Acta Biomaterialia 8 (2012) 2899–2910

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Design and characterization of sulfobetaine-containing terpolymer biomaterials

Daniel E. Heath, Stuart L. Cooper *

Department of Chemical and Biomolecular Engineering, Koffolt Labs, Room 125A, The Ohio State University, 140 W. 19th Avenue, Columbus, OH 43210, USA

ARTICLE INFO

Article history:
Received 12 September 2011
Received in revised form 29 March 2012
Accepted 31 March 2012
Available online 11 April 2012

Keywords:
Blood compatibility
Methacrylic terpolymer
Zwitterionic
Sulfobetaine methacrylate
Endothelial cells

ABSTRACT

A methacrylic terpolymer system with non-fouling interfacial properties was synthesized by the random copolymerization of hexyl methacrylate, methyl methacrylate and sulfobetaine methacrylate (a monomer bearing a zwitterionic pendant group). Polymers were synthesized from feeds containing 0–15 mol.% of the zwitterion-containing methacrylate. Proton nuclear magnetic resonance verified the incorporation of sulfobetaine methacrylate into the polymer structure. Water absorption studies illustrate that the hydrophilicity of the material increases with increasing zwitterion concentration. The biological properties of the polymer were probed by fibrinogen adsorption, human umbilical vein endothelial cell adhesion and growth, and platelet adhesion. Strong resistance to protein adsorption and cell and platelet attachment was observed on materials synthesized from 15 mol.% sulfobetaine methacrylate. Results were compared to the non-fouling behavior of a PEGylated terpolymer formulation and it was observed that the poly(ethylene glycol)-containing materials were slightly more effective at resisting human umbilical vein endothelial cell adhesion and growth over a 7 day incubation period, but the zwitterion-containing materials were equally effective at resisting fibrinogen adsorption and platelet adhesion. The zwitterion-containing materials were electrospun into three-dimensional random fiber scaffolds. Materials synthesized from 15 mol.% of the zwitterion-containing monomer retained their non-fouling character after fabrication into scaffolds.

1. Introduction

One of the primary questions in the field of biomaterials is how to create a blood-compatible interface. Active research has been undertaken in this area for 50 years, yet the answer is still elusive. For instance, recipients of a blood-contacting biomedical device still require the administration of anticoagulants, no successful small diameter grafts have been developed and devices such as extracorporeal membrane oxygenators cause blood damage [1,2]. Current research in our laboratory focuses on the generation of polymeric biomaterials which specifically bind endothelial progenitor cells (EPCs), adult stem cells found in circulation which have the capacity to differentiate into cells with endothelial phenotype yet still retain the high proliferation capacities and rates compared to mature endothelial cells [3–12]. We hypothesize that the adherent stem cells will divide, differentiate and endothelialize such a biomaterial resulting in a blood compatible interface. Specifically, we are interested in developing this material for small diameter vascular graft applications. Though many new biomaterials systems are designed to be biodegradable, our system, a methacrylic terpolymer is biostable because one could envision a biodegradable vascular graft affected by aneurysm and rupture as the polymer deteriorates [6].

A phage display library was screened to discover several polypeptide ligands which bind EPCs but not other commonly occurring blood cell types [10]. These ligands were covalently incorporated into a novel methacrylic terpolymer biomaterial which we refer to simply as "terpolymer". Increased adhesion of the EPCs was observed on one of these peptide-containing materials, but only in medium not containing serum, most likely due to the adsorption of dissolved proteins to the biomaterial surface which acted to bury the peptides and undermine the specificity of the material [11].

To help resist the adsorption of serum proteins, we modified the terpolymer system to create an interface with non-fouling properties. The first generation of non-fouling terpolymer was created by copolymerizing in a monomer which bears an oligo-ethylene oxide pendant group. Terpolymer polymerized from $\geqslant$15 mol.% of the oligo-ethylene oxide monomer showed robust non-fouling interfacial properties [12]. Although PEGylation is a powerful and commonly used technique for imparting non-fouling interfacial properties to a biomaterial, this technology does have limitations. Most notably, poly(ethylene glycol) (PEG) suffers from oxidative degradation in the presence of oxygen or transition metal ions such as Cu(II) and Fe(III) [13–15]. Since we propose to use this material

* Corresponding author. Tel.: +1 614 247 8015; fax: +1 614 247 8323.
E-mail address: Coopers@chbmeng.ohio-state.edu (S.L. Cooper).

1742-7061/$ - see front matter © 2012 Acta Materialia Inc. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.actbio.2012.03.052