Supporting Information for Bacterium-Mimicking Nanoparticle Surface Functionalization with Targeting Motifs

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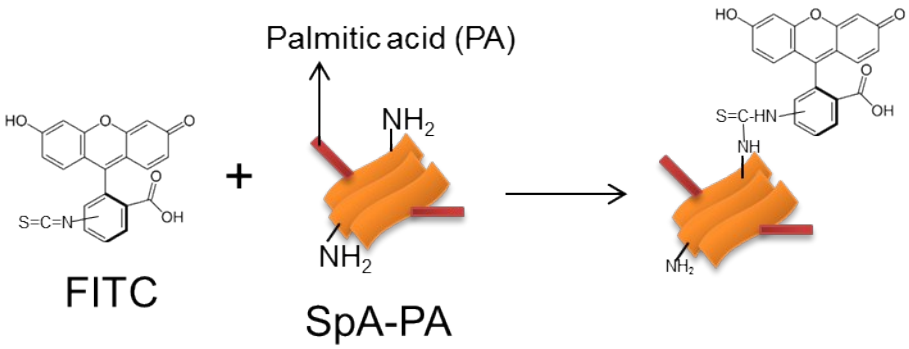
Materials were purchased from Sigma-Aldrich (USA) and used without further purification unless otherwise specified.

SpA-PA labeled with fluorescein (Scheme S1). First, 400 μl SpA-PA was suspended in PBS at 2.73 mg ml^{-1}, and 12.96 μl FITC solution (10 mg ml^{-1} in dimethyl sulfoxide (DMSO)) was added into the SpA-PA suspension. The mixture was incubated at room

temperature in the dark for 40 min with stirring. Afterward, the solution was dialyzed in a dialysis cassette (Thermo Scientific, MWCO 3000) against PBS at 4 ° C for two days. Finally, the product was concentrated with a centrifugal filter (Amicon® Ultra 3K device, Millipore Corporation) and re-suspended in PBS containing 0.1 wt% NaN_3 at a concentration of 1.26 mg ml^{-1}.



Scheme S1. Schematic description of chemical conjugation of 5(6)-fluorescein isothiocyanate (FITC) to SpA-PA.

Antibody labeled with rhodamine. Next, 150 µL anti-VCAM-1 solution (CD106) at 500 µg ml^{-1} PBS was mixed with 30.15 µL rhodamine B isothiocyanate (RITC) at 5 mg ml^{-1} DMSO, and the mixture was incubated at room temperature in the dark for 2 hours. The excess free rhodamine was removed by dialyzing the raw product against PBS at 4 °C for 2 days, and then the sample was concentrated with a centrifugal filter (Amicon® Ultra 3K device, Millipore Corporation). The concentrate was re-suspended with PBS equal to the antibody concentration at 500 µg ml^{-1}.

Details about the surface modification of SPR chip. A gold sensor chip (GE Healthcare) was modified to present a 11-mercaptoundecanoic acid (MUA) monolayer by

immersing the chip in 1 mM MUA solution overnight to form a self-assembled monolayer. The carboxylic groups of the MUA monolayer were then activated by injecting the mixture of 0.4 M 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC, Thermo Scientific) and 0.1 M *N*-hydroxysuccinimide (NHS) (1:1, v/v) into the flow cell in a Biacore 3000 (GE Healthcare) for five minutes at 5 μl min^{-1}. After activation, recombinant human VCAM-1 (R&D Systems) or recombinant human integrin $\alpha_v\beta_3$ (R&D Systems) was chemically linked to the MUA layer by flowing the solution at 2 μl min^{-1} until the response unit (RU) was saturated. The remaining NHS-ester groups on the MUA surface were blocked by injecting 1.0 M ethanolamine into the flow cell at 5 μl min^{-1}.

