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Polyelectrolyte multilayer film on decellularized porcine aortic valve can reduce the adhesion of blood cells without affecting the growth of human circulating progenitor cells

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ABSTRACT

Polyelectrolyte multilayer film modification could be an effective method to reduce the immunological and inflammatory response of the xenogeneic scaffold in vivo, and may also be applied to tissue-engineered heart valve in contact with blood. The objectives of this study are to test heparin–chitosan multilayer film as an antithrombotic coating reagent for decellularized aortic heart valve and the biocompatibility of the modified valvular surface. The adhesion and geometric deformation of platelets were demonstrated by scanning electron microscopy. The quantitative assay of platelet activation was determined by measuring the production of soluble P-selectin. Moreover, the leukocytes' adhesion, erythrocyte hemolysis, and whole blood clotting time studies were performed to gain information on the hemocompatibility of this biomaterial. Human-blood-derived endothelial progenitor cells (EPCs) were cultured and the adhesion and growth of EPCs on the surface-modified PDAV were assessed. The results showed that heparin–chitosan multilayer film could be coated on the decellularized valvular scaffolds, and improved their hemocompatibility with respect to a substantial reduction of platelet adhesion and activation. The modified valve also significantly reduced leukocytes adhesion, erythrocyte hemolysis, and whole blood clotting time. Seeding with EPCs achieved a confluent monolayer on the surface of the decellularized matrix. The in vitro studies performed in this work suggest that it may be reasonable to use heparin–chitosan multilayer film as a means of surface modification to improve the blood compatibility of decellularized valvular scaffold.

1. Introduction

Heart valve disease remains a major medical problem throughout the world. Valve replacement is a standard treatment for heart valve disease. Despite the excellent long-term results, currently available heart valve prostheses have limitations which are mainly related to life-long anticoagulation of mechanical valves and the degeneration of biological prostheses [1]. Tissue engineering is an evolution which is related to various disciplines, including materials, chemistry and cell biology [2]. Based on the concept of tissue engineering, tissue-engineered heart valves (TEHVs) are constructed by seeding cells on a valvular scaffold, and may finally regenerate to a self-organ in vivo, holding promise for replacing the current valve substitutes [3].

Two categories of materials are used as the scaffold to construct TEHV, namely biomaterials and synthetic materials [4]. Among these, decellularized porcine aortic valve (DPAV) appears more attractive because of its natural anatomical geometry and rich source [5]. However, the results of clinical trials were catastrophic, with severe inflammation and fibrosis of the scaffold in vivo [6]. One of the reasons might be the thrombogenicity of xenogenic extracellular matrix, which causes platelet deposition and inflammatory responses. Recent experiments confirmed that DPAV can induce platelet adhesion and activation [7–9]. Seeding with endothelial cells can effectively abolish the platelet adhesion and activation; however, in vitro repopulation with these cells is limited by several issues, including the source of endothelial cells, the risk of contamination, time-consuming cell culture, and the retention of cells in the flow circumstance. Recent experiments with decellularized heart valves in sheep demonstrated that host endothelial cells are detectable after implantation [10]. The source of endothelial cells might be endothelial progenitor cells (EPCs), which circulate in peripheral blood [11]. Therefore, an antithrombotic and biocompatible covering may serve as a transitional surface to reduce the formation of thrombus before being repopulated by EPCs in vivo.

For the past two decades, polyelectrolyte multilayer film (PEM) has emerged as a new strategy of surface modification [12]. It is constructed by the alternate adsorption of oppositely charged

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