Supporting Information

Intracellular Thiol-Responsive Nanosized Drug Carriers Self-assembled by Poly(ethylene glycol)-*b*-Poly(ε-caprolactone)-*b*-Poly(ethylene glycol) Having Multiple Bioreducible Disulfide Linkages in Hydrophobic Block

Seung Yeon Moon[a,†], Yeon Su Choi[a,†], Jung-Kyo Cho[a], Minjong Yu[b], Eunji Lee[b], Kang Moo Huh[c], Don Haeng Lee[d,e], Jong-Ho Kim[f,*], Han Chang Kang[a,*]

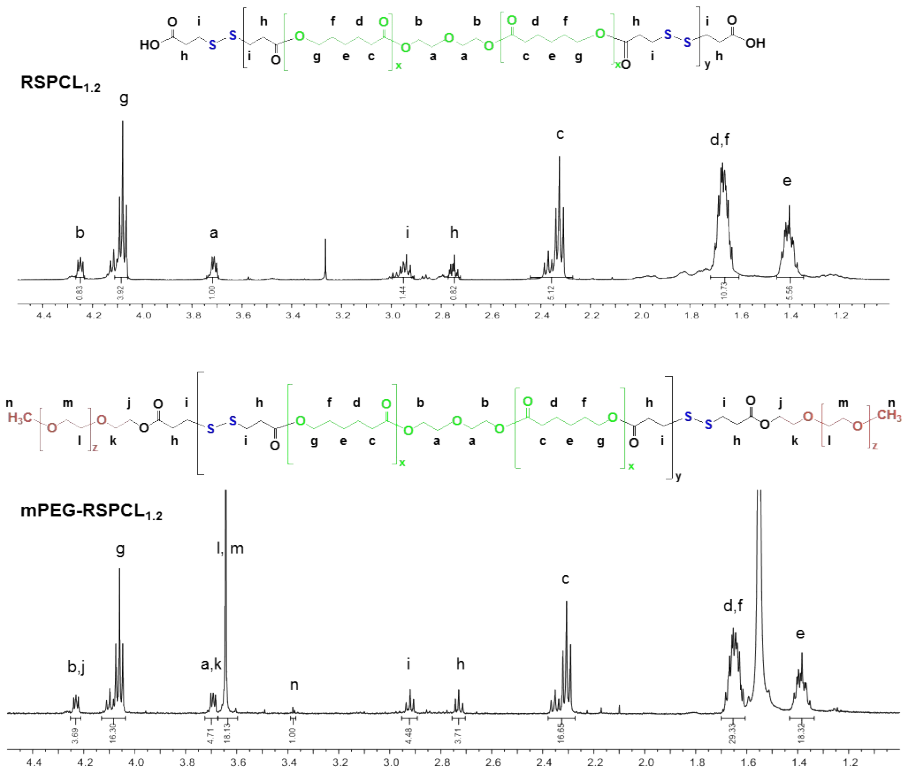
[a] Department of Pharmacy and Integrated Research Institute of Pharmaceutical Sciences, College of Pharmacy, The Catholic University of Korea, 43 Jibong-ro, Wonmi-gu, Bucheon-si, Gyeonggi-do 420-743, Republic of Korea
[b] Graduate School of Analytical Science and Technology, Chungnam National University, 99 Daehak-ro, Yuseong-gu, Daejeon 305-764, Republic of Korea
[c] Department of Polymer Science and Engineering, Chungnam National University, 99 Daehak-ro, Yuseong-gu, Daejeon 305-764, Republic of Korea
[d] Division of Gastroenterology and Hepatology, Department of Internal Medicine, Inha University Hospital, 27 Inhang-ro, Jung-gu, Incheon 400-712, Republic of Korea
[e] Utah-Inha Drug Delivery Systems and Advanced Therapeutics Research Center, 9 Songdomirae-ro, Yeonsu-gu, Incheon 406-840, Republic of Korea
[f] Department of Pharmaceutical Sciences, Kyung Hee University, 26 Kyungheedae-ro, Dongdaemoon-gu, Seoul 130-701, Republic of Korea

[†] SYM and YSC equally contributed this work.