PHEA-*g*-C_{18} micelles labeled with rhodamine. Next, 1 ml PHEA-*g*-C_{18} dissolved in 10 mg ml^{-1} DMSO was mixed with 0.135 ml RITC dissolved in 10 mg ml^{-1} DMSO. The mixture was incubated at room temperature in the dark for 24 hours. The excess RITC was removed by dialyzing the raw product against water for 3 days. Then, the sample was lyophilized to get a powder product.

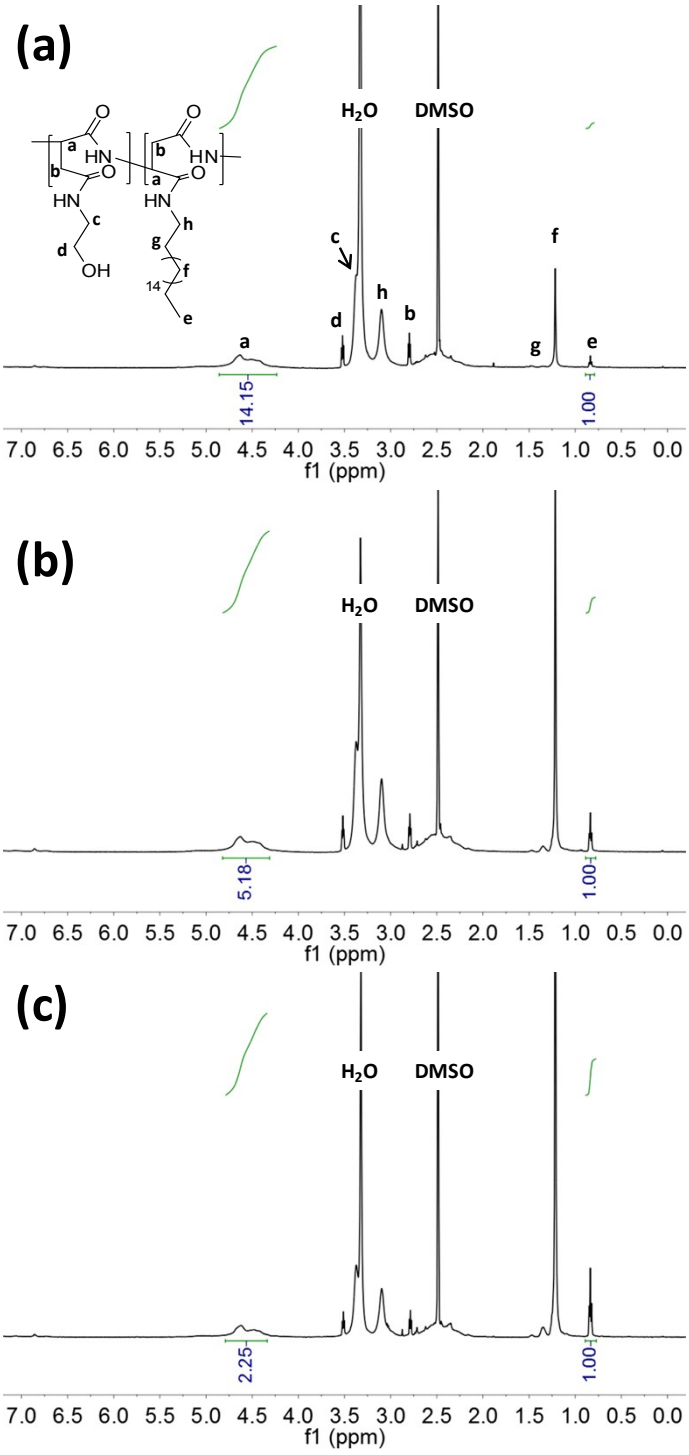


Fig. S1 ^{1}H NMR spectra of PHEA-g-C_{18} polymers with DS_{C18} of 2.4 mol % **(a)**, DS_{C18} of 6.4 mol % **(b)**, and DS_{C18} of 14.8 mol % **(c)** in DMSO-d_6.

