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Moving Electrospun Nanofibers and Bioprinted Scaffolds toward Translational Applications

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Over the past two decades, electrospun nanofibers have been actively explored for a range of applications, including those related to biomedicine, environmental science, energy harvesting, catalysis, photonics, and electronics. Regarding biomedical applications, one can readily produce nanofiber-based scaffolds with controlled compositions, structures, alignments, and functions by varying the material, design of collector, number of spinnerets, and electrospinning parameters. This report highlights both preclinical and translational applications of electrospun nanofibers and bioprinted constructs presented at the 2019 International Conference on Electrospinning, together with some perspectives on their future development.

1. Introduction

Electrospinning is a simple and versatile technique for producing nanofibers from a wide variety of materials, including synthetic polymers, natural macromolecules, ceramics, and even small molecules.[1–4] In addition to the variations in composition, electrospun nanofibers can be further engineered to take different orientations (e.g., random vs aligned) and secondary structures (e.g., pore, groove, protrusion, hollow interior, and core–shell configuration), while their surfaces can be functionalized with bioactive agents and nano/microscale particles.[4] As a result, it has been a vibrant field of research for people to develop electrospinning as a fabrication technique while exploring the use of electrospun nanofibers to solve a broad range of clinical problems. Owing to their small diameters (e.g., 50–500 nm, similar to the collagen fibers in a native extracellular matrix, ECM) and architecture (i.e., a 3D network of fibrous structures), electrospun nanofibers are immediately useful in a range of biomedical applications, including regenerative medicine and tissue engineering. By engineering the electrospun nanofibers, one can easily and conveniently create a scaffold to recapitulate the microenvironment in a native tissue. At the 2019 International Conference on Electrospinning held at Donghua University in Shanghai, China (June 19–21), researchers from all over the world gathered to share ideas and showcase recent progress in the development of electrospinning techniques and functionalization of electrospun nanofibers for a variety of applications. In this report, we only highlight the research presented at the symposia on "Electrospinning Techniques" and "Nanofibers for Medical and Biology."

2. New Materials and Methods for Electrospinning

Recently, a number of new variants of the traditional electrospinning setup have been demonstrated to meet the requirements for future clinical applications. For example, to endow the nonwoven mats of nanofibers with enhanced mechanical strength and tunable degradability, researchers have applied hydrogel-based materials to electrospinning. To this end, Cui and co-workers from Shanghai Jiao Tong University School of Medicine, China, have demonstrated the use of gelatin methacryloyl (GelMA) in the fabrication of photo-crosslinkable, hydrogel-based nanofibers (**Figure 1**).[5] Scaffolds made of such nanofibers showed adjustable mechanical strength and degradation rate, holding great potential for use in tissue repair and regeneration, including the induction of vascularization, acceleration of wound healing, and promotion of spinal cord repair.[5–7]

Researchers have also engineered the structure and/or orientation of electrospun nanofibers by changing the design of collector to make them better suited for the repair of tissues with highly orientated structures, such as nerve, muscle, tendon, and blood vessel, among others. In general, a high-speed rotating mandrel or a U-shaped, stainless-steel frame with a gap between the edges is often used as the collector to produce uniaxially aligned nanofibers. In these cases, the alignment still needs to be improved in terms of precision. To this end, the Zhang group at Donghua University, China,

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developed a rectilinear jet-enabled method for electrospinning (termed stable jet electrospinning) to obtain highly orientated nanofibers.[8] The success of this method mainly relies on suppressing the occurrence of bending instability and thus extending the straight section to an adequate length sufficient for manipulation during electrospinning by tuning the formulation of solution and parameters for electrospinning. They further applied the uniaxially aligned nanofibers to induce tenolineage differentiation for human-induced pluripotent stem cells during Achilles tendon regeneration and promote phenotypic expression of human umbilical arterial smooth muscle cells for vascular repair, respectively.[9,10]

Since the traditional electrospinning setup typically relies on the use of a relatively large and heavy power supply with low portability, one cannot generate nonwomen mats of electrospun nanofibers whenever and wherever needed, greatly limiting their use in certain applications such as military and special medicine. To address this issue, the Long group from Qingdao University, China, developed and commercialized a handheld electrospinning device. Remarkably, their battery-operated electrospinning apparatus only involved the use of two mercury-free alkaline AAA batteries and one voltage converter to provide the high voltage instead of the traditional power supply (**Figure 2**).[11] The handheld device has also been successfully applied to the in situ treatment of skin wounds.[12]

