Electropolymerization of dopamine for constructing bioactive cardiovascular stent coatings

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Introduction

Although percutaneous coronary intervention with stenting has been widely used for the treatment of symptomatic coronary disease, there are still several urgent issues to be addressed, such as in-stent restenosis (ISR) and late stent thrombosis (LAST). Our recent studies indicated selectively promoting migration and proliferation of endothelial cell to accelerate re-endothelialization provides a promising approach to prevent the ISR and LAST [1, 2]. However, the poor cytocompatibility of metallic cardiovascular stents often lead to the inefficiency of re-endothelialization. Surface functionalization of the metallic surface which is absent in reactive groups is a great challenge. Inspired by the redox reactions of dopamine, which play key roles in the formation of poly(dopamine) under basic conditions, we develop an electrochemistry-based method for the rapid surface modification of metallic cardiovascular stents with complex, three-dimensional shapes. A high bioactive coating can be obtained after immobilization of VEGF, which is a highly specific mitogen for vascular endothelial cells.

Method

- The electropolymerization of dopamine was conducted in a standard three-electrode electrochemical cell using the 316L stainless steel stent as a working electrode.
- Proliferation, migration, functional development (nitric oxide secretion) and maintenance of endothelial phenotype of HUVECs on various surfaces were studied.
- The formation of electropolymerized poly(dopamine) coating was characterized by cyclic voltammograms, electrochemical impedance spectroscopy, ellipsometer and fluorescently labeled BSA.

Results

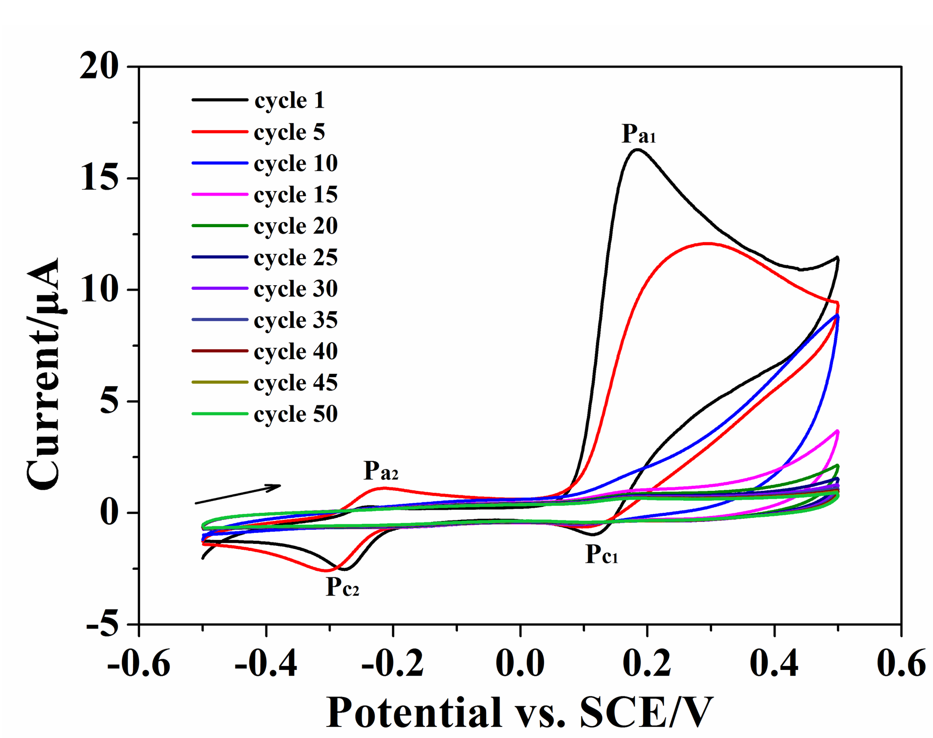

Fig. 1 *Cyclic voltammograms of dopamine solution (1 g/L) under a nitrogen atmosphere as a function of the number of voltammetric cycles. The scan rate was of 20 mV/s.*

An insulating electropolymerized poly(dopamine) (ePDA) coating was formed on the working electrode.

