The modulation of biodistribution of stem cells by anchoring lipid-conjugated heparin on the cell surface

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The modulation of biodistribution of stem cells by anchoring lipid-conjugated heparin on the cell surface

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Abstract

Heparin is a bioactive glycosaminoglycan that can interact with various extracellular matrix (ECM) proteins and growth factors. Lipid-conjugated heparin was synthesized, and was used to coat adipose-derived stem cells (ADSCs) by physical insertion on the cell membrane. Coating of lipid-conjugated heparin with two lipid moieties on ADSCs was stable for 24 hr *in vitro*. Biodistribution of heparin-coated ADSCs upon intravenous injection in mice was analyzed by In-Vivo Imaging System (IVIS), and showed enhanced accumulation in the liver and spleen while reduced entrapment in the lung. Thus, the coating of ADSCs with lipid-conjugated heparin could significantly modulate the biodistribution of cells.

Keyword: lipid-conjugated heparin, cell surface engineering, biodistribution, stem cell.

1. Introduction

Cell therapy is one of the ideal therapeutic modalities that can provide a fundamental cure by reconstructing damaged tissues and their functions. Cell therapy has been applied to many diseases including diabetes, cirrhosis, chronic liver failure, muscular dystrophy, myocardial infarction, and neurological disorders, which may not be cured by the currently available chemical or protein drugs [1]. Especially, stem cells including induced pluripotent stem cells (iPSCs) are regarded as the ultimate source of cell therapy due to their unique properties such as autologous source, self-renewal, homing, and differentiation ability. Moreover, several cases of stem cell based products are commercialized and available in the market for the treatment of myocardial infarction, damaged cartilage, anal fistula in Crohn's disease, and amyotrophic lateral sclerosis [2].

Expansion of stem cells *in vitro* is inevitable to get enough cells for cell therapy. Natural homing ability of stem cell is reduced during cell culture *in vitro* [3]. In addition, increasing the amount of cells in systemic treatment has a limitation for increasing therapeutic cells at target sites, because the entrapment of injected cells in the lung also increases by increasing the number of injected cells [3]. Thus, increasing the affinity of injected cells to target sites is desired to provide the enhanced accumulation of injected cells at the target sites. Cell surface