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Visible light controls cell adhesion on a photoswitchable biointerface

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ABSTRACT

Bioactive surfaces with specific interactions with cells have been greatly interested due to their potential applications in biosensors and tissue engineering. Herein, we fabricated a dopamine contained photoswitch molecule (compound **1**) which could form self-assembled monolayer (SAM) on substrates. The SAM showed a good photoswitch ability and manifested excellent fatigue resistance, which displayed its potential application as a biologically friendly surface coating. Contact angle analysis and cell experiments exhibited that the SAM surface was hydrophobic before irradiation which favored cell adhesion, while, it turned hydrophilic and induced cell unfouling or detachment after light irradiation. The uses of visible light stimulation (λ_{ex} = 530 nm) and the reversible regulation on cell adhesion and detachment should open up new avenues for bioacitve surfaces in biomedical applications.

1. Introduction

Research on the interactions between cell and materials is necessary for tissue engineering and basic cell biology. Among which, cell adhesion on materials plays key role that subsequent decides cell fate, such as proliferation, differentiation, migration and apoptosis [1,2]. Both chemical and physical properties on the surface of materials influence cell adhesion [3–6]. Learned from the extracellular matrix (ECM) characters that can continuously provide spatiotemporally changed chemical, physical and mechanical cues, various strategies have been used to engineer materials to present dynamic environments to direct cell adhesion and tissue functions [7–13]. Especially, photolithography technique has proven to be a powerful tool to modulate the chemical and physical properties on material surface because it allows for the remote control in high spatiotemporal resolutions [14–17]. In fact, light has been extensively used to pattern and control cell adhesion in various substrates.

Up to now, both irreversible and reversible photoresponsive moieties have been successfully used to control the physical or chemical properties on substrates, thereby control the cell adhesion or detachment [18–23]. For example, Zhu et al. reported to use a coumarin phototrigger to trigger the charge changes on a hydrogel surface, which regulated the electrostatic interaction with proteins and thus finally achieved protein guided cell adhesion and detachment upon light irradiation as desired [24]. Liu and Jiang et at. used photoswitchable spiropyran to reversibly control the hydrophobicity of a hydrogel surface to guide cell pattern, since cells prefer to adhering and spreading on hydrophobic surfaces[25,26]. Azobenzene photoswitches were also widely selected to regulate the presence of adhesive ligands on substrates, thus to get reversible control on cell adhesion [27–29]. Up to now, most of reported photoresponsive moieties are UV-sensitive that would somewhat limit its application due to the potential cytotoxicity of UV light to cells. Alternatively, visible light excitation has superiority in biocompatibility and penetration with cells or tissues. For example, Wang and co-workers recently reported a near-infrared responsive surface, on which the regulated wettability induced the control of cell adhesion [30].

Recently, Alaniz group designed a new class of visible light activated photochromes (DASA), it underwent conformation conversion from the hydrophobic triene to hydrophilic zwitterionic cyclopentenone when irradiated upon visible light (λ_{ex} > 520 nm), and subsequently recovered when kept in dark [31]. Given its excellent photoreversibility and the large polarity change, we are encouraged to introduce this photoswitch on material surface, and expect to control cell adhesion and detachment by visible light manipulation. Herein, as illustrated in Scheme 1, a bifunctional compound **1** containing a surface anchoring dopamine moiety and a visible light excitable photoswitch DASA was designed. We applied compound **1** on a glass or quartz substrate to form a self-assembly monolayer (SAM), the hydrophobic property of DASA was expected to facilitate cell adhesion, while the hydrophilic transformation

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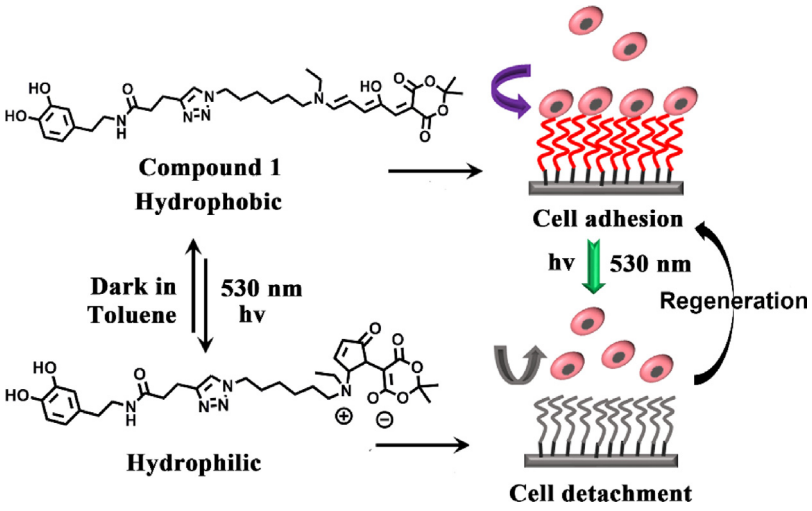