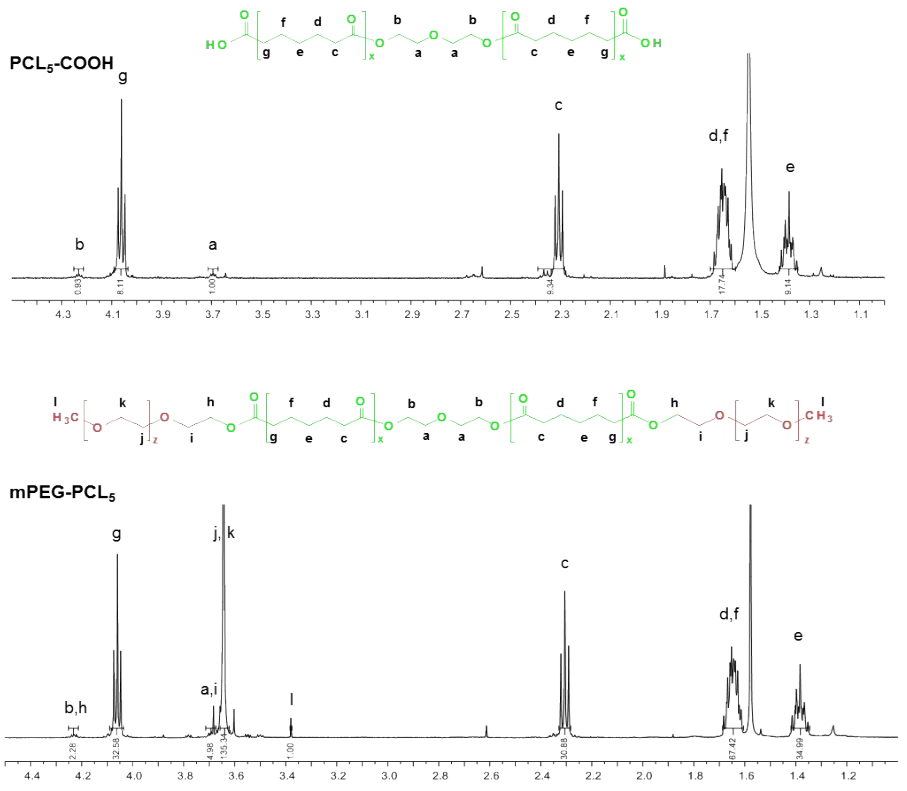
* Co-correspondence to:
Professor Han Chang Kang, Ph.D., Department of Pharmacy and Integrated Research Institute of Pharmaceutical Sciences, College of Pharmacy, The Catholic University of Korea, 43 Jibong-ro, Wonmi-gu, Bucheon-si, Gyeonggi-do 420-743, Republic of Korea
Tel: +82-2-2164-6533; Fax: +82-2-2164-4059
E-mail address: hckang@catholic.ac.kr

Professor Jong-Ho Kim, Ph.D., Department of Pharmaceutical Sciences, Kyung Hee University, 26 Kyungheedae-ro, Dongdaemoon-gu, Seoul 130-701, Republic of Korea
Tel: +82-2-961-9312-; Fax: +82-2-966-3885
E-mail address: jonghokim@khu.ac.kr

(a)



(b)



(c)