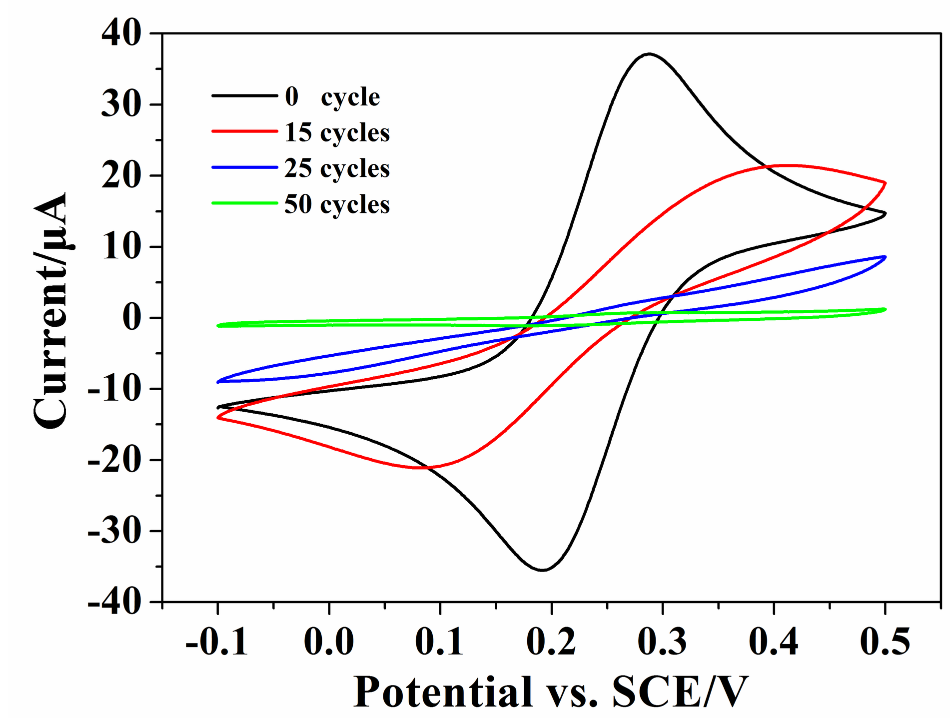

Fig.2 *Cyclic voltammograms of the electrode modified with ePDA in solution containing 5 mM $[Fe(CN)_6]^{3-/4-}$ as a function of the number of performed voltammetric cycles of ePDA. The scan rate was 50 mV/s.*

Formation of a continuous ePDA coating

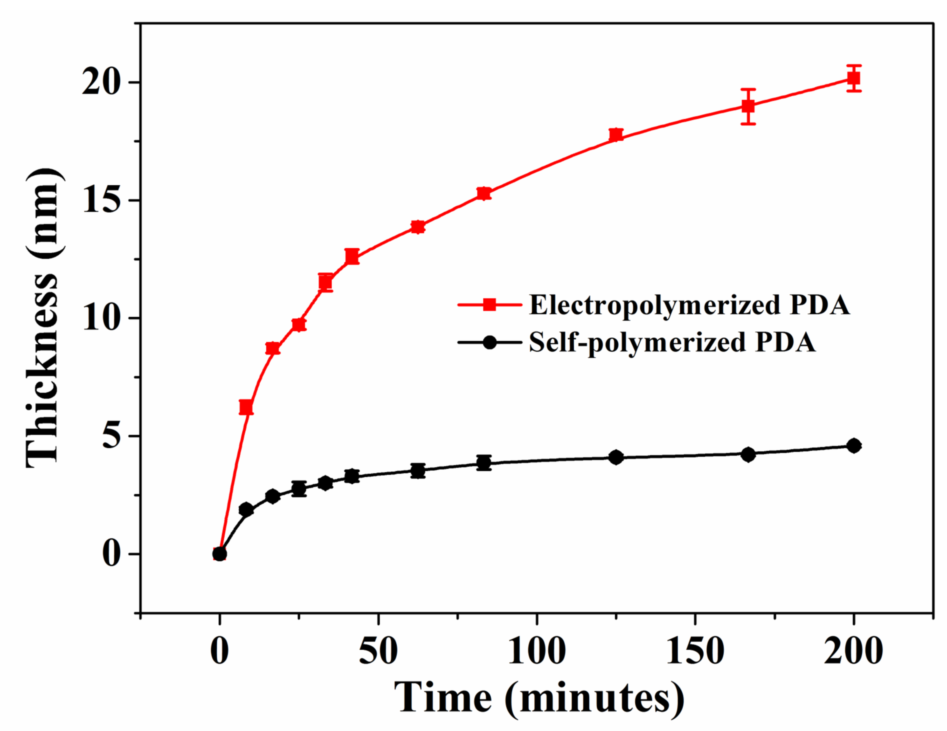

Fig. 3 *Ellipsometric thickness of electropolymerized poly(dopamine) and self-polymerized poly(dopamine) as a function of time.*