In terms of translational medicine, 2D nonwoven mats of nanofibers are not well-suited for the repair of bulk tissues. In this regard, 3D scaffolds consisting of nanofibers are of great importance. Recently, 3D aerogels made of short nanofibers and directly expanded 3D nanofibrous scaffolds have been developed for use in tissue repair and regeneration.[13–16] For example, the Mo Group at Donghua University, China, demonstrated the fabrication of superabsorbent 3D scaffolds from short nanofibers made of a blend of gelatin and poly(lactic acid) (PLA). Their protocol involves four major steps: i) electrospinning of gelatin/PLA nanofibers, ii) cutting the nanofibers to short pieces, iii) homogenizing and freeze-drying, and iv) crosslinking.[14] After further modification with hyaluronic acid, such scaffolds were successfully used to repair the cartilage defects at 12 weeks postsurgery in rabbits. Similarly, the Li and Ding groups from Donghua University, China, also reported the development of 3D elastic scaffolds made of chitosan-wrapped SiO_2 nanofibers[16] or chitosan-crosslinked SiO_2-CaO nanofibers.[17] Such scaffolds hold great potential in the repair of subchondral bone sites and the regeneration of bone tissues.

In addition to the post treatment of short nanofibers, the Xie group at University of Nebraska Medical Center, USA, developed a general method to directly expand 2D mats of nanofibers into 3D scaffolds while preserving the imparted anisotropic features of a variety of shapes and sizes.[18] They explored a modified gas foaming strategy through the use of $NaBH_4$ solution to generate hydrogen bubbles for the expansion of nanofiber mats. Using this simple method, they successfully realized cell penetration into and neovascularization in the bulk of a nanofiber-based scaffold.[19] This strategy was further extended to transform 2D nanofiber mats in the shapes of rectangle, triangle, semicircle, and arche into cylinder (**Figure 3**), circular cone, sphere, and hollow sphere, respectively.[20] They also realized the expansion by depressurizing the subcritical CO_2 fluid to avoid the use of any aqueous solution and chemical reaction.[21] As such, this new approach can reduce the loss of bioactivity of the biological molecules encapsulated in the scaffold and be used to expand the nanofiber mats made of hydrophilic polymers. The 3D scaffolds fabricated using this method were able to greatly promote

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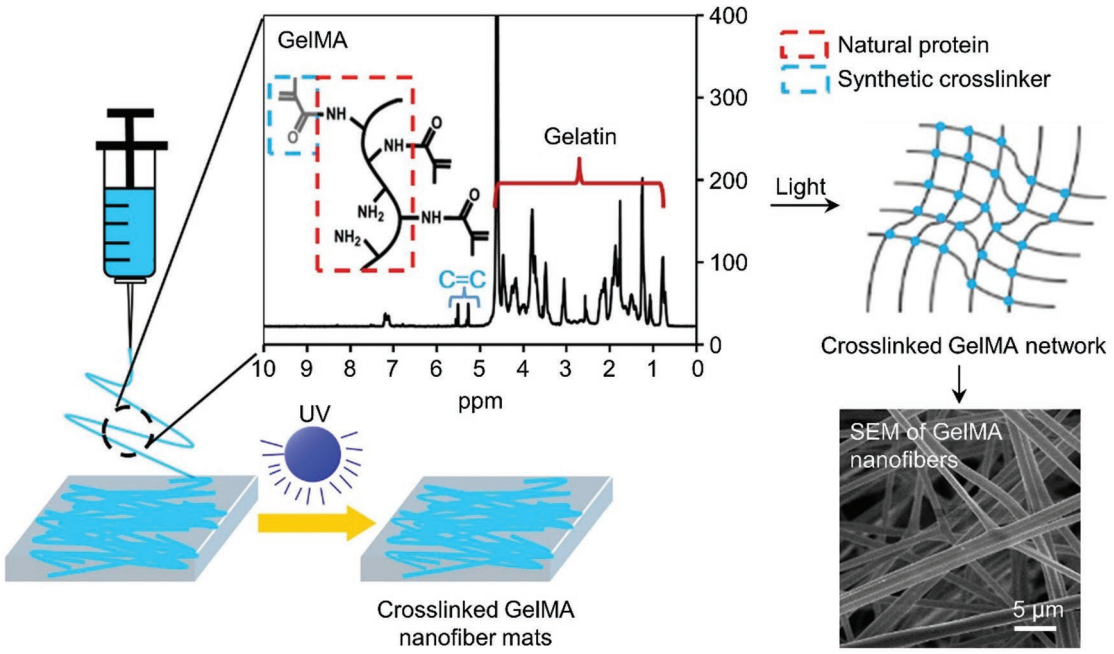

Figure 1. Schematic illustration showing the fabrication of nonwoven mats of GelMA nanofibers by electrospinning and subsequent photo-crosslinking. The box shows the nuclear magnetic resonance (NMR) spectrum of the as-synthesized GelMA. The gelatin component (red dashed box) was modified to contain methacryloyl groups (blue dashed box) for cross-linking the GelMA network upon light exposure. The scanning electron microscopy (SEM) image shows the typical morphology of the cross-linked GelMA nanofibers. Reproduced with permission.[5] Copyright 2017, Elsevier.

the cellular infiltration, neovascularization, and positive host response after subcutaneous implantation in rats.