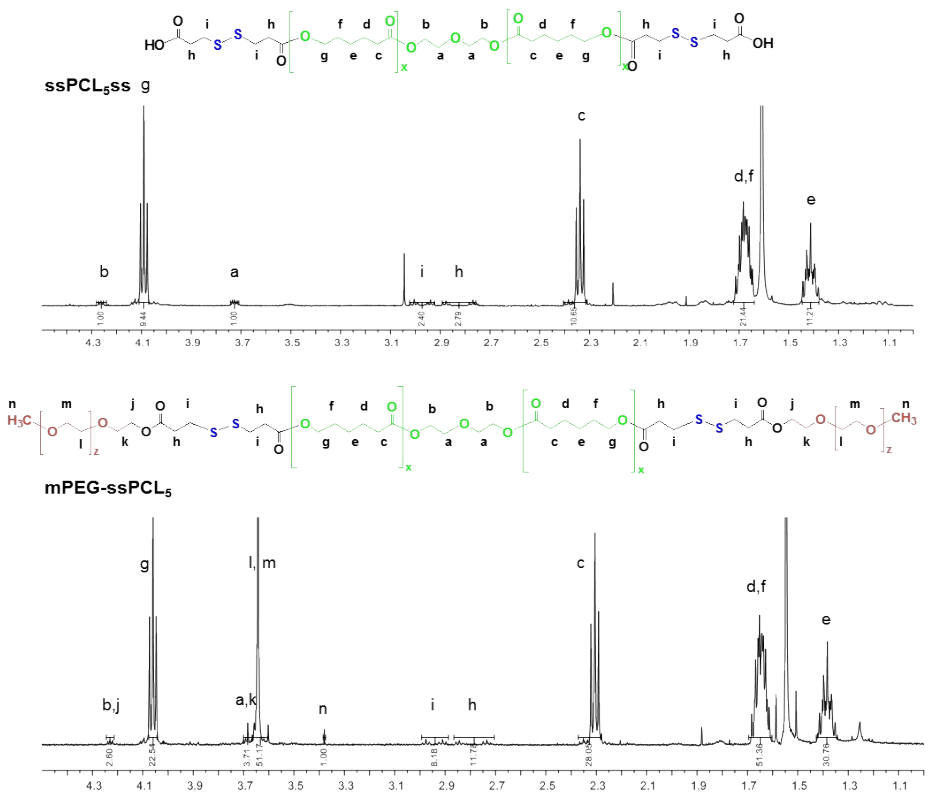
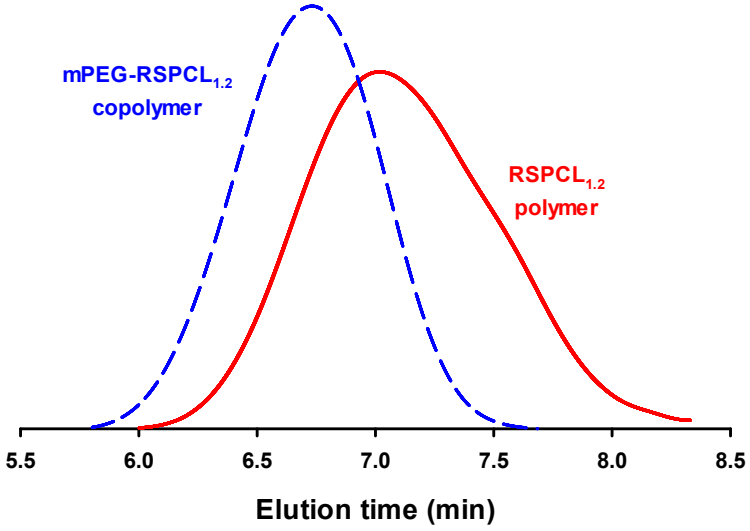
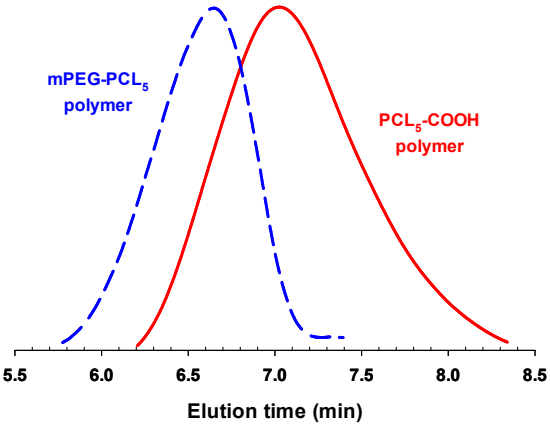


Figure S1. ^{1}H-NMR spectra of (a) the synthesized $RSPCL_{1.2}$ polymers and mPEG-$RSPCL_{1.2}$ copolymers, (b) the commercially-available PCL_5-COOH polymers and the synthesized mPEG-PCL_5 copolymers, and (c) the synthesized ssPCLss polymers and mPEG-$ssPCL_5$ copolymers in $CDCl_3$.