Rapid increase in thickness of the ePDA coating

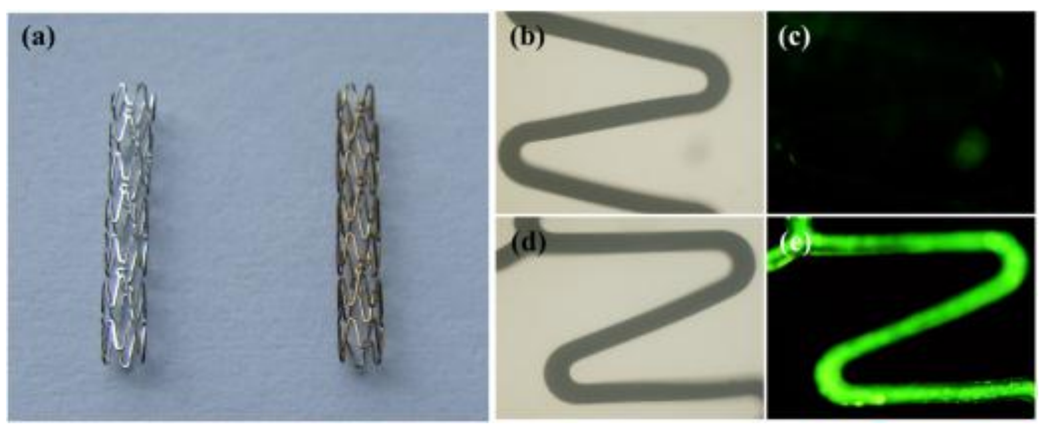

Fig. 4 *(a) Optical images of the bare stent (left) and ePDA-coated stent (right). Typical optical (b, d) and fluorescent (c, e) micrographs of the bare stent (b, c) and ePDA-coated stent (d, e) after immobilization of BSA-FITC.*

Successful surface modification of stent *via* ePDA

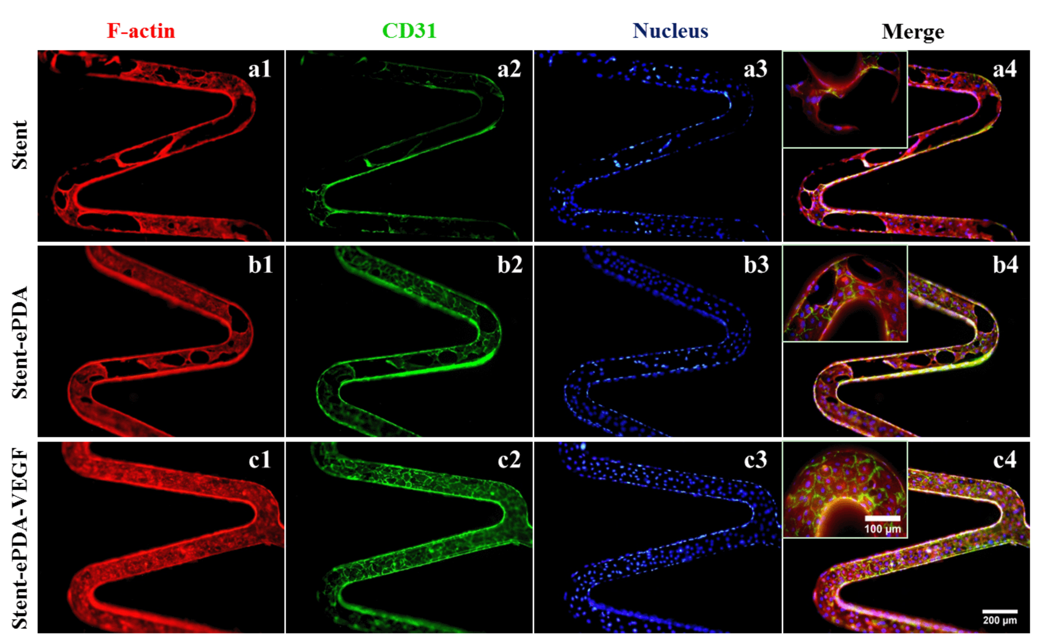

Fig. 5 *Fluorescent images of HUVEC on the surfaces of bare stent (a1~a4), ePDA-modified stent (b1~b4) and ePDA-modified stent immobilized with VEGF (c1~c4) after 6 days of culture.*

VEGF-functionalized stent greatly promoted the proliferation and phenotype maintenance of HUVEC.