3. Scaffolds Based upon Electrospun Nanofibers for Biomedical Applications

Owing to the rapid progress of materials and methods for electrospinning, scaffolds made of electrospun nanofibers have been developed for a rich variety of biomedical applications, among which tissue repair and cancer diagnosis are the most promising fields.

The Xia group at the Georgia Institute of Technology, USA, have carried out a series of studies to maximize neurite outgrowth for the purpose of repairing injured peripheral nerves. They have demonstrated that both planar mats and multitubular nerve guidance conduits (NGCs) made of uniaxially aligned, poly(ε-caprolactone) (PCL) nanofibers promoted the differentiation of bone marrow stem cells (BMSCs) into Schwann cells.[22,23] The aligned nanofibers, upon preseeding with the BMSCs-derived Schwann cells, significantly promoted the extension of neurites from the chick dorsal root ganglion bodies.[22] They also developed a near-infrared (NIR)-triggered release system with the use of a phase-change material (PCM) and a NIR dye.[24] The payloads could be released on-demand when the temperature was elevated to slightly pass the melting point of the PCM in response to the laser. The PCM particles loaded with nerve growth factors (NGFs) were then sandwiched between two layers of PCL nanofibers to boost the outgrowth of neurites. In addition to cells and growth factors, they also investigated the impacts of physical cues on neurite extension. For example, they demonstrated the functionalization of uniaxially aligned PCL microfibers with electrosprayed microparticles of fatty acids.[25] Due to the surface roughness and chemical cues derived from the microparticles of fatty acids, the outgrowth of neurites was significantly enhanced. Upon integration, this new platform is expected to find use in the repair of peripheral nerves.

The You group at Donghua University, together with the Ye and Zhao groups at Shanghai Jiao Tong University School of Medicine, China, developed a hybrid, small-diameter vascular graft to investigate its performance in inhibiting intimal hyperplasia.[26] Such a vascular graft was constructed from a layer of decellularized vessel and a layer of rapamycin-loaded, electrospun PCL nanofibers. Rapamycin, a drug approved by the Food and Drug Administration (FDA), has been reported to be able to ameliorate in-stent thrombosis and restenosis.[27] Upon blending in the PCL nanofibers, the rapamycin could be slowly released in a localized region. After integrated with the decellularized vessel, the hybrid vascular graft was transplanted into the abdominal aorta in a rat model. At 12 months post implantation, the rapamycin-loaded vascular graft significantly decreased neo-intimal hyperplasia relative to the case of a hybrid graft without the incorporation of rapamycin, without the impairing of re-endothelialization (**Figure 4**). These results suggest that the rapamycin-loaded, hybrid vascular grafts have great translational potential for the repair of small-diameter blood vessels.

The He group at Fudan University Affiliated Zhongshan Hospital, China, developed a patch for the repair of abdominal wall. The patch was constructed from electrospun nanofibers made of a blend of poly(L-lactide-*co*-caprolactone) and porcine