(a)



(b)



(c)

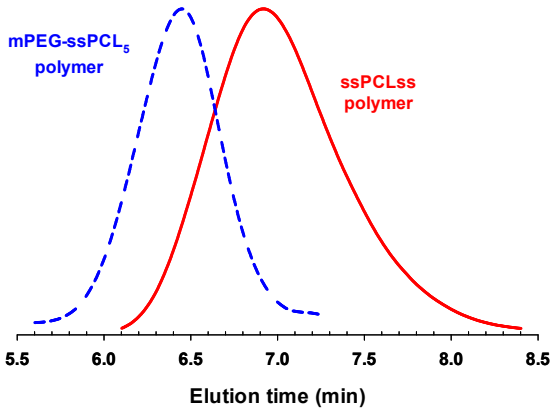


Figure S2. GPC chromatograms of (a) the synthesized $RSPCL_{1.2}$ polymers and mPEG-$RSPCL_{1.2}$ copolymers, (b) the commercially-available PCL_5-COOH polymers and the synthesized mPEG-PCL_5 copolymers, and (c) the synthesized ssPCL_5ss polymers and mPEG-ssPCL_5 copolymers in THF.

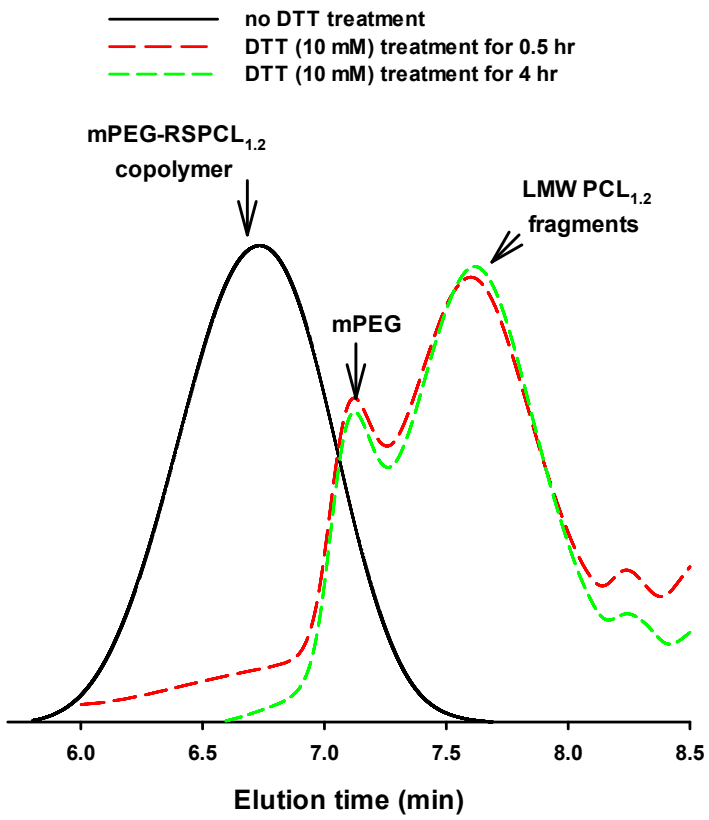


Figure S3. Thiol-induced MW change of mPEG-RSPCL$_{1.2}$ copolymers in drug-free mPEG-RSPCL$_{1.2}$ NPs. The degradation experiment was carried out at 37 ^{o}C and was analyzed by GPC chromatograms. ([mPEG-RSPCL$_{1.2}$ NP] = 0.25 mg/mL, [DTT] = 10 mM)