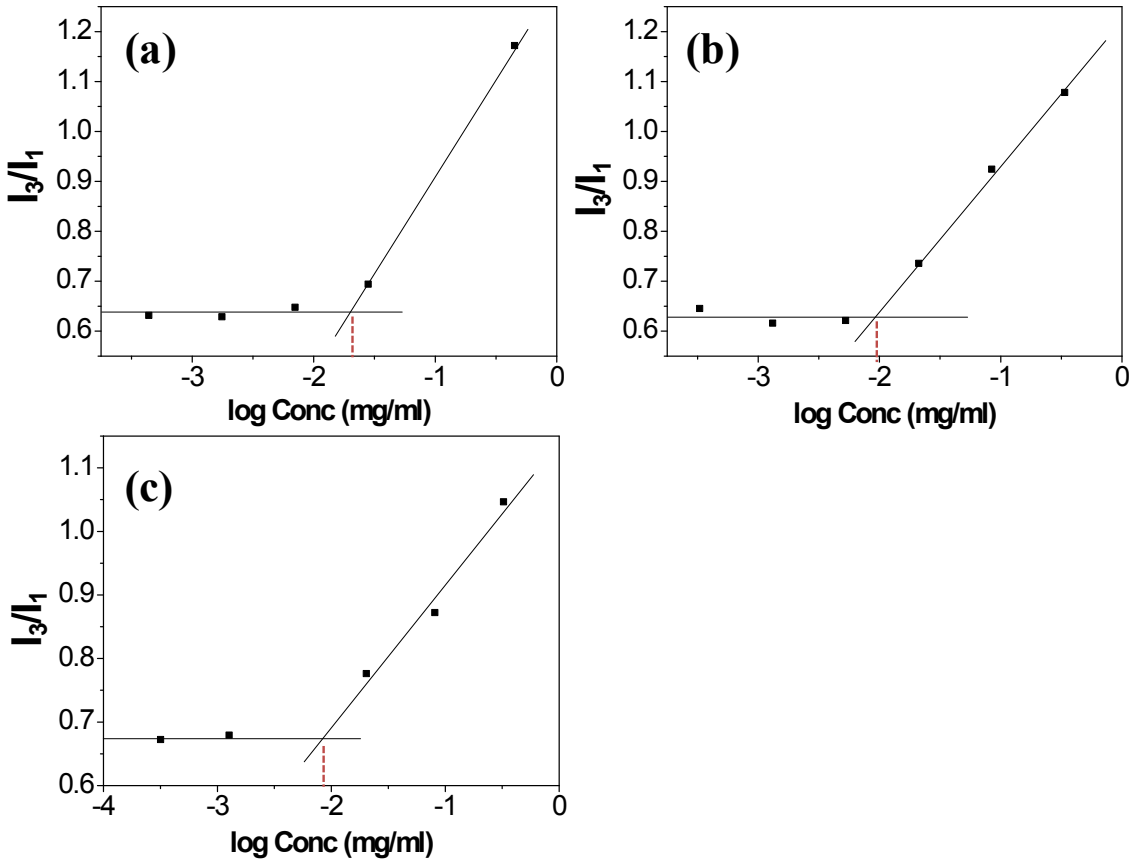


Fig. S2 Fluorescent analysis to determine the critical micelle concentration (CMC) of PHEA-*g*-C_{18} polymers with DS_{C18} of 2.4 mol % **(a)**, DS_{C18} of 6.4 mol % **(b)**, and DS_{C18} of 14.8 mol % **(c)** in PBS. First, pyrene molecules were incorporated into the mixture of PHEA-g-C_{18} and water. Then, the CMC value was determined by the onset of increasing I_3/I_1, where I_3 and I_1 represent the pyrene emission intensity measured at the wavelength of 385 and 373 nm, respectively.

