

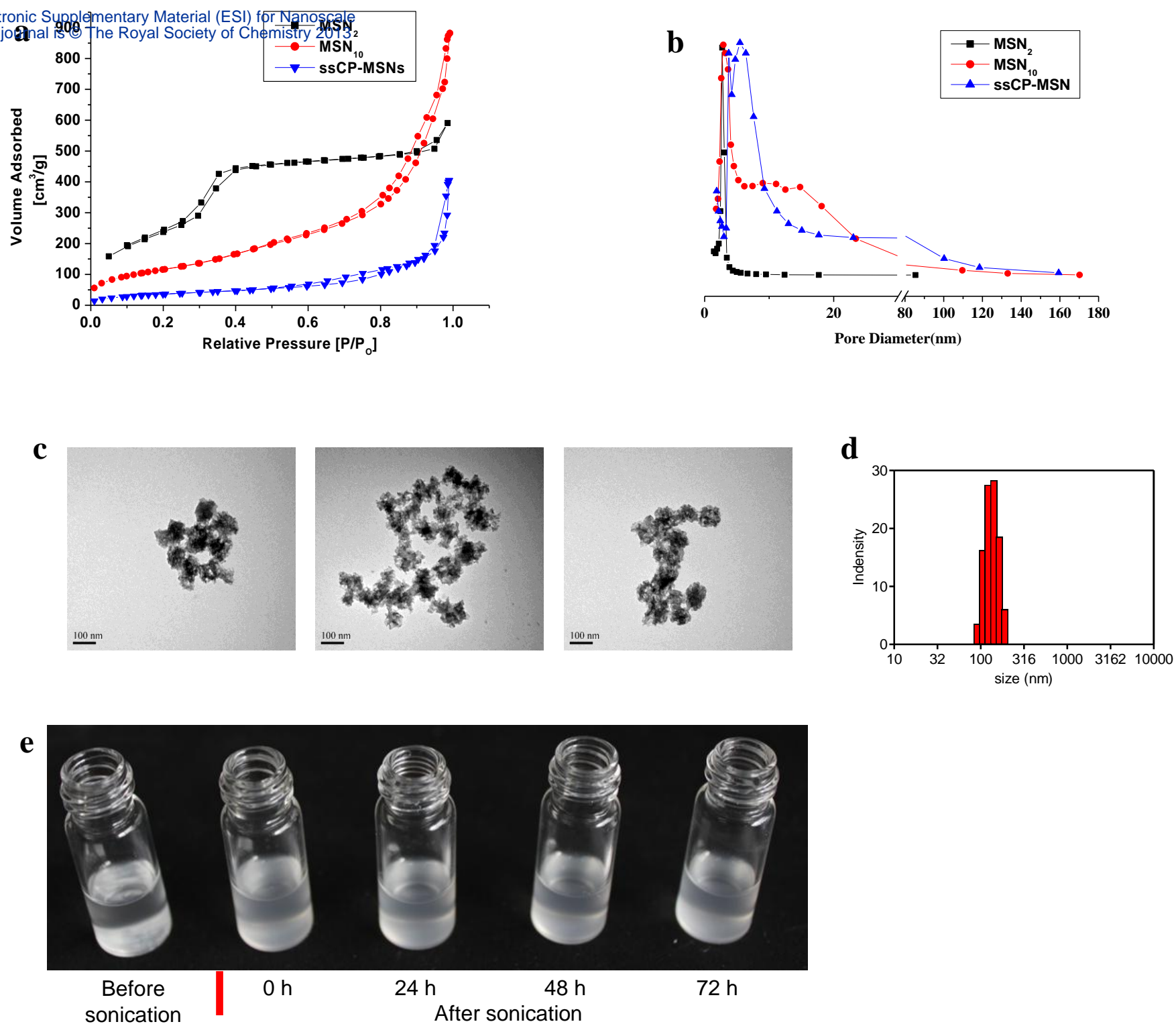
## Experimental

### Loading ssCP-MSNs with Rhodamine B (RhB) and gel retardation assay of ssCP-MSNs/RhB

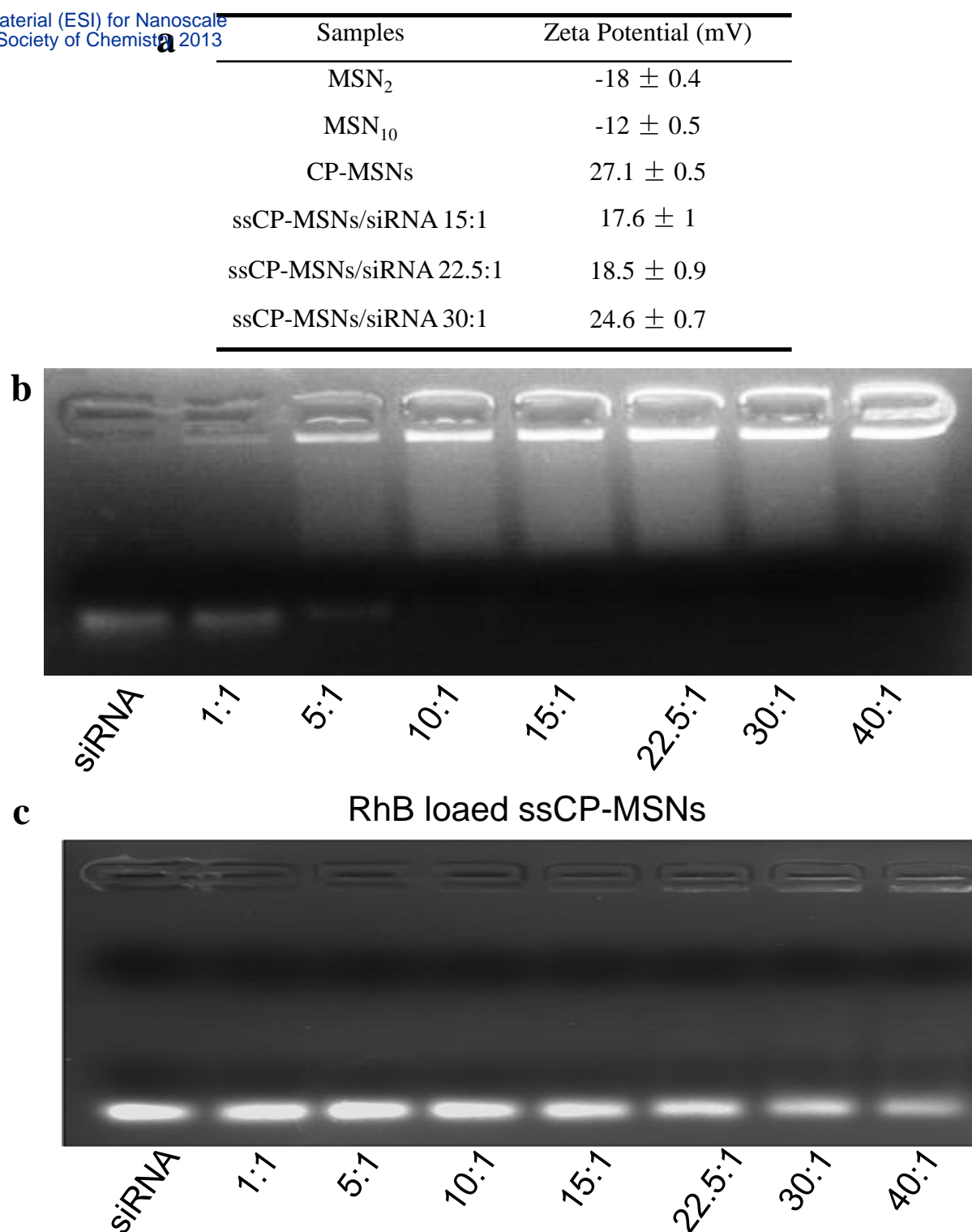
The ssCP-MSNs (0.15 g) was added to 3.00 mL anhydrous ethanol solution of RhB (5.00 mM). The solution mixture was stirred at room temperature for 24 h to allow RhB to be encapsulated by ssCP-MSNs. The resulting ssCP-MSNs/RhB was filtered and washed thoroughly with ethanol, and dried under high vacuum. The loading of RhB (25  $\mu\text{mol/g}$ ) was calculated by subtracting the amount of RhB in the ethanol solution and combined washings from the amount of RhB initially added to the reaction<sup>1</sup>. The concentration of RhB was measured by UV-Vis spectrophotometer with absorbance at 554 nm. Surface areas, pore volumes and pore sizes were determined by BET and BJH method.