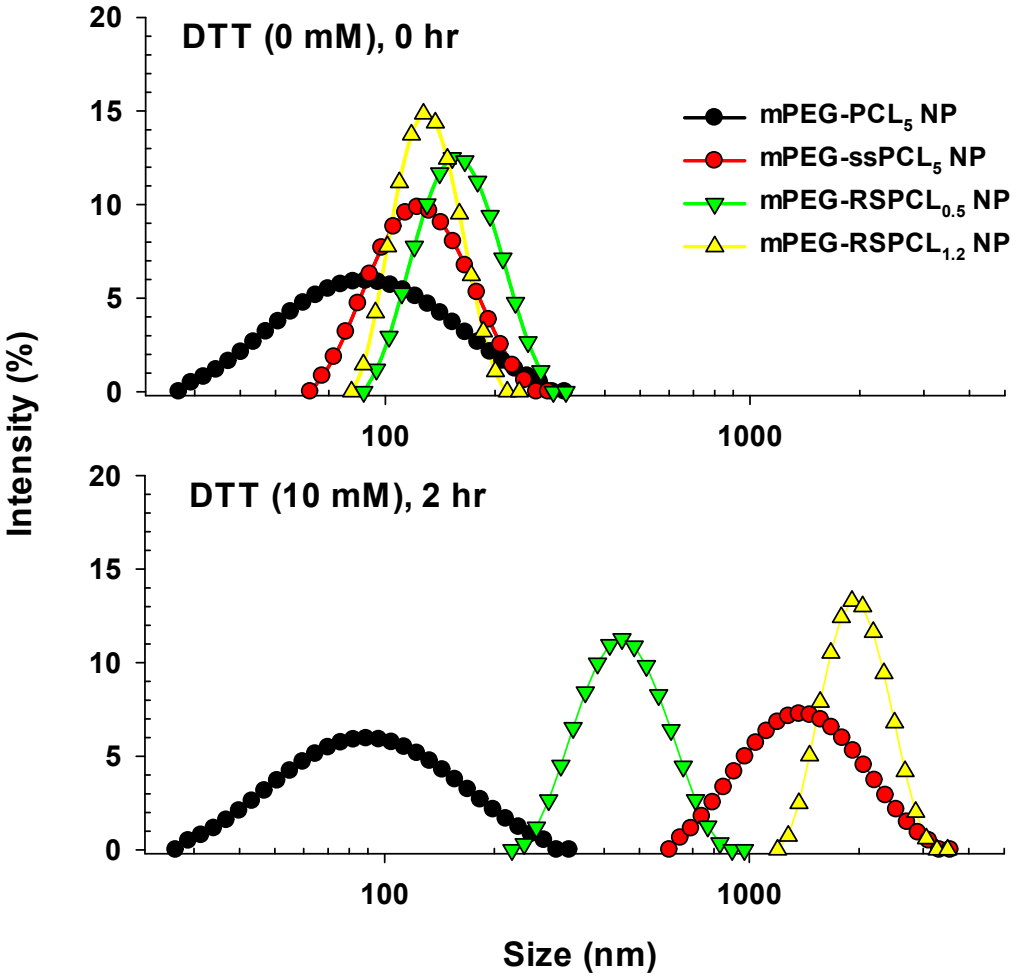


Figure S4. Thiol-induced size (intensity average) change of various NPs such as mPEG-PCL_5 NPs, mPEG-ssPCL_5 NPs, mPEG-RS$PCL_{0.5}$ NPs and mPEG-RS$PCL_{1.2}$ NPs in DTT-containing DPBS (50 mM, pH 7.4). The degradation experiment was performed at 37 °C for 2 hrs. ([Polymer] = 0.25 mg/mL, [DTT] = 10 mM)