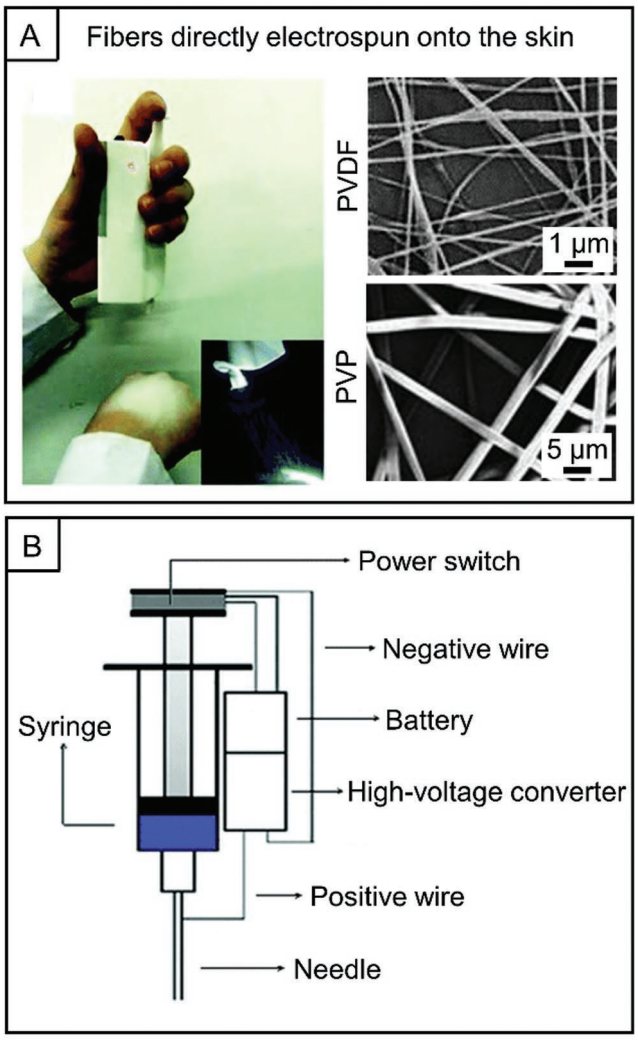

Figure 2. A) Photographs (left panel) showing the fibers directly electrospun onto the skin using a battery-operated, portable handheld electrospinning apparatus. The inset shows the spinning process in a dark environment. SEM images (right panel) showing the poly(vinylidene fluoride) (PVDF) and poly(vinyl pyrrolidone) (PVP) fibers electrospun using the apparatus. B) Schematic diagrams showing the portable apparatus. Reproduced with permission.[11] Copyright 2015, The Royal Society of Chemistry.

fibrinogen. The optimized blend with a weight ratio of 4:1 for the poly(L-lactide-*co*-caprolactone) and porcine fibrinogen showed the best physical properties in terms of shrinkage, mechanical strength, porosity, and hydrophilicity. Then, they applied such a patch to in vivo investigation in a canine abdominal wall defect model. After 36 weeks, the patch effectively induced the regeneration of abdominal skeletal muscles. In particular, the degradation rate of the patch and the rate of new tissue in-growth could reach a balance, and the biomechanical strength was able to return to the baseline within two weeks of implantation. Such patches have been commercialized as class III medical devices by the P&P Biotech Company.[28]

The Yang group at Radboud University Medical Center, Netherlands, has been developing nanomaterials for electrospinning and/or electrospraying to produce scaffolds for drug delivery and/or defected tissue repair.[29–31] At the meeting, they reported the preparation of drug-loaded poly (lactic-*co*-glycolic acid) (PLGA) microspheres by electrospraying, which showed advantages such as a short exposure time of drugs to organic solvents and a high encapsulation efficiency. By tuning the solvent used for electrospraying and/or the characteristics (e.g., end group and molecular weight) of PLGA, they were able to obtain PLGA microspheres with different shapes and variable drug release profiles.[31] Because both tumors and wounds generated high levels of hydrogen peroxide, they further modified the surface of PLGA microspheres with catalase. The as-modified microspheres showed a self-guided movement in response to the gradient of hydrogen peroxide, with great potential for wound healing and cancer treatment.

The Zhang group from North Carolina Agricultural and Technical State University, USA, investigated the antifungal functionality of electrospun polyacrylonitrile nanofibers. Compared with the film and microfiber mat made of the same polymer, the mat of polyacrylonitrile nanofibers adversely affected the growth, morphology, and viability of yeast cells without any aid from antifungal agents, providing exciting promise as the next-generation material that can control fungal growth through physical contact. Such nanofiber mats, as antifungal nanofibrous materials, have been granted by a U.S. patent.[32]

Besides their use as scaffolds for tissue regeneration, electrospun nanofibers have also been used for efficient capture and release of circulating tumor cells (CTCs), with potential for clinical cancer diagnosis.[33] At the meeting, the Shi group from Donghua University, China, reported DNA aptamer-functionalized, magnetic short nanofibers comprised of polyethyleneimine-stabilized Fe_3O_4 nanoparticles and poly(vinyl alcohol) for efficient capture and release of CTCs. It was shown that the fibers were able to specifically capture and nondestructively release MCF-7 cells, with capture and release efficiencies as high as 87% and 90%, respectively.

With or without involving the use of electrospinning, several new techniques have also been reported to fabricate scaffolds for preclinical and translational use. Among them, 3D printing (in particular, bioprinting) is emerging as a powerful technique for the fabrication of biomimetic scaffolds.[34] In one example, the Mo group at Donghua University, China, used short electrospun nanofibers made of a blend of gelatin and PLGA as inks for 3D printing. Post printing and freeze drying, the nanofiber-based inks were successfully constructed into 3D scaffolds with precisely controlled shapes and large pores, in addition to a fibrous surface similar to that of a native ECM.[35] The Swieszkowski group from Warsaw University of Technology, Poland, reported that short electrospun nanofibers could be loaded with growth factors and then used as bioactive reinforcing fillers to fabricate 3D hydrogel scaffolds by bioprinting. They successfully fabricated vascular scaffolds made of GelMA-alginate hydrogels reinforced with short polymeric fibers with length less than 50 μm, which were preloaded with vascular endothelia growth factors.