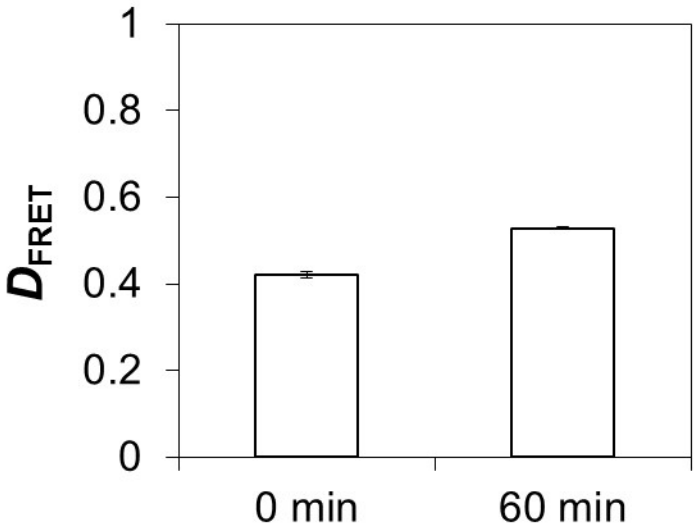


Fig. S3 The degree of FRET (D_{FRET}) for the mixture of antibodies with SpA-PA-coupled DS-14.8 micelles right after mixing (0 min) and after incubation in serum-supplemented media at 37 °C for 60 min. The serum concentration in the media was 80 wt%. The scheme of FRET experiment was displayed in **Fig 3a**.

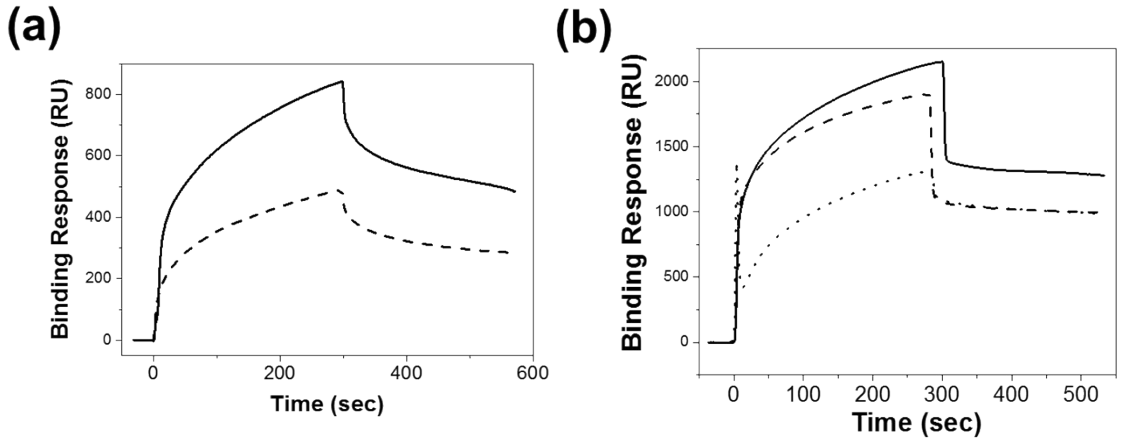


Fig S4 (a) SPR sensorgrams for binding of SpA-PA-coupled DS-14.8 micelles coated by antibodies (solid line) and DS-14.8 mcelles simply mixed with antibodies (dashed line) with the substrate. The substrate was conjugated with VCAM-1 and antibodies to VCAM-1 (i.e., anti-VCAM-1) was used. **(b)** SPR sensorgrams for the binding of SpA-PA-coupled DS-14.8 micelles coated by anti-VCAM-1 (solid line), DS-14.8 micelles chemically linked with anti-VCAM-1 (dashed line), and free anti-VCAM-1 (dotted line) with the targeted substrate. The substrate was conjugated with VCAM-1.

