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Incorporation of phosphate group modulates bone cell attachment and differentiation on oligo(polyethylene glycol) fumarate hydrogel

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ABSTRACT

In this work, we have investigated the development of a synthetic hydrogel that contains a negatively charged phosphate group for use as a substrate for bone cell attachment and differentiation in culture. The photoreactive, phosphate-containing molecule, bis(2-(methacryloyloxy)ethyl)phosphate (BP), was incorporated into oligo(polyethylene glycol) fumarate hydrogel and the mechanical, rheological and thermal properties of the resulting hydrogels were characterized. Our results showed changes in hydrogel compression and storage moduli with incorporation of BP. The modification also resulted in decreased crystallinity as recorded by differential scanning calorimetry. Our data revealed that incorporation of BP improved attachment and differentiation of human fetal osteoblast (hFOB) cells in a dose-dependent manner. A change in surface chemistry and mineralization of the phosphate-containing surfaces verified by scanning electron microscopy and energy dispersive X-ray analysis was found to be important for hFOB cell attachment and differentiation. We also demonstrated that phosphate-containing hydrogels support attachment and differentiation of primary bone marrow stromal cells. These findings suggest that BP-modified hydrogels are capable of sustaining attachment and differentiation of both bone marrow stromal cells and osteoblasts that are critical for bone regeneration.

1. Introduction

Creation of a functional polymer surface that mimics the bone extracellular matrix is necessary to direct biomineralization and stimulate cell adhesion, migration and proliferation [1,2]. Hydroxyapatite- and phosphate-containing coatings have been studied extensively to better integrate biomaterial implants with bone for applications such as hip replacement, dental implants and screws for fracture fixation [3,4]. These coatings provide a bone-like mineral matrix that stimulates the in vivo bone environment. More specifically, a bone-like mineral has been shown to be prerequisite to the attachment of osteoblasts and bonding of orthopedic implant materials to bone tissue (osteoconductivity) and may drive osteogenic differentiation of adult stem cells (osteoinductivity) [5]. Hydroxyapatite coatings adsorb many proteins and other macromolecules and lead to a biological layer that favors cell attachment and osteogenic differentiation [6]. However, there are disadvantages associated with the coating of minerals on the polymer surfaces, including poor adhesion and the lack of a structural relationship between the surface and mineral layer [7,8]. More recent studies have focused on chemically altering the polymer interface [9–11]. These approaches include post-processing of the polymer matrix to initiate mineral nucleation and/or creating mineralization nucleators with covalent linkages within the polymer network.

Polyethylene glycol (PEG)-based hydrogels have been extensively studied for their use in tissue engineering and regenerative medicine applications [12–14]. The drawback of PEG-based hydrogels is a low cell attachment rate as a result of the formation of a hydrated surface layer that inhibits adsorption of adhesion proteins such as fibronectin. Investigators have applied a variety of techniques to improve cell adhesion on PEG-based hydrogels. This includes incorporation of adhesion peptides such as arginine-glycine-aspartic acid (RGD)-peptide [15–18] and electrical charge [19–21]. Oligo(polyethylene glycol) fumarate (OPF) is an injectable and biodegradable PEG-based hydrogel previously used in our group for cartilage tissue engineering and nerve regeneration [19,22]. We have reported that the physical and chemical properties of OPF hydrogels can be modified by incorporation of a positively

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