

NANOFIBER MATRIX BASED MICROCHIP FOR HUMAN MESENCHYMAL STEM CELL CULTURE

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ABSTRACT

Integrated biomimetic systems with nanofiber polymer networks and microfluidic chips were fabricated and cellular behaviors were observed by changing surface characteristics of nanofiber matrices and flow rates of microchannels. Human MSCs were seeded on the nanofiber matrices and a morphological investigation with actin filament staining and SEM was performed. Integration of nanofiber matrices into the microchannels provides the useful tools for mimicking cellular microenvironments and elucidating basic questions of cell and ECM assembly and interactions.

KEYWORDS: Biomimetic system, Nanofiber, Human mesenchymal stem cell, Cell culture chip

INTRODUCTION

The three-dimensional electrospun nanofiber matrix integrated into PDMS-based microfluidic chip may offer the multifunctional benefits from a microfluidic channels providing effective transport and exchange of cell culture medium for development of three-dimensional scaffold, which help cell to grow and provide the effective diffusion of nutrients, metabolites, and growth factors[1]. A combination of microfluidic technology and electrospun nanofiber matrix can provide a biomimetic cell culture environment[2].

EXPERIMENTAL

The PDMS-based cell chip, in which AA-grafted electrospun nanofiber matrix were integrated as ECM, was fabricated and its 3-D schematics is shown in figure 1. The cell chip consisted of two layers (lower: microfluidic channel, upper: cell culture chamber) which were fabricated by the standard PDMS process[3] and the hydrophilic electrospun nanofiber matrix was incorporated between the layers. Here we have observed the diffusion and spreading of rhodamine B flowing beneath electrospun nanofiber matrix and the chip including un-treated group was prepared as control (figure 2 and 3). AA-grafted electrospun produced the potential to provide a better environment for human mesenchymal stem cell (hMSC) culture, Herein, the influence of surface modification on the hMSCs cultured on electrospun nanofiber matrix was investigated by morphological observation and quantitative measurement

of proliferation and viability of bone marrow derived stem cells.

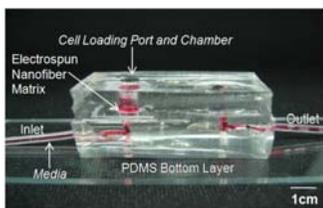


Figure 1. Schemes of cell chip integrated with electrospun nanofiber matrix

RESULTS AND DISCUSSION

Figure 2(a) shows that the experimental flow and saturation profiles agree reasonably well with figure 2(b) for surface diffusion control in the cell chip. The experiment diffusivities depended on the hydrophilicity of the electrospun nanofiber matrix in cell culture chip. The saturation time of fluorescence was very rapid as the hydrophilicity of surface and flow rate of microchannels increase. The AA-grafted electrospun nanofiber matrix and higher flow rate showed largest value. The reason may be due to the affinity between the dye molecules and the surface of nanofiber matrix by carboxylic group. These results may suggest that diffusion of media molecules is controllable by the integration of microfluidic chip and ECM-like nanofiber matrix.

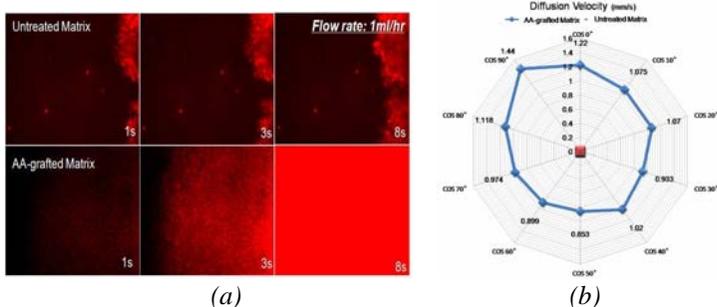


Figure 2. (a) The comparison of diffusion rates under the different flow conditions; the fluorescence images of diffused by rhodamine B solutions through the chip, (b) relative diffusivities of water on matrix in the static condition

Figure 3 (c) and (f), The cellular morphology on untreated nanofiber matrix appears to be mostly localized and nonproliferated along the seeding framework. Alternatively, cellular morphology on AA-grafted surface appeared to be widely spread with the cytoskeleton framework of the cell. SEM was used to observe the morphological differences more clearly. In the figure 3(a), (b), (d) and (e) illustrates SEM images of the hMSCs cultured on untreated and AA-grafted nanofiber matrix. And then, the surface area of the attached hMSCs was calculated in figure 3(g).

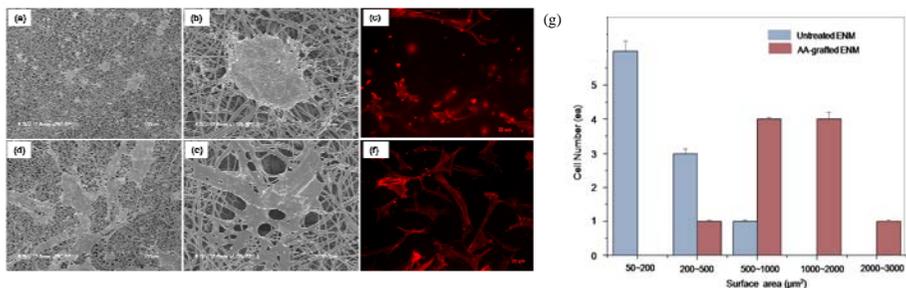


Figure 3. Cellular morphology of hMSCs cultured on the untreated (a–c) and AA-grafted (d–f) surfaces. Cellular morphology was observed with SEM (a, b, d, and e) and actin filaments (c and f), (g) measurement of hMSC spreading on the chips. Cell areas were measured from SEM images and cell area

CONCLUSIONS

The cellular study revealed the AA-grafted polyurethane nanofiber matrix integrated cell chip greatly promoted the hMSC adhesion, migration, and proliferation without affecting the desired bulk properties of the ECM-like structure embedded microchip. In the developed the hydrophilic nanofiber matrix integrated cell chip, the nutrients, growth factors or other materials can be supplied to the cells from all directions and a more biomimetic cell culture environment can be provided.

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