The Xu group from Tsinghua University, China, reported a series of studies involving the development of 3D bioprinting and made lots of efforts in preclinical translation.[36–41] In one study, they combined biomimetic shape,

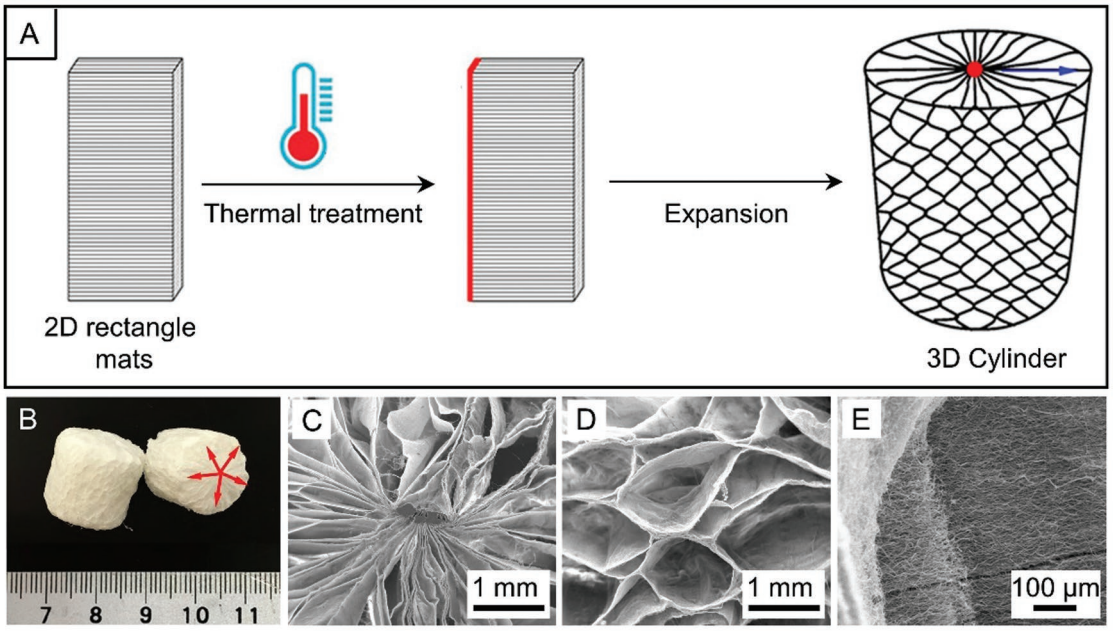

Figure 3. A) Schematic illustration showing how a 2D rectangular mat, with one side fixed, is expanded using a gas-foaming technique for the generation of a cylindrical shape. B) Photograph of the resultant cylinders. Arrows indicate the direction of fiber alignment. C,D) SEM images showing the top and side surface of the cylinder. E) SEM image showing the fibrous structure on the side surface in a magnified view. Adapted with permission.[20] Copyright 2019, American Chemical Society.

autogenous bone matrix, and autogenous cells in one step for patient-specific repair through the use of 3D bioprinting.[41] The clinical advantages of such a strategy include the inherent biosafety of autogenous materials and cells, and the heterogeneous structures realized via 3D bioprinting. They have demonstrated precise replication of mandibular ramus, partial frontal bone with supraorbital ridge, and atlas. Using the 3D-printed scaffolds containing autogenous bone materials and marrow-derived mesenchymal stem cells, they observed the regeneration of mature bone with endogenetic blood vessels and enhanced mineralization in a critical-sized skull defect model in vivo at three months post repair. Finally, they explored the potential of 3D bioprinting in the construction of in vitro models for studying lung cancers and proposed to integrate 3D bioprinting with electrospinning for the creation of 3D scaffolds with autogenous materials and cells, and nanofibrous structures for clinical translation.

