Bio-Smart Surfaces Prepared by SET-LRP and Host-Guest Interaction

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Statement of Purpose: Stimuli-responsive surfaces or so-called "smart surfaces" which can undergo a dramatic change in physicochemical properties in response to specific environmental stimuli are good candidates for bio-applications.[1] So far, the most commonly used and best studied thermoresponsive polymer is poly(*N*-isopropylacrylamide) (PNIPAAm), because of its ability of controlling protein adsorption and cell adhesion at temperatures below or above the lower critical solution temperature (LCST). However, the protein adsorption based on hydrophobic interaction is hardly considered as selective immobilization, which will hinder its applications. Glycocalyx-mimicking glycopolymer brushes, with "cluster glycoside effect", have found their application of recognizing specific proteins and repelling non-specific proteins/cells.[2] Therefore, the introduction of glycopolymers to PNIPAAm surface can greatly enhance the selective protein adsorption. For preparing ligand-bearing copolymers, the post-modification of polymer backbone via host-guest interaction is a new versatile and robust methodology, with the ability to tune ligand valency, type, orientation and location, or even allowing the reversible binding.[3,4] Among the host-guest pairs, β-cyclodextrin (β-CD) and adamantane are strong pairs, and have been used as linkers in many applications. Here we synthesized poly(*N*-isopropylacrylamide-*co*-1-adamantan-1-ylmethyl acrylate) [poly(NIPAAm-*co*-Ada)] via surface-initiated single electron transfer living radical polymerization (SET-LRP), which further attached β-CD-(mannose)$_7$ onto the surface via host-guest interactions as shown in Figure 1A. The host-guest approach may provide possibility to build a series of functional smart surfaces just by changing ligands on the β-CD ring based on the same pre-surface of poly(NIPAAm-*co*-Ada).

Methods: The procedures reported in our previous work were followed in the pretreatment of silicon wafers for the immobilization of initiator.[5] Surface-initiated SET-LRP of NIPAAm and Ada copolymer was carried out in a glovebox purged with nitrogen, using 4:1 mixture of isopropanol and water as solvent and Me_6-TREN/CuCl as catalyst. The addition of H_2O was required as it serves to increase the polarity of the medium and initiate the disproportionation of Cu(I)Cl, driven by strong thermodynamics of crystallisation, thereby accelerating the polymerization rate. Static water contact angle measurement was used to conform the inclusion of β-CD-(mannose)$_7$.The radioiodine labeling method was used to investigate the specific adsorption of ConA and the nonspecific adsorption of HSA on poly(NIPAAm-*co*-Ada)/β-CD-(mannose)$_7$ surface.

Results: To take the copolymer surface with Ada feed ratio of 4.76% as an example, the LCST of poly(NIPAAm-*co*-Ada) was too low to measure; while after complexion with β-CD-(mannose)$_7$, the LCST shifted to 16.5 ^oC, and surface became more hydrophilic, indicating the successful inclusion of β-CD-(mannose)$_7$ onto the surface (Figure 1B). The protein adsorption on sugar modified PNIPAAm surface at 37 and 4 ^oC were compared. ^{125}I-ConA adsorption on sugar surface was 8.4 times of that on PNIPAAm surface at 37 ^oC, and the specific adsorption reduced 75 % at 4 ^oC (Figure 2A). Meanwhile, the nonspecific HSA adsorption on sugar surface was at a very low level, even lower than that on PNIPAAm surface at both tempratures (Figure 2B).

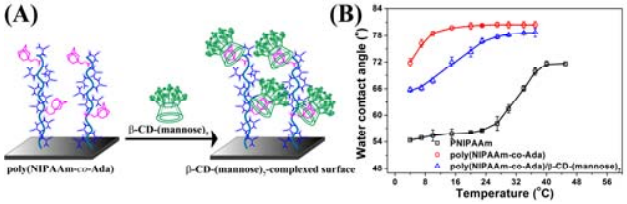

Figure 1. (A) Scheme of the inclusion of Si-poly(NIPAAm-*co*-Ada) with β-CD-(mannose)$_7$; (B) Wettability transition behaviors of surfaces with and without β-CD-(mannose)$_7$.

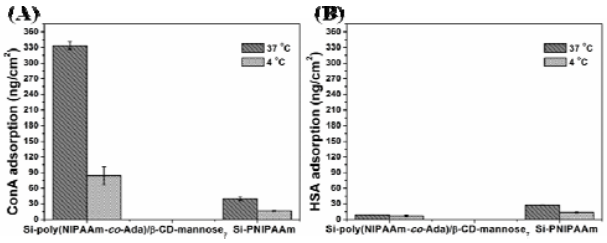

Figure 2. Protein adsorption on Si-poly(NIPAAm-*co*-Ada)/β-CD-(mannose)$_7$ and Si-PNIPAAm. (A)0.3 mg/mL ConA in PBS (10 mM, pH 7.4, containing 1 mM Ca^{2+} and 1 mM Mn^{2+}); (B) 0.5 mg/mL HSA in PBS at 37 and 4 ^oC for 3 h.

Conclusions: The NIPAAm and adamantane copolymer was successfully prepared on silicon surface for the first time by surface-initiated SET-LRP. β-CD-mannose$_7$ was then successfully introduced onto the copolymer surface. The thermoresponsive glycoplymer surface prepared by host-guest interaction has the ability of specifically recognizing ConA, thermoresponsively controlling its adsorption, and greatly reducing nonspecific protein adsorption.

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