Scheme 1. Schematic illustration of photoswitching of compound **1** and controllable cell release of the SAM upon irradiation of visible light.

induced the unfouling or detachment of cells upon visible light irradiation. The use of reversible photoswitch provides not only the spatiotemporal control on cell adhesion but also the regeneration for the next cycles, and the use of visible light (λ_{ex} = 530 nm) improves the biocompatibility of the manipulation, especially for the processes with living cells. This visible light-triggered cell adhesion/detachment may afford smart surfaces with significant potential applications in tissue engineering and biosensors.

2. Experimental

2.1. Materials

All chemical reagents were purchased from commercial available sources such as Aldrich or Fisher and used without further purification. All air- or moisture-sensitive reactions were performed using oven-dried or flame-dried glassware under an inert atmosphere of dry argon. Dry dichloromethane (DCM) was distilled from calcium hydride; triethylamine (TEA) was redistilled and stored over KOH pellets prior to use. Deionized water was used to prepare all aqueous systems. The buffer used in all the experiments is 0.01 M PBS buffer (pH = 7.2).

2.2. Methods

Proton and carbon magnetic resonance spectra (^{1}H, ^{13}C NMR) were recorded on a Bruker Avance 500 (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm) downfield from the Me_4Si resonance which was used as the internal standard when recording ^{1}H NMR spectra. Mass spectra were recorded on a Micromass GCTTM and a Micromass LCTTM. Absorption spectra were recorded on a Lambda 950 UV–vis spectrometer. Contact angles (CA) were measured with an OCA20 contact angle system (Data Physics, Germany). Water drop volumes were 2 μL. X-ray photoelectron spectra (XPS) was measured with a Thermo Escalab250 Xi spectrophotometer. Confocal luminescence imaging was performed with an A1R Nikon confocal microscope with 10× or 4× objective lens.

2.3. Preparation of photoswitchable compound *1*

Compound 12,11 and 10 were prepared as reported previously [31].

The synthesis of compound 7. Compound 9 (2 g, 24.0 mmol) and 8 (3.5 g, 24.0 mmol) were added to 30 mL H_2O and the mixture was heated to 75 °C for 2 h. A yellow solid appeared during the process of the reaction. The mixture was filtrated and the solid was obtained

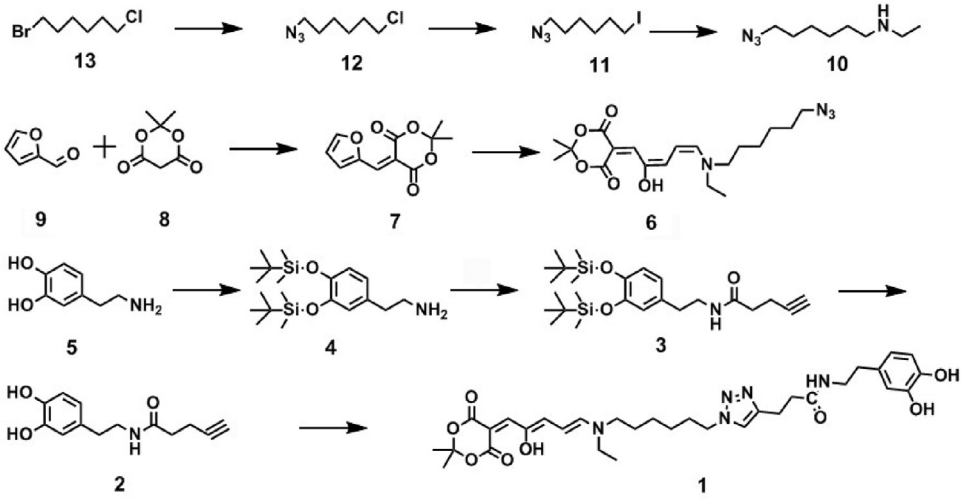

Fig. 1. The schematic synthesis of photoswitchable compound **1**.