Biomaterials 33 (2012) 4988–4997

Contents lists available at SciVerse ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

Micropatterning of mammalian cells on inorganic-based nanosponges

Chung-Yao Yang [a], Tzu-Chun Liao [b], Hung-Hsun Shuai [a], Tang-Long Shen [c,d,***], J. Andrew Yeh [a,**], Chao-Min Cheng [a,*]

[a] Institute of Nanoengineering and MicroSystems, National Tsing Hua University, Hsinchu 30013, Taiwan
[b] Department of Power Mechanical Engineering, National Tsing Hua University, Hsinchu 30013, Taiwan
[c] Department of Plant Pathology and Microbiology, National Taiwan University, Taipei 10617, Taiwan
[d] Center for Biotechnology, National Taiwan University, Taipei 106, Taiwan

ARTICLE INFO

Article history:
Received 8 March 2012
Accepted 21 March 2012
Available online 6 April 2012

Keywords:
Mammalian cell micropatterning
Nanosponges
Nanofabrication
Cell fusion

ABSTRACT

Developing artificial scaffolding structures *in vitro* in order to mimic physiological-relevant situations *in vivo* is critical in many biological and medical arenas including bone and cartilage generation, biomaterials, small-scale biomedical devices, tissue engineering, as well as the development of nanofabrication methods. We focus on using simple physical principles (photolithography) and chemical techniques (liquid vapor deposition) to build non-cytotoxic scaffolds with a nanometer resolution through using silicon substrates as the backbone. This method merges an optics-based approach with chemical restructuring to modify the surface properties of an IC-compatible material, switching from hydrophilicity to hydrophobicity. Through this nanofabrication-based approach that we developed, hydrophobic oxidized silicon nanosponges were obtained. We then probed cellular responses—examining cytoskeletal and morphological changes in living cells through a combination of fluorescence microscopy and scanning electron microscopy—via culturing Chinese hamster ovary cells, HIG-82 fibroblasts and Madin–Darby canine kidney cells on these silicon nanosponges. This study has demonstrated the potential applications of using these silicon-based nanopatterns such as influencing cellular behaviors at desired locations with a micro-/nanometer level.

1. Introduction

This paper describes the micropatterning of mammalian cells onto inorganic-based surfaces––silicon surface in this study, a commonly used material in IC manufacturing industry––with nanometer-scale regular features made via nanofabrication. The ability to modulate cell–substrate interactions has provided a number of exciting insights in cell-relevant research including stem cell differentiation, cell survival, mechanotaxis, and biomaterials [1,2]. Cell–substrate interactions are closely determined by adhesive molecular events at the cell–material interface. These adhesive molecules (e.g., transmembrane proteins such as integrins or syndecan-4) influence various cellular behaviors including cell migration, growth, division, and differentiation [3,4]. Studies probing cell–substrate interactions at a nanometer scale can be summarized by two catalogues: (i) those that examine the influences of substrate stiffness and substrate topography on various cellular responses (physical cue) [5–9]; and (ii) those that investigate the immobilization of adhesion molecules on various substrates as the molecular scaffolding for cell adhesion (chemical cue) [10–13]. A number of reports have been published that delve into the influences of engineered surfaces with a variety of geometries at a micro-/nano-meter scale to include the examination of columns [14,15], sharp tips [16,17], pores [18,19], and dots [20,21], and their respective effects on a range of cellular responses at either a molecular level (e.g., cytoskeletal remodeling [6]) or a single-cell level (e.g., cell adhesions through integrin or syndecan-4, and cell proliferation and motility [22–24]). The purpose of this study is twofold: (i) establish and refine an IC-compatible nanofabrication method to create nanometer-scale regular features on silicon surfaces with surface characteristics of hydrophobicity, attempting to apply the current IC-based manufacturing process with the feature of mass production in biotechnology and, (ii) successfully micropattern a variety of mammalian cells (Chinese hamster ovary cells, HIG-82 fibroblasts, and Madin–Darby canine kidney

* Corresponding author. No. 101, Sec. 2, Kuang-Fu Rd., Hsinchu 30013, Taiwan. Tel.: +886 3 571 5131x80555; fax: +886 3 574 5454.
** Corresponding author. No. 101, Sec. 2, Kuang-Fu Rd., Hsinchu 30013, Taiwan. Tel.: +886 3 571 5131x42912; fax: +886 3 574 5454.
*** Corresponding author. No.1, Sec.4, Roosevelt Road, Taipei 10617, Taiwan. Tel.: +886 2 3366 4998; fax: +886 2 2363 6490.
E-mail addresses: shentl@ntu.edu.tw (T.-L. Shen), jayeh@mx.nthu.edu.tw (J.A. Yeh), chaomin@mx.nthu.edu.tw (C.-M. Cheng).

0142-9612/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.biomaterials.2012.03.071