Material-driven differentiation of induced pluripotent stem cells in neuron growth factor-grafted poly(ε-caprolactone)-poly(β-hydroxybutyrate) scaffolds

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The potential of constructs comprising induced pluripotent stem (iPS) cells and biopolymers can be high for neurological surgery practice, if the systematic activity of neuronal regeneration is clarified. This study shows a guided differentiation of iPS cells toward neurons in neuron growth factor (NGF)-grafted poly(ε-caprolactone) (PCL)-poly(β-hydroxybutyrate) (PHB) scaffolds. The porosity of PCL-PHB scaffolds enhanced with increasing the concentration of salt particles (porogen) and the weight percentage of PCL. An increase in the graft concentration of NGF elevated the atomic ratios of N/C and O/C on the surface of NGF-grafted PCL-PHB scaffolds. In addition, incorporating heparin and NGF promoted the adhesion and viability of iPS cells in constructs. When the weight percentage of PCL increased, the viability of iPS cells reduced; however, more PCL in constructs benefited the adhesion of iPS cells. Under the influence of heparin and NGF, a high weight percentage of PCL and a long inductive period improved iPS cells to differentiate into neuron-like cells carrying βIII tubulin and inhibited other differentiation(s). The material-driven differentiation in NGF-grafted PCL-PHB constructs can be promising in guiding iPS cells to produce neurons for nerve tissue engineering.

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1. Introduction

Cell transplantation therapy is an emerging biomedical method for regenerating neurons in injured nervous system [1,2]. For example, infiltration of bone narrow stromal cells could repair a traumatic spinal cord with the cells attaching onto spinal surface and invading the lesion, yielding a reduced cavity volume and raised blood–brain barrier locomotor scores (improved behavioral function) [3]. In addition, stem cell implantation could activate neurosphere cells, stimulate axonal growth, and retrieve the capability for signal transmission among neural fibers in vertebrates [4,5]. However, a proper manipulation of stem cells for designated and/or preferred biological characteristics is a thorny problem. In neural tissue engineering, a cell culture using polymeric biomaterials was regarded as a feasible approach to the control over proliferation, differentiation, and migration of stem cells [6–9].

Various biopolymers, such as poly(lactide-co-glycolide), alginate, chitosan, gelatin, and poly(β-hydroxybutyrate) (PHB), have been employed to meliorate neuronal survivals and bridge wounded spinal zones [10–14]. Poly(ε-caprolactone) (PCL) also exhibited an efficient regulation in differentiating neural stem cells via a specific lineage pathway [15]. Moreover, hydrogel scaffolds composed of dextran with macroporous structure were used for enhancing cell penetration, cell adhesion, and neurite outgrowth [16]. In addition to polymers, growth factors can be important to the induction of stem cell differentiation. In fact, insulin-like growth factor I, epithelial growth factor, platelet-derived growth factor, epidermal growth factor, and hepatocyte growth factor displayed critical impacts on the differentiation of human adipose tissue-derived multipotent stem cells, human mesenchymal stem cells, embryonic stem (ES) cells, and putative hepatic stem cells [17–20]. Furthermore, basic fibroblast growth factor and neuron growth factor (NGF) have been shown to play an important role in inducing differentiation of stem cells toward neurons [21,22].

The aim of this study is to unveil the differentiation of induced pluripotent stem (iPS) cells in NGF-grafted PCL-PHB scaffolds for neuronal regeneration. iPS cells are reprogrammed cells bearing the differentiation ability similar to ES cells [23]. In a recent scientific evaluation, iPS cells have been demonstrated to evolve into electrophysiologically functional neurons, astrocytes, and oligodendrocytes by neural induction [24]. Therefore, iPS cells can be a promising cell source to reconstruct nervous system. However, little is known about their traits after contacts with biomaterials, leaving the particular identity of iPS cell-polymer construct...