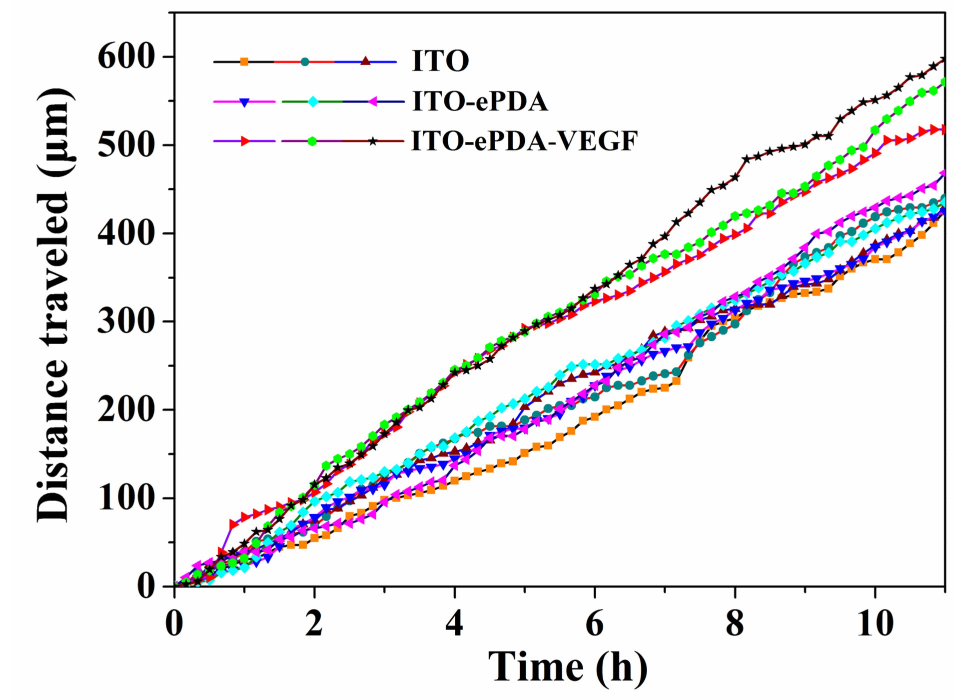

Fig. 6 *Migration behavior of HUVEC on various surfaces. (a) Traveled distance profiles of three representative cells on the ITO substrate, ePDA coating and VEGF-bound surface.*

Significant increase in cell migration on VEGF-functional surface

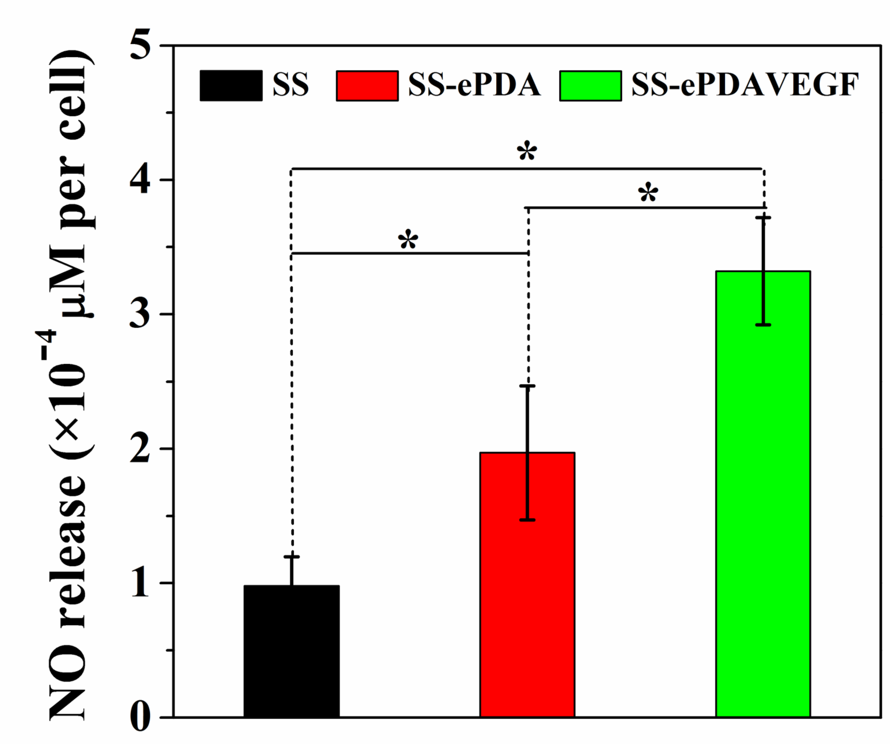

Fig. 7 *NO levels released in the culture media after 5 days of culture. Data presented as mean ± SD, n = 3 (* $p < 0.05$, t test).*

Significantly increase in NO secretion on VEGF-functionalized surface

Conclusion

Here we presented a facile and effective method to construct bioactive cardiovascular stent coatings via the electropolymerization of dopamine and subsequently immobilizing VEGF. Compared to bare 316L stainless steel stent, the proliferation, migration and nitric oxide secretion of HUVEC were greatly enhanced on the the VEGF-functionalized stent. Due to its simplicity and high efficiency, electropolymerization of dopamine has great potentials for applications in the surface modification and functionalization of the metallic medical devices.

Acknowledgements

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References

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[2] H Chang , KF Ren, J Ji, *et al*. **Biomaterials** 2013, 34, 3345.