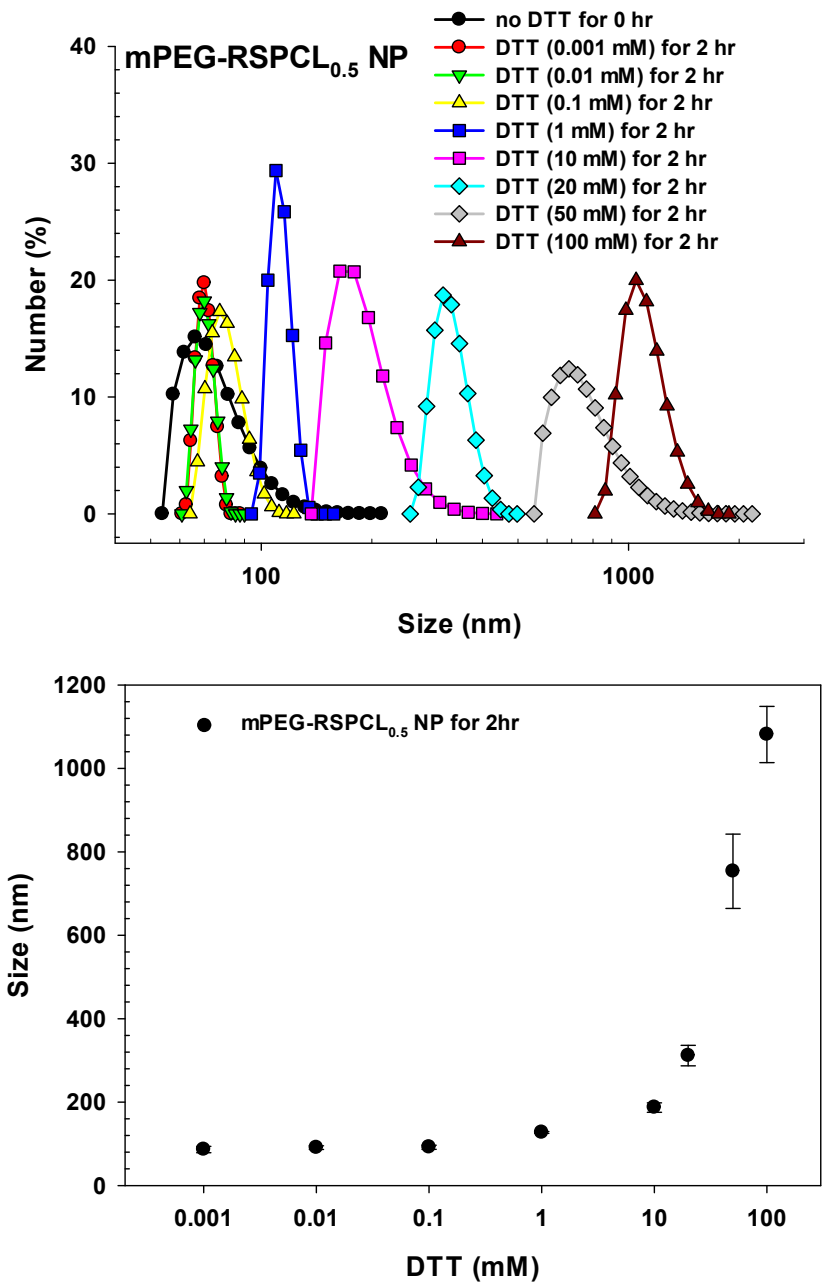


Figure S5. Size change of mPEG-RSPCL$_{0.5}$ NPs was monitored as a function of DTT concentration (1 μM-100 mM) for 2 hr at RT (n=3).