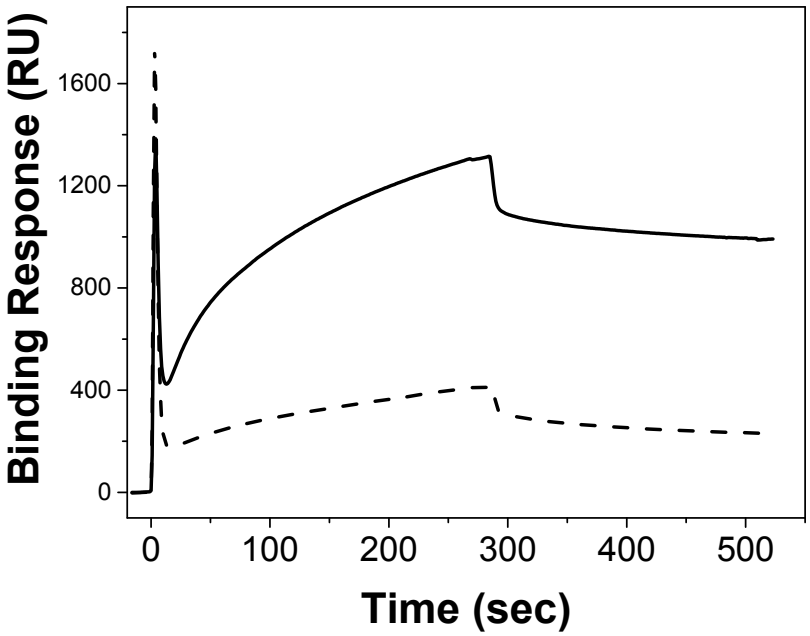


Fig. S5 SPR sensorgrams for bindings of the anti-VCAM-1 (solid line) and anti-integrin α_v (dashed line) with substrates conjugated with VCAM-1 and integrin $\alpha_v\beta_3$, respectively.

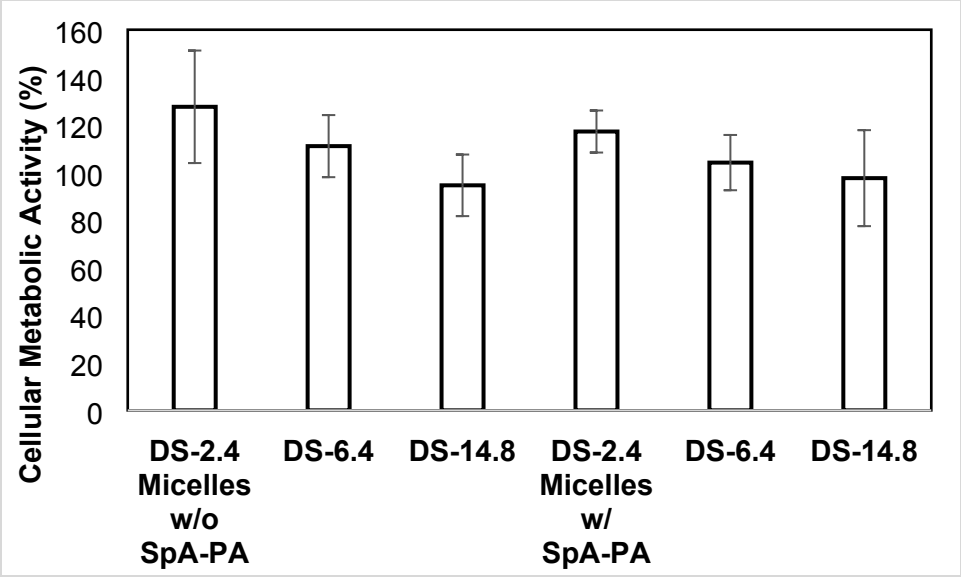


Fig. S6 Cellular metabolic activity of C166 mouse endothelial cells analyzed with the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, ATCC) reagent. The cellular metabolic activity level was calculated by normalizing the absorbance at 570 nm for each condition to the absorbance at 570 nm for cells never exposed to micelles.