Plaetelet Adhesion and Bacterial Adhesion on PEG-Modified Textured Biomaterial Surfaces

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Statement of Purpose: The long term use of synthetic polymeric biomaterials in blood-contacting devices is complicated by the potential for thromboembolic events and microbial infection. Topographical change and chemical modification have been the efficient strategies for controlling these biological responses. To our knowledge, strategies for surface modification have generally focused on either physical approach or chemical modification. This work seeks to control the biological responses on biomaterial surfaces through a combination of topographical change and chemical modification. The integration of chemical and physical modification techniques produces a unique environment on the biomaterial surface and greatly enhances the biocompatibility of materials, and may provide a new strategy and concept for improvement of biomaterials.

Methods: Poly(urethane urea) (PUU) biomaterial surfaces were first textured with ordered arrays of pillars using a soft lithography technique[1]. These textured PUU films were then reacted with hexamethylene diisocyanate (HMDI) in the presence of triethylamine as a catalyst to form PUU-NCO on surface, and finally polyethylene glycol (PEG) was grafted to PUU surface. Two submicron textured patterns with round pillars of diameter and separation of 400 and 400 nm, 500 and 500nm were used. Platelet adhesion and bacterial adhesion (*S. epidermidis* RP62A) were examined in a microwell plate under static condition in PBS or under 75% PPP (platelet poor plasma) solutions for 1 hr at 37°C. Platelets and bacteria adhered were fixed and labeled with appropriate fluorescence, and examined by optical fluorescence microscopy.

Results / Discussion:

Fabrication and characterization of PEG-textured PUU surfaces: PUU films were first physically textured with ordered arrays of pillars using a soft lithography two-stage replication molding technique, and then were grafted with PEG with a terminal –OH and molecular weight of 1500. The surfaces were characterized by SEM and AFM (Fig. 1). The fractions of total surface area covered by pillar tops are reduced to 27.5% and 24.5% of the nominal surface area for patterns 400/400 nm and 500/500 nm, respectively. After PEG modification, the pillars were found to be deformed (Fig. 1b), and the height of pattern is reduced from ~700nm to 350-400 nm. XPS analysis confirmed the surface chemistry grafted with PEG.

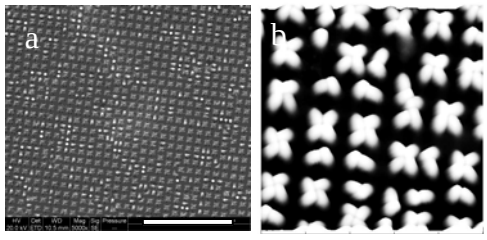

Fig. 1 Topographic images of PEG modified 500/500 nm textured PUU surface (a) SEM, bar = 20μm, and (b) AFM, image size: 10×10μm^2.

PEG-textured PUU surfaces inhibit platelet adhesion and activation: Compared to non-PEG modified PUU surfaces, both PEG modification and surface texturing reduced platelet adhesion and activation in PBS and PPP solutions, suggesting that chemical modification and topographical modification can significantly control platelet adhesion (Fig. 2). PEG modification on textured surfaces presented a further reduction in platelet adhesion with reduction rate of platelet adhesion on PEG-textured surfaces increasing from 71% to 86%. Results suggest combination of PEG modification and surface texturing may have a synergistic effect on reducing platelet adhesion.

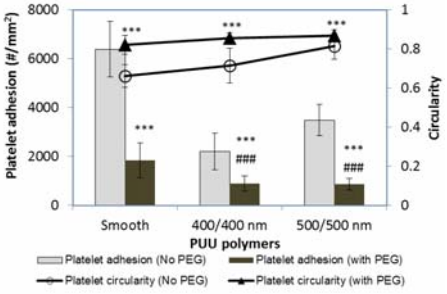

Fig. 2 Platelet adhesion and activation on PUU surfaces in PBS.

PEG-textured PUU surfaces reduce bacterial adhesion and biofilm formation: Significant reductions in bacterial adhesion were observed on all textured and PEG modified PUU surfaces compare to regular smooth PUU surface in PBS and 75% PPP solutions. Similar to platelet adhesion, the greatest inhibition of bacterial adhesion was found on PEG-textured surface with 500/500nm pattern. The reduction rate of bacterial adhesion on PEG-500/500 nm patterned surface reached 97% in PBS, higher than on PEG-smooth, and 500/500 nm textured surface, suggesting that a combination of PEG modification and surface texturing has a synergistic effect on inhibition of bacterial adhesion (Fig.3). Biofilm experiments carried out in a rotating disk system showed that biofilm formed on regular smooth PUU surface within 2 days, however, no biofilm was observed on PEG-textured PUU surfaces even after 8 days, and only a small number of individual bacterial cells seen.

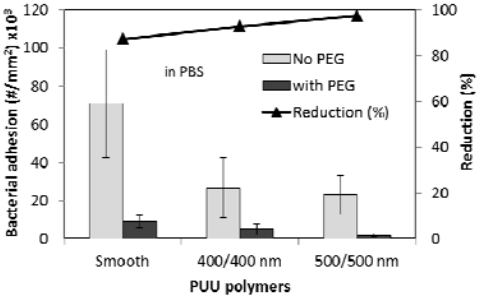

Fig. 3 Bacterial adhesion on PUU surfaces in PBS. Reduction in adhesion is shown as marker+line.

Conclusion:

Submicron textured biomaterial surfaces grafted with PEG dramatically increase the efficiency in inhibiting platelet adhesion/ activation, and bacterial adhesion/biofilm due to the synergistic effect of physical topography and grafted PEG. The combination of chemical and physical modifications improves the efficiency in treating microbial infection and blood coagulation, and thereby enhances the hemocompatibility of biomaterials.

Reference:

1. Xu and Siedlecki, *Acta Biomateriialia*, 2012, 8, 72.