Fabrication of tunable micropatterned substrates for cell patterning via microcontact printing of polydopamine with poly(ethylene imine)-grafted copolymers

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ABSTRACT

Cell patterning is an important tool for biomedical research. In this work, we modified a technique combining mussel-inspired surface chemistry and microcontact printing (μCP) to modulate surface chemistry for cell patterning. Polymerized dopamine on poly(dimethylsiloxane) stamps was transferred to several cell-unfavorable substrates via μCP. Since cells only attached to the polydopamine (PDA)-imprinted areas, cell patterns were formed on a variety of cell-unfavorable surfaces. The stability of PDA imprints was proved under several harsh conditions. The cell affinity of PDA was modulated by co-deposition with several poly(ethylene imine) (PEI)-based copolymers, such as PEI, PEI-g-PEG (poly(ethylene glycol)) and PEI-g-galactose. The imprints of PDA/PEI-g-PEG provide the formation of cell patterns on cell-favorable substrates. Neuronal PC12 cells were patterned via imprinting of PDA/PEI, while HepG2/C3A cells were arranged on the imprint of PDA/PEI-g-galactose. Finally, co-culture of HepG2/C3A cells and L929 fibroblasts was accomplished by our micropatterning approach. This study demonstrated this simple and economic technique provides a powerful tool for development of functional patterned substrates for cell patterning. This technique should profit the preparation of cell patterns to study fundamental cell biology and to apply to biomedical engineering such as cell-based biosensors, diagnostic devices and tissue engineering.

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1. Introduction

Cell patterning on artificial substrates can be applied to the fundamental study of cell biology, as well as biomedical engineering applications, such as cell-based biosensors, diagnostic devices and tissue engineering [1]. The basic principle of cell patterning is to create cell-favorable and -unfavorable regions on substrates to control the spatial arrangement of cells. A variety of microfabrication techniques have been applied to create surface chemical or topographical patterns in order to regulate cell attachment and functions, as reviewed previously [2,3]. The most commonly used microfabrication techniques include photolithography [4–6], microcontact printing (μCP) [7,8], microfluid patterning [9] and transfer lithography [10–12]. A strategy of transfer photolithography has recently been developed to generate surface patterns that has the advantage of persistently localizing cells in the pre-designed patterns, though at the cost of several fabrication procedures. In contrast, μCP is an easy, rapid and economic technique for cell patterning, though the cell patterns only persist for a relatively short time. This technique is based on contact transfer of the material of interest from a poly(dimethylsiloxane) (PDMS) stamp onto a surface only on the areas contacted by the stamp. A variety of molecules, such as alkanethiols [8], proteins [13], polymers [14] and nanoparticles [15], have been employed as the ink to create micropatterned surfaces via μCP. We suggest that an imprinting material that could adhere to a wide variety of substrates with adjustable cell affinity would have great advantages for patterning diverse cell types.

Recently, a technique based on the adhesive mechanism of marine mussels provides a simple and versatile tool for biomaterials surface modification [16]. Marine mussels bind tightly to the various surfaces on which they reside in an aqueous environment, a process which relies on the much repeated 3,4-dihydroxy-L-phenylalanine-lysine (DOPA-K) motif found in mussel adhesive proteins [17,18]. A dopamine molecule containing a catechol and an amine simulates the functional moieties of the DOPA-K motif. Dipping substrates in an alkaline dopamine solution (e.g. pH 8.5) creates a spontaneous coating of a thin adhesive film via the oxidative polymerization of the dopamine [16]. An attractive character of polydopamine (PDA) for surface modification is its strong adhesive bonding to a wide range of organic and inorganic materials [16]. Furthermore, a thin PDA film is capable of promoting protein