4. Future Outlook

The continuous development of materials and methods for electrospinning has enabled the utilization of electrospun nanofibers in various biomedical applications. Among them, the nanofibers hold great promise as scaffolds to manipulate cell behaviors for tissue repair or regeneration, and as in vitro tissue/organ models to study cancers or screen drugs for cancer diagnosis and treatment. However, to reach the translational goal, there is still a long way to go in transforming the laboratory results into commercial products. Some of the major obstacles include the long-term biocompatibility and potential immunogenicity of the materials when applied to humans. In this regard, autogenous matrixes and cells, as well as the materials approved by FDA should receive the highest priority. Another major concern related to the clinical translation is the obvious variation between animal models and the patients who really carry the disease. For example, the patients who suffer from the same disease more or less have individual differences, especially for those with severe immunodeficiency and complications. It will be very difficult to develop a "versatile" product suitable for the therapy of all patients throughout the world. In this regard, a large number of preclinical trials should be carried out before the products will be brought to the market. In addition, the regeneration of 3D tissues still remains a challenge due to their hierarchical structures and multiple functions. As such, the integration of electrospinning with bioprinting techniques would offer a practical route to the fabrication of nanofiber-based 3D scaffolds with any desired shapes and dimensions, even with the use of materials extracted from the autogenous matrixes to meet the needs for repairing different types of tissues. The last but not least, the invention of portable electrospinning devices would provide an easier way for the commercialization of translational products, in particular, for field use and special medicine. It is hoped that the concepts and examples presented in this report will provide motivation and insight for moving electrospun nanofibers toward more translational applications.

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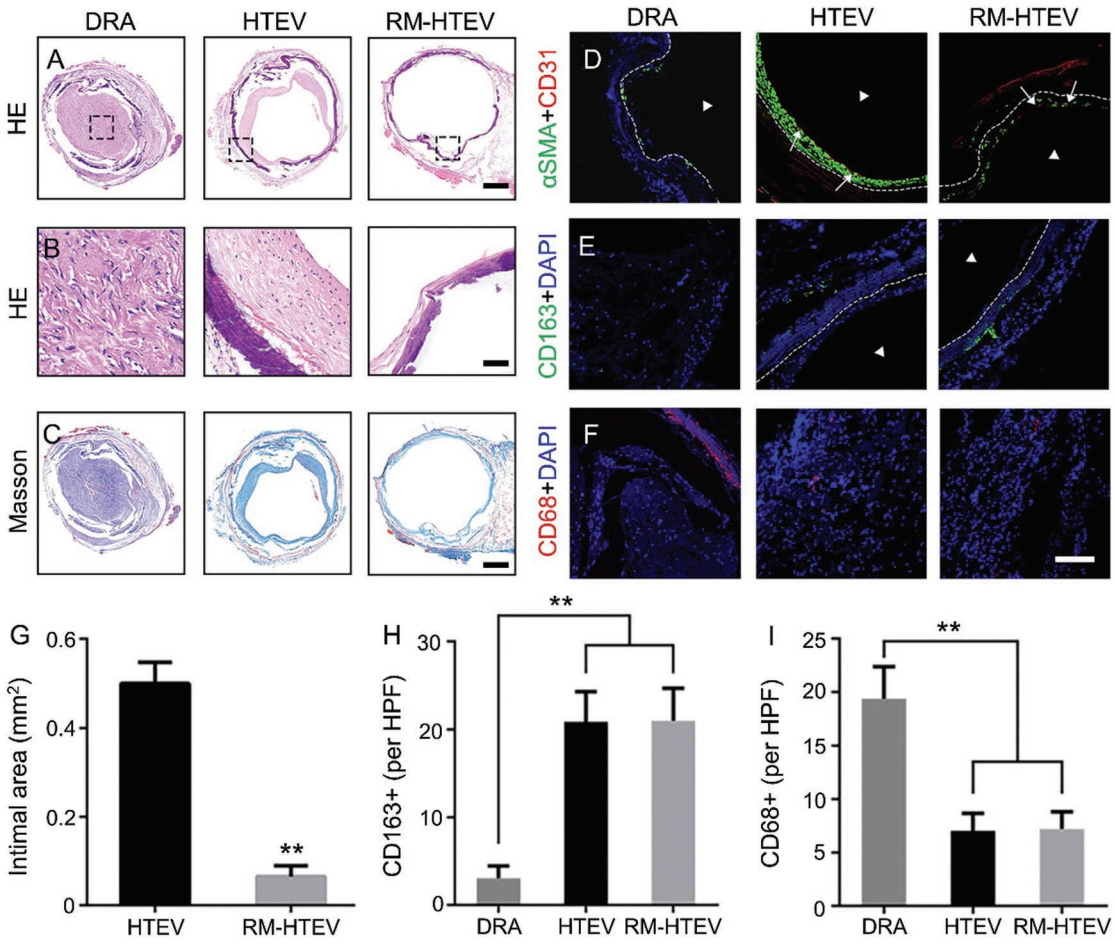

