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Adhesion and differentiation of adipose-derived stem cells on a substrate with immobilized fibroblast growth factor

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ABSTRACT

Control of cell–matrix interactions plays a role in the regulation of stem cell function. In this study basic fibroblast growth factor (bFGF) linked to maltose-binding protein (MBP) was designed as a matrix for cell adhesion. MBP–FGF was immobilized on polystyrene (PS) surfaces by spontaneous adsorption. The amount of MBP–bFGF immobilized on the PS surface increased with increasing protein concentration, being 158 ng cm^{-2} at 10 μg ml^{-1} protein. Human adipose-derived stem cell (hASC) adhesion to MBP–bFGF immobilized on a PS surface (PS–MBP–bFGF) was inhibited by heparin. Integrin signaling and cell spreading of hASC on PS–MBP–bFGF were down-regulated compared with those on fibronectin-coated surfaces or tissue culture polystyrene (TCP). hASC differentiated into adipocytes, which stained positive for lipid vacuoles with Oil Red, more readily on PS–MBP–bFGF than on TCP. In contrast, hASC hardly differentiated into osteoblast on PS–MBP–bFGF or on TCP. These results suggest that the mechanism of hASC adhesion to MBP–bFGF immobilized on a PS substrate is mediated by a specific interaction between bFGF and heparin, and that the adhesion mechanism might provide an insight into the design of biomaterials to control the fate of stem cells.

1. Introduction

Mesenchymal stem cells (MSC) are found in the stromal–vascular fraction (SVF), which can be centrifugally separated from homogenized adipose tissue, as well as bone marrow and umbilical cord blood. A population of adherent MSC obtained from the SVF is termed adipose-derived stem cells (ASC). Human adipose-derived stem cells (hASC) are regarded as an attractive cell source in regenerative medicine, including cell therapies and tissue engineering, as adipose tissue is available in much larger quantities than cord blood or bone marrow. hASC are isolated from adipose tissue by liposuction and have been shown to differentiate along a variety of lineages, such as osteoblasts, adipocytes, chondrocytes, and endothelial cells [1,2].

Cell adhesion to the extracellular matrix (ECM) is critical in determining cellular fates, such as proliferation, migration, and differentiation, in the living body or culture environment [3]. Of interest in stem cell and tissue engineering research, studies involving cellular adhesion to an artificial ECM artificial ECM have recently increased. For example, ex vivo expansion of bone marrow-derived mesenchymal stem cells on a denatured collagen type I matrix resulted in the retention of adipogenic differentiation potential [4]. Significant progress has been made in the use of naturally derived ECM components or modified ECM molecules as cell adhesion matrices. Synthetic biomimetic materials have been designed as artificial ECM to stimulate cell adhesion and particular cellular functions. The resulting field has been termed "matrix engineering" [5]. Specifically, Arg–Gly–Asp (RGD), as well as many other oligopeptides that bind to cell surface integrins, have been incorporated into biomaterials to control cell adhesion, cell morphology, and other specific functions [6,7]. In other strategies non-adhesive bioactive polypeptides, such as growth factors and cytokines, and cell-recognizing carbohydrates have been fused with materials in an effort to generate artificial ECM to enhance selective interactions between the materials and cells [8–11].

Classically proteins have been immobilized on surfaces via physico-chemical or chemical interactions between the protein and the surface [12–14]. However, directly immobilizing a protein to a surface can result in partial or complete loss of protein activity due to the random orientation and structural deformation [15]. In an effort to avoid improper folding of proteins linkers have been employed in the form of chimera proteins to immobilize growth factors on surfaces. For example, several investigators have used an IgG Fc-containing vector to design Fc-linked fusion proteins, because the hydrophobic Fc domain can be immobilized on

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