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#### ACCEPTED MANUSCRIPT

# Fucoidan/VEGF-Based Surface Modification of Decellularized Pulmonary Heart Valve Improves the Antithrombotic and Re-endothelialization Potential of Bioprostheses

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- 17 Key words: Fucoidan; VEGF; Polyelectrolyte multilayer film; Re-endothelialization; Antithrombotic; Heart
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#### 20 Abstract

21 Decellularized porcine heart valves offer promising potential as biocompatible prostheses.

However, this procedure alter matrix fibres and glycans, leading to lower biomechanical 22 resistance and increased their thrombotic potential. Therefore, their durability is limited due to 23 calcification and weak regeneration in vivo. Surface modifications are highly requested to 24 improve the scaffolds re-endothelialization required to restore functional 25 and haemocompatible heart valve. Fucoidan, a natural sulphated polysaccharide, carries 26 antithrombotic and anti-inflammatory properties and is known to enhance endothelial 27 adhesion and proliferation when associated with vascular endothelial growth factor (VEGF). 28 Based on these features, we constructed fucoidan/VEGF polyelectrolyte multilayer film 29 (PEM) coated valve scaffold in an attempt to develop functional heart valve bioprosthesis. We 30 investigated the haemocompatibility of the PEM coated valve scaffolds, the adhesion and 31 growth potential of endothelial cells (HUVECs) in flow, as well as long term culture with 32 stem cells. Fucoidan/VEGF PEM coated scaffolds demonstrated antithrombotic and non-33 calcifying properties. The PEM application increased HUVECs adhesion in flow (6 h) and 34 HUVECs viability over time (72 h). HUVECs were well spread and aligned in flow direction. 35 Interestingly, stem cells infiltration was improved by the PEM coating at 21 days. Thus, the 36 fucoidan/VEGF PEM is a promising surface modification to obtain valve bioprostheses for 37 clinical applications with increased antithrombotic and re-endothelialization potential. 38

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