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Nanopatterned polymer substrates promote endothelial proliferation by initiation of β-catenin transcriptional signaling

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ABSTRACT

Control of endothelial phenotype involves a variety of signaling pathways and transcriptional regulators, including the junctional protein β-catenin. This multifunctional signaling molecule is part of adhesion contacts in the endothelium and is able to translocate into the nucleus to activate genetic programs and control proliferation and the fate of the cells. We investigated the influence of laser-generated nanopatterns on polymeric cell culture substrates on endothelial tissue architecture, proliferation and β-catenin signaling. For our experiments human microvascular endothelial cells or $CD34^+$ endothelial progenitor cells, isolated from human adipose tissue, were cultured on polyethylene terephthalate (PET) substrates with oriented nanostructures with lateral periodicities of 1.5 μm and 300 nm, respectively. The surface topography and chemistry of the PET substrates were characterized by electron microscopy, atomic force microscopy, water contact angle measurement and X-ray photoelectron spectroscopy. Analysis of cell phenotype markers as well as β-catenin signaling revealed that short-term culture of endothelial cells on nanostructured substrates generates a proliferative cell phenotype associated with nuclear accumulation of β-catenin and activation of specific β-catenin target genes. The effects of the nanostructures were not directly correlated with nanostructure-induced alignment of cells and were also clearly distinguishable from the effects of altered PET surface chemistry due to photomodification. In summary, we present a novel mechanism of surface topology-dependent control of transcriptional programs in mature endothelium and endothelial progenitor cells.

1. Introduction

Cell adhesion to and interaction with polymer surfaces has been recognized as a determinant of tissue architecture and, consequently, of cell fate [1,2]. The potential impact of certain surface topologies on the proliferation and differentiation of adherent cells is of great interest for applications in medicine and biotechnology. Novel medical and biological technologies such as tissue engineering and cell biochips require control over interactions between cells as well as cells and substrate to allow reasonable cell expansion and functionality.

In classical tissue culture polymer substrates substitute for the extracellular matrix and affect cell behavior via surface chemistry [3–5]. Numerous previous studies have focused on modifying the surface chemistry to improve the biocompatibility of polymers, enhance cell adhesion to the substrate and promote proliferation [6–8]. Adhesion and proliferation can be substantially enhanced by choosing suitable substrates, and it has been shown that the substrate also has an impact on cell differentiation and gene expression [9–11]. Substrate modification can be achieved by exposure of the polymer surface to various types of radiation, including plasmas [12], γ-rays [13] and UV photons [14,15]. The enhanced biocompatibility of the modified polymer surfaces is based on the incorporation of new chemical groups into the surface and the

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