Supplementary Data

## ReductivelyDegradableα-AminoAcid-BasedPoly(esteramide)-Graft-GalactoseCopolymers:FacileSynthesis,Self-Assembly,and Hepatoma-TargetingDoxorubicinDelivery

Jiaolong Lv<sup>1</sup>, Huanli Sun<sup>1</sup>, Yan Zou<sup>1</sup>, Fenghua Meng<sup>1,\*</sup>, Aylvin A. Dias<sup>2</sup>, Marc Hendriks<sup>2</sup>, Jan Feijen<sup>1,3</sup>, and Zhiyuan Zhong<sup>1,\*</sup>

<sup>1</sup> Biomedical Polymers Laboratory, and Jiangsu Key Laboratory of Advanced Functional Polymer Design and Application, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou, 215123, P. R. China.

<sup>2</sup>DSM Biomedical, Koestraat 1, Geleen 6167 RA, The Netherlands.

<sup>3</sup> Department of Polymer Chemistry and Biomaterials, Institute for Biomedical Technology and Technical Medicine (MIRA), Faculty of Science and Technology, University of Twente, Enschede, The Netherlands.

\* Corresponding authors. Tel/Fax: +86-512-65880098, Email: <u>fhmeng@suda.edu.cn</u> (F. Meng); <u>zyzhong@suda.edu.cn</u> (Z. Zhong)



Scheme S1 Synthetic pathway of Phe(TDE)·2TsOH. Conditions: TsOH·H<sub>2</sub>O, Toluene, refluxing 8 h.



Scheme S2 Synthetic pathway of VSC(HD)·2TsOH. Conditions: (i) Methanol, 30°C, 3 d; (ii) TsOH·H<sub>2</sub>O, Toluene, 130°C, 8 h.



Fig. S1 <sup>1</sup>H NMR (400 MHz) (A) and <sup>13</sup> C NMR (100 MHz) (B) of Phe(TDE)·2TsOH (DMSO-*d*<sub>6</sub>).



Fig. S2 <sup>1</sup>H NMR spectrum (400 MHz, D<sub>2</sub>O) of vinylsulfone substituted cysteine (VSC).



Fig. S3 <sup>1</sup>H NMR (400 MHz) (A) and <sup>13</sup> C NMR (100 MHz) (B) of VSC(HD)·2TsOH (DMSO-*d*<sub>6</sub>).



Fig. S4 FTIR spectrum of vinylsulfone substituted cysteine (VC).

FTIR spectrum (**Fig. S4**) displayed the characteristic absorption bands of  $NH_3^+$  stretch from cysteine unit (~3000 cm<sup>-1</sup>), C=O stretch of carboxyl groups (~1760 cm<sup>-1</sup>), C-O stretch of carboxyl groups (~1417 cm<sup>-1</sup>), O=S=O stretch (~1332 and 1125 cm<sup>-1</sup>), NH<sub>3</sub><sup>+</sup> bend from cysteine unit (~1579 and 1500 cm<sup>-1</sup>), O-H bend of carboxyl groups (~1293 cm<sup>-1</sup>), and =C-H bend of vinyl groups (988 and 926 cm<sup>-1</sup>).



Fig. S5 The change in size distribution profiles of PEA-Gal<sub>42</sub> nanoparticles in response to 10 mM GSH in PBS (10 mM, pH 7.4).



Fig. S6 Cytotoxicity of SSPEA-Gal42 and PEA-Gal42 nanoparticles against HepG2 (A) and MCF-7 (B) cells by MTT assays at 48 h incubation. Data are presented as the average ± SD (n = 4).