Zhang | Email: fzhang12@ncsu.edu