Modular polymer design to regulate phenotype and oxidative response of human coronary artery cells for potential stent coating applications

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1. Introduction

The physico-chemical and mechanical properties of biomaterials modulate the response of the cells and tissues with which they interact [1–4]. In particular, polymers can be designed to control cell activity and fate through structure–function relationships [4]. Copolymerization techniques provide a means for tuning polymer properties by incorporating subunits with different characteristics and varying their molar ratios, thereby controlling micro and macro structures [4]. By understanding the effect of each subunit on the resulting polymer properties, as well as the ability of each subunit to modulate a cellular response, polymer properties can be precisely optimized to control a specific biological function.

Implantation of a vascular stent is crucial to reduce human morbidity and mortality resulting from vascular disease-induced localized blood flow constriction [5]. Current stent technologies include bare metal stents, polymers, and drug eluting stents (e.g. bare metal stents with a surface coating of polymers and drugs), yet each of these technologies poses a specific set of issues that has prevented its dominance of the clinical market. For example, bare metal stents are non-biodegradable and have been shown to cause restenosis, certain types of polymer stents can produce by-products that stimulate an inflammatory response, and drug eluting stents promote late thrombosis resulting from delayed re-endothelialization [5,6]. Therefore, much attention has recently been paid to design instructive, bioactive, and biodegradable materials as a solution to the problems associated with classical treatments [7]. The ideal properties of a stent material include sufficient mechanical strength, moderate degradation kinetics, resorbable by-products, and regulation of cellular activities (i.e. proliferation and viability), each of which can be precisely controlled by understanding how the polymer chemistry affects the subsequent cellular response.

In order to design polymers for potential coronary stent coating applications, an insight into how these materials modulate the response of the cells with which they interact is of the utmost importance. The vasculature is primarily comprised of smooth muscle cells (SMC) and endothelial cells (EC). In general, healthy vascular SMC proliferate at a very low rate and assume a contractile phenotype that is characterized by smooth muscle myosin heavy chain (smMHC) expression, and a spindle-like morphology [8,9]. In contrast, unhealthy, “dedifferentiated” SMC assume a circular, cobble