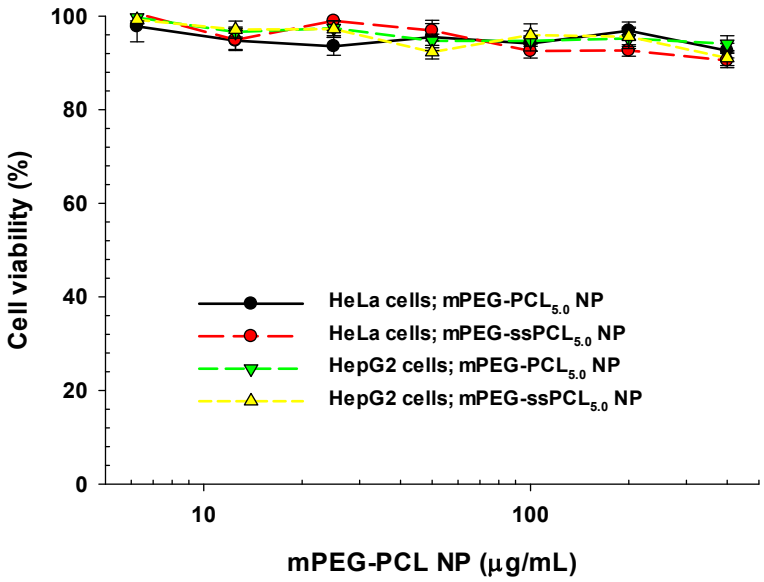


Figure S6. In vitro cytotoxicity of drug-free mPEG-PCL_5 NPs and mPEG-ssPCL_5 NPs in HeLa and HepG2 cells 48 hr post-treatment. Various concentrations of NPs were used to treat the cells for 48 hr, and the data are expressed as the mean ± standard error of the mean (SEM) (n=12).

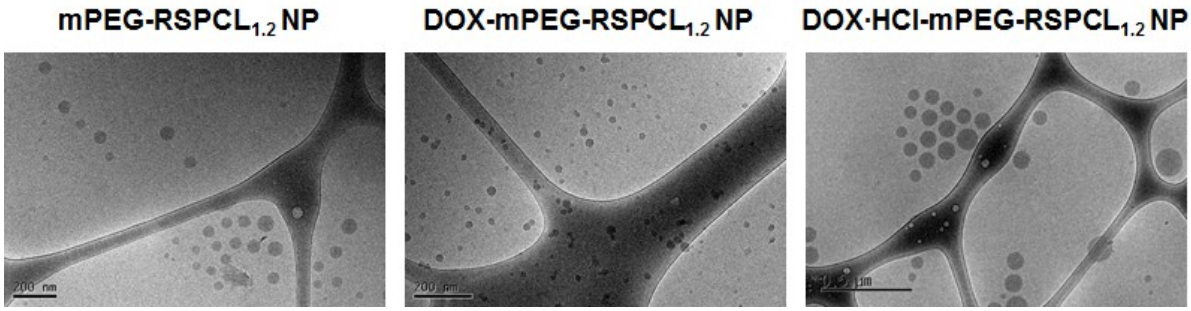


Figure S7. CryoTEM images of drug-free mPEG-$RSPCL_{1.2}$ NPs and drug-loaded mPEG-$RSPCL_{1.2}$ NPs.

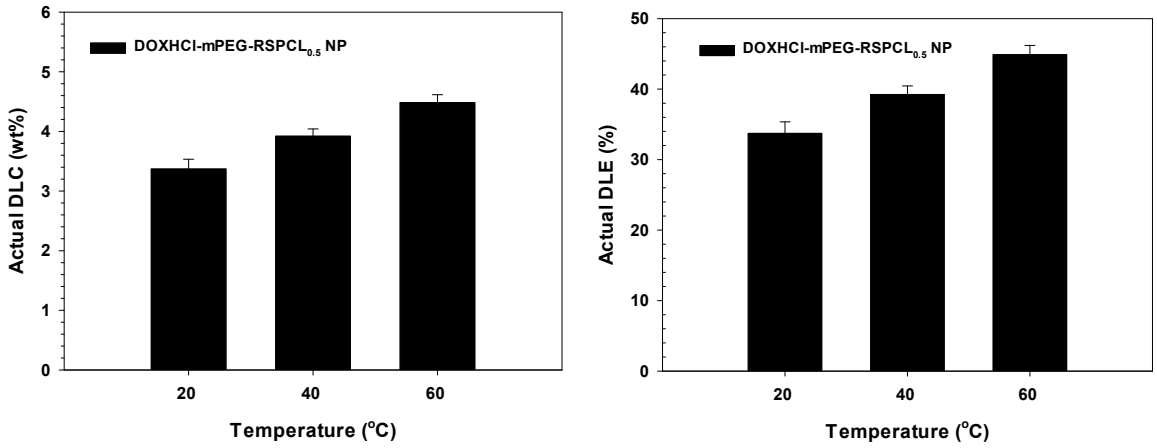


Figure S8. Drug loading content (DLC, %) and efficiency (DLE, %) of DOX·HCl-mPEG-RSPCL$_{0.5}$ NPs as a function of temperature (n=3).