Understanding the cell behavior on nano-/micro-patterned surfaces

Aim: This article reports on studies conducted in the same laboratory on interactions between patterned substrates with different pattern dimensions and chemistries, and various types of cells. **Materials & methods:** In order to compare the influence of various parameters, bone marrow stromal cells, retinal pigment epithelial cells, human corneal stromal cells (keratocytes), Saos-2 (human osteosarcoma cells), human microvascular endothelial cells and vascular smooth muscle cells were tested on surfaces with different physical patterns and chemical properties. **Results:** It was observed that cell type and surface topography are more influential than surface chemistry in determining the alignment tendency of a cell on a substrate surface. Low walls (several microns high) could not confine cells into the microgrooves of the films but alignment was still possible if the cells had a natural alignment property. **Conclusion:** This information is very useful in designing tissue engineering scaffolds and in the long-term success of implants.

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KEYWORDS: micropatterning ■ nanopatterning ■ surface modification ■ tissue engineering

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This study offers a compilation of some of the research carried out at the Biomaterials and Tissue Engineering Research Group (BIOMAT) at the Middle East Technical University (METU) over the last 10 years, to draw conclusions on the influence of various parameters on the behavior of a number of cells on micro- and nano-patterned polymeric surfaces.

The attachment, orientation, proliferation and differentiation of cells on nano- and micro-patterned surfaces are very important stages of tissue–material interactions and the success of the biomaterial to be used in the field of tissue engineering and regenerative medicine has to achieve optimum levels in each stage. It is reported that the extracellular matrix may influence the differentiated state of connective tissue cells through physical, as well as chemical effects [1]. It has been shown that under certain conditions, cartilage cells maintain their differentiated character and produce cartilage but when the cells are scarce on a surface and stay as a monolayer, they transform from a round to a flat shape, and start producing type I collagen-like osteoblasts instead of type II, which is an important signature of cartilage [2]. Thus the cells become fibroblastic. When these cells are grown in a dish of agar they revert back to cartilage phenotype indicating that the phenotype changes as a result of cell-to-cell contact as well as with contact with the microenvironment. Since most cell types, especially those of the connective tissue, secrete their own extracellular matrix (ECM), they ensure their own stability and their neighbors' phenotype. In addition it is known that animal cells will not divide unless they are anchored to a surface. The ability of a cell to divide is related with the ability to spread on a surface. Thus, adhesion and spreading are critical issues for the success of an implant.

Over the last decade, explorations into the mechanisms and results of cell-surface interaction experiments have resulted in new methods for mediating cell differentiation [3–5] and controlling tissue orientation [6,7]. Although there are a number of reviews on the adherence of cells to surfaces designed in the form of micropatterns [8,9], a thorough comparison of a limited number of cell types on a limited number of micro-patterned surfaces should prove to be very valuable because the variables are in manageable numbers. In order to understand the specific nature of the cell–surface interactions and to draw conclusions from our results it is necessary to understand the basics of a how a cell interacts with its surroundings.

It is vital to understand the shape and the internal structure of a cell in order to fully appreciate the mechanisms that are involved in the interactions with other cells or substrates. The main structural support of the cell is provided by the cytoskeleton, which is made up of a network

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