Figure 4. Inhibitory effect of a rapamycin-loaded, hybrid tissue-engineered vascular (RM-HTEV) graft on intimal hyperplasia. The RM-HTEV graft was comprised of a layer of decellularized vessel and a layer of rapamycin-loaded, electrospun PCL nanofibers. Optical microscopy images of representative A,B) hematoxylin and eosin staining and C) Masson's trichrome staining at 12 weeks post-implantation. The results indicated that the intimal hyperplasia of the RM-HTEV group was inhibited relative to the HTEV and decellularized rat aorta (DRA) groups. The scale bars are 400 µm in (A) and (C), and 40 µm in (B). Images showing the immunofluorescence staining for D) αSMA (green) and CD31 (red), E) CD163 (green) and DAPI (blue), and F) CD68 (red) and DAPI (blue). White arrows indicate the CD31-positive cells. White triangles indicate the vessel lumens. The scale bar is 50 µm. G) Quantified assessment of the intimal area for the RM-HTEV and HTEV grafts from (A)–(C). $^{**}P < 0.01$ as compared with that of the HTEV graft. H,I) Quantified assessment of the CD163- and CD68-positive cells for the different groups from (D)–(F). $^{**}P < 0.01$ as compared with that of the DRA. Reproduced with permission.[26] Copyright 2019, Elsevier.

Conflict of Interest

The authors declare no conflict of interest.

Keywords

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[1] F. Anton, *U.S. Patent 2,160,962*, **1939**.
[2] J. Doshi, D. H. Reneker, *J. Electrostat.* **1995**, *35*, 151.
[3] F. Anton, *U.S. Patent 2,349,950*, **1944**.
[4] J. Xue, T. Wu, Y. Dai, Y. Xia, *Chem. Rev.* **2019**, *119*, 5298.
[5] X. Zhao, X. Sun, L. Yildirimer, Q. Lang, Z. Y. W. Lin, R. Zheng, Y. Zhang, W. Cui, N. Annabi, A. Khademhosseini, *Acta Biomater.* **2017**, *49*, 66.
[6] X. Sun, Q. Lang, H. Zhang, L. Cheng, Y. Zhang, G. Pan, X. Zhao, H. Yang, Y. Zhang, H. A. Santos, W. Cui, *Adv. Funct. Mater.* **2017**, *27*, 1604617.
[7] C. Chen, J. Tang, Y. Gu, L. Liu, X. Liu, L. Deng, C. Martins, B. Sarmento, W. Cui, L. Chen, *Adv. Funct. Mater.* **2019**, *29*, 1806899.
[8] H. Yuan, S. Zhao, H. Tu, B. Li, Q. Li, B. Feng, H. Peng, Y. Zhang, *J. Mater. Chem.* **2012**, *22*, 19634.
[9] C. Zhang, H. Yuan, H. Liu, X. Chen, P. Lu, T. Zhu, L. Yang, Z. Yin, B. C. Heng, Y. Zhang, H. Ouyang, *Biomaterials* **2015**, *53*, 716.
[10] H. Yuan, J. Qin, J. Xie, B. Li, Z. Yu, Z. Peng, B. Yi, X. Lou, X. Lu, Y. Zhang, *Nanoscale* **2016**, *8*, 16307.
[11] S. C. Xu, C. C. Qin, M. Yu, R. H. Dong, X. Yan, H. Zhao, W. P. Han, H. D. Zhang, Y. Z. Long, *Nanoscale* **2015**, *7*, 12351.

