Supporting Information

Detail on synthesis and characterization of PHEA-g-C_{18}

Polysuccinimide (PSI, Mw 19,000 g/mol, PDI 1.5) was synthesized through the acid-catalyzed polycondensation process of $_{L}$-aspartic acid (Sigma-Aldrich) described previously as the starting chemical for PHEA-g-C_{18} synthesis. The $_{L}$-aspartic acid was dissolved in dried sulfolane with existence of 85% phosphoric acid and reacted at 170 °C for 7 hours, refluxed under dry nitrogen atmosphere with the Dean-Stark trap setup. The precipitates from the reaction was filtered out and washed with methanol and deionized water in sequence until the suspension was neutral. Then, the product was dialyzed (Fisher Scientific, MWCO 3,500) against deionized water for two days and freeze-dried (Labconco, FreeZone 6) to obtain powder.

PSI was aminolyzed with octadecylamine (ODA) (Sigma-Aldrich) and ethanolamine (Sigma-Aldrich) sequentially into poly(2-hydroxyethyl aspartamide) grafted with octadecyl chains (PHEA-g-C_{18}). PSI was dissolved in dimethylformamide (DMF) at concentration of 1.5 mmol PSI per 5 mL DMF. Then, PSI was reacted with the designed amount of ODA at 70 °C for 24 hours. After the mixture was cooled down, the calculated volume of ethanolamine was added and further reacted for 6 hours at room temperature. The final product was collected and dialyzed (Fisher Scientific, MWCO 3,500) against deionized water for 2 days followed by freeze-drying (Labconco, FreeZone 6) to obtain the dry powder.

The structure of PHEA-g-C_{18} was characterized by ^{1}H NMR spectra, from which the degree of substitution of octadecyl chains (DS_{C18}) on the PHEA backbone was calculated by using [Eq. (1)]:

$$DS_{C_{18}} = \frac{Integration\ of\ spectra\ from\ 0.80\ to\ 0.86\ /3}{Integration\ of\ spectra\ from\ 4.36\ to\ 4.70} \quad \text{Eq. (1)}$$

where the integration of spectra from 0.80 ppm to 0.86 ppm represents the methyl group on octadecyl chain containing three protons; the integration of spectra from 4.36 ppm to 4.7 ppm represents the proton on the polymer backbone with one per polymer unit.

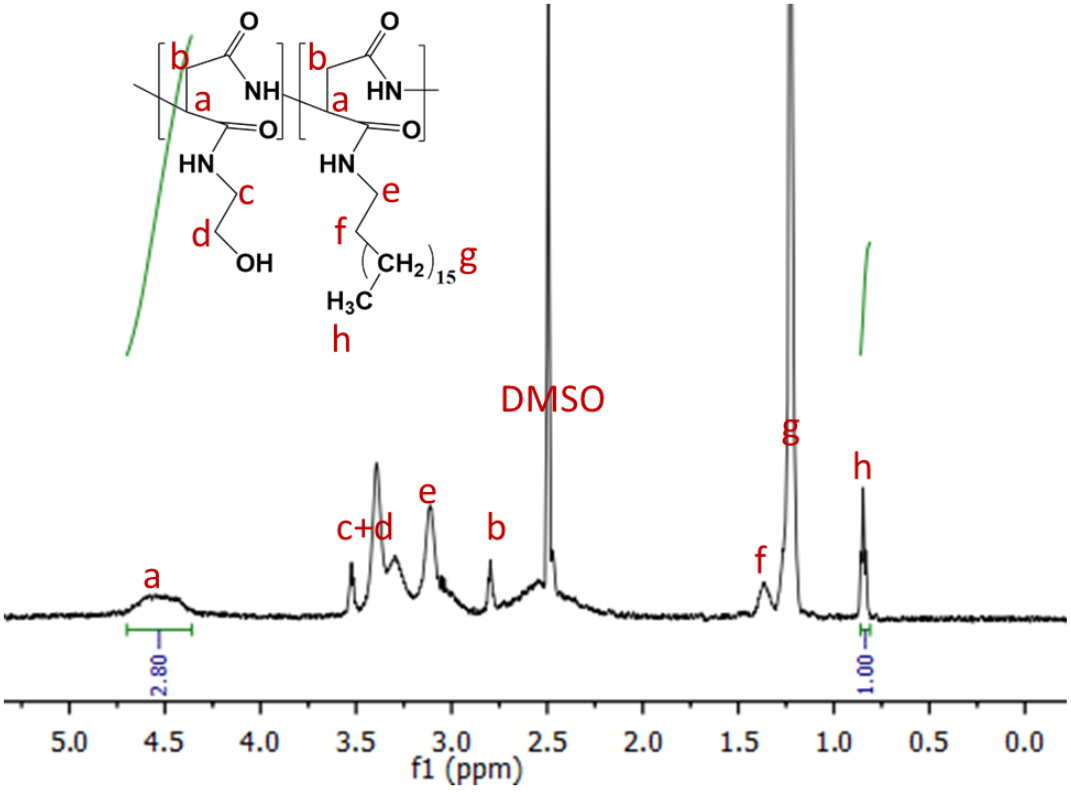

Figure S1. ^{1}H NMR spectra of PHEA-g-C_{18} labeled with corresponding peaks of the protons and integration of protons at positon a and h on the polymer.

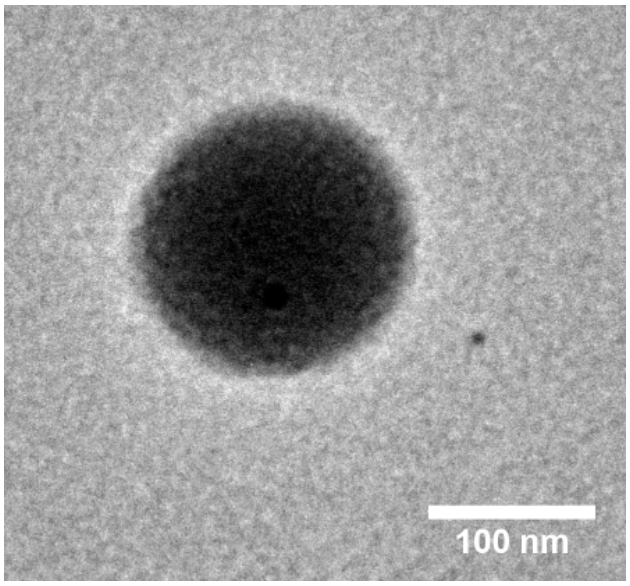

Figure S2. Transmission electron microscopy image of the PLGA nanoparticle.