[12] R. H. Dong, Y. X. Jia, C. C. Qin, L. Zhan, X. Yan, L. Cui, Y. Zhou, X. Jiang, Y. Z. Long, *Nanoscale* **2016**, *8*, 3482.
[13] G. Duan, S. Jiang, V. Jérôme, J. H. Wendorff, A. Fathi, J. Uhm, V. Altstädt, M. Herling, J. Breu, R. Freitag, S. Agarwal, A. Greiner, *Adv. Funct. Mater.* **2015**, *25*, 2850.
[14] W. Chen, S. Chen, Y. Morsi, H. El-Hamshary, M. El-Newhy, C. Fan, X. Mo, *ACS Appl. Mater. Interfaces* **2016**, *8*, 24415.
[15] B. Sun, Z. Zhou, T. Wu, W. Chen, D. Li, H. Zheng, H. El-Hamshary, S. S. Al-Deyab, X. Mo, Y. Yu, *ACS Appl. Mater. Interfaces* **2017**, *9*, 26684.
[16] L. Wang, Y. Qiu, H. Lv, Y. Si, L. Liu, Q. Zhang, J. Cao, J. Yu, X. Li, B. Ding, *Adv. Funct. Mater.* **2019**, *29*, 1901407.
[17] L. Wang, Y. Qiu, Y. Guo, Y. Si, L. Liu, J. Cao, J. Yu, X. Li, Q. Zhang, B. Ding, *Nano Lett.* **2019**, *19*, 9112.
[18] S. Chen, M. A. Carlson, Y. S. Zhang, Y. Hu, J. Xie, *Biomaterials* **2018**, *179*, 46.
[19] J. Jiang, Z. Li, H. Wang, Y. Wang, M. A. Carlson, M. J. Teusink, M. R. MacEwan, L. Gu, J. Xie, *Adv. Healthcare Mater.* **2016**, *5*, 2993.
[20] S. Chen, H. Wang, A. McCarthy, Z. Yan, H. J. Kim, M. A. Carlson, Y. Xia, J. Xie, *Nano Lett.* **2019**, *19*, 2059.
[21] J. Jiang, S. Chen, H. Wang, M. A. Carlson, A. F. Gombart, J. Xie, *Acta Biomater.* **2018**, *68*, 237.
[22] J. Xue, J. Yang, D. M. O'Connor, C. Zhu, D. Huo, N. M. Boulis, Y. Xia, *ACS Appl. Mater. Interfaces* **2017**, *9*, 12299.
[23] J. Xue, H. Li, Y. Xia, *Macromol. Biosci.* **2018**, *18*, 1800090.
[24] J. Xue, C. Zhu, J. Li, H. Li, Y. Xia, *Adv. Funct. Mater.* **2018**, *28*, 1705563.
[25] J. Xue, T. Wu, J. Li, C. Zhu, Y. Xia, *Angew. Chem., Int. Ed.* **2019**, *58*, 3948.
[26] Y. Yang, D. Lei, H. Zou, S. Huang, Q. Yang, S. Li, F. L. Qing, X. Ye, Z. You, Q. Zhao, *Acta Biomater.* **2019**, *97*, 321.
[27] G. W. Stone, J. F. Sabik, P. W. Serruys, C. A. Simonton, P. Généreux, J. Puskas, D. E. Kandzari, M. C. Morice, N. Lembo, W. M. Brown III, D. P. Taggart, A. Banning, B. Merkely, F. Horkay, P. W. Boonstra, A. J. Van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P. Buszman, A. Bochenek, E. Schampaert, P. Pagé, O. Dressler, I. Kosmidou, R. Mehran, S. J. Pocock, A. P. Kappetein, *N. Engl. J. Med.* **2016**, *375*, 2223.
[28] http://www.nmpa.gov.cn/WS04/CL2056/329889.html (accessed: August 2018).
[29] M. Ali, X. F. Walboomers, J. A. Jansen, F. Yang, *J. Drug Delivery Sci. Technol.* **2019**, *52*, 263.
[30] J. Shao, B. Wang, J. Li, J. A. Jansen, X. F. Walboomers, F. Yang, *Mater. Sci. Eng., C* **2019**, *98*, 1053.
[31] J. Wang, L. Helder, J. Shao, J. A. Jansen, M. Yang, F. Yang, *Int. J. Pharm.* **2019**, *564*, 1.
[32] L. Zhang, D. R. LaJeunesse, N. Sirelkhatim, *U.S. Patent 10,412,962*, **2019**.
[33] Y. Xiao, M. Shen, X. Shi, *J. Mater. Chem. B* **2018**, *6*, 1420.
[34] L. Moroni, T. Boland, J. A. Burdick, C. De Maria, B. Derby, G. Forgacs, J. Groll, Q. Li, J. Malda, V. A. Mironov, C. Mota, M. Nakamura, W. Shu, S. Takeuchi, T. B. F. Woodfield, T. Xu, J. J. Yoo, G. Vozzi, *Trends Biotechnol.* **2018**, *36*, 384.
[35] W. Chen, Y. Xu, Y. Liu, Z. Wang, Y. Li, G. Jiang, X. Mo, G. Zhou, *Mater. Des.* **2019**, *179*, 107886.
[36] M. Albanna, K. W. Binder, S. V. Murphy, J. Kim, S. A. Qasem, W. Zhao, J. Tan, I. B. El-Amin, D. D. Dice, J. Marco, J. Green, T. Xu, A. Skardal, J. H. Holmes, J. D. Jackson, A. Atala, J. J. Yoo, *Sci. Rep.* **2019**, *9*, 1856.
[37] J. Diao, C. Zhang, D. Zhang, X. Wang, J. Zhang, C. Ma, K. Deng, T. Jiang, W. Jia, T. Xu, *Biofabrication* **2019**, *11*, 025006.
[38] J. He, J. Shao, X. Li, Q. Huang, T. Xu, *Bioprinting* **2018**, *11*, e00036.
[39] J. I. Rodriguez-Devora, B. Zhang, D. Reyna, Z. D. Shi, T. Xu, *Biofabrication* **2012**, *4*, 035001.
[40] X. Dai, C. Ma, Q. Lan, T. Xu, *Biofabrication* **2016**, *8*, 045005.
[41] H. Chen, J. Zhang, X. Li, L. Liu, X. Zhang, D. Ren, C. Ma, L. Zhang, Z. Fei, T. Xu, *Biofabrication* **2019**, *11*, 045007.