To compare with the un-blocked ssCP-MSNs, the weight of ssCP-MSNs/RhB was converted to the weight of ssCP-MSNs according to the RhB loading ratio of ssCP-MSNs (25  $\mu\text{mol/g}$ ). To prepare each ssCP-MSNs/siRNA complexes, 0.5  $\mu\text{g}$  siRNA was incubated with a predetermined amount of ssCP-MSNs at r.t. in DEPC for 1h. Then the complexes were mixed with 4  $\mu\text{L}$  of 6  $\times$  loading buffer (Takara Biotechnology, Dalian, Liaoning Province, China), and then the mixture was loaded onto 2% agarose gel containing 5  $\mu\text{g/mL}$  ethidium bromide. Electrophoresis was carried out at a voltage of 120 V for 20 min in 1  $\times$  TAE running buffer. Finally, the results were recorded at UV light wavelength 254 nm with image master VDS thermal imaging system (Bio-Rad, Hercules, CA).

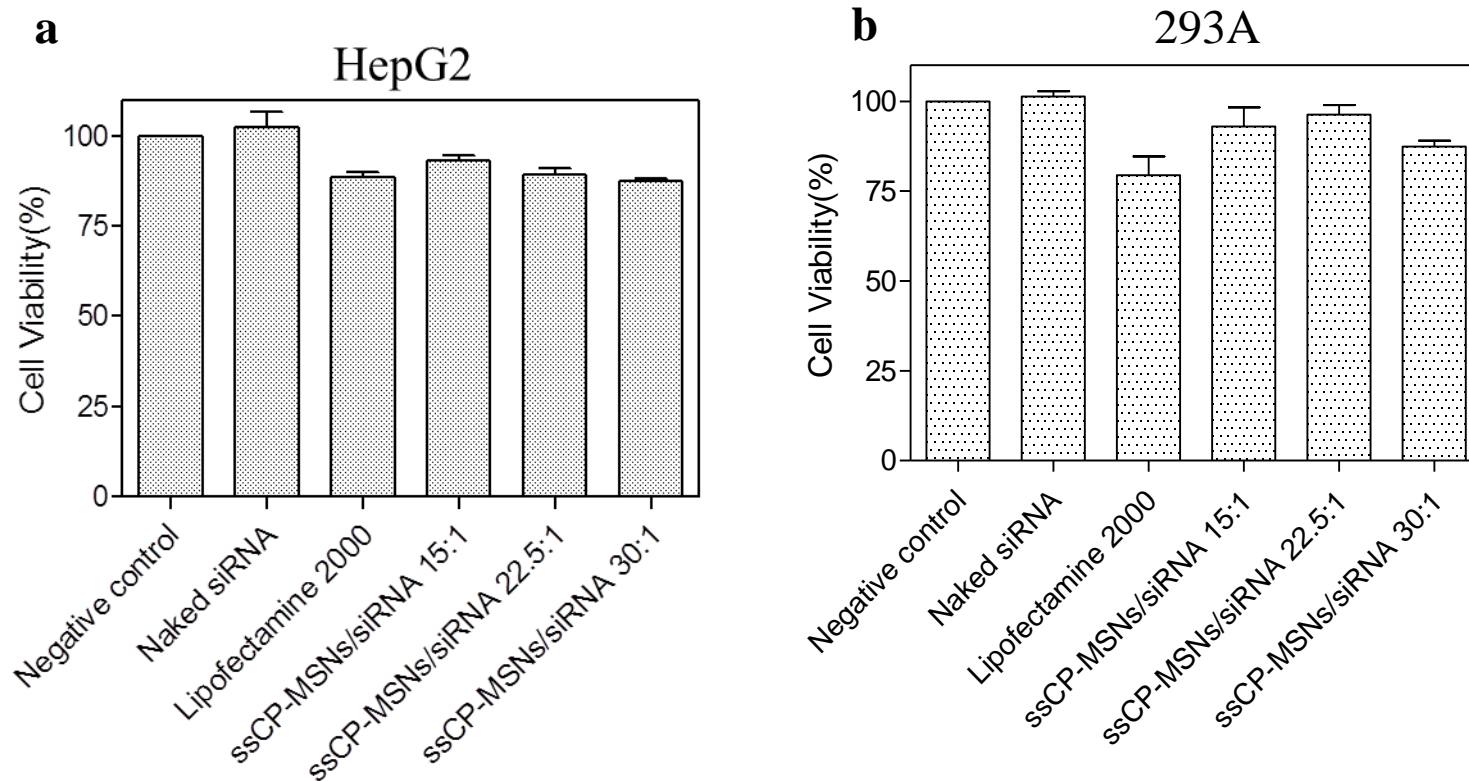
1. Y. N. Zhao, B. G. Trewyn, Slowing, II and V. S. Y. Lin, *Journal of the American Chemical Society*, 2009, **131**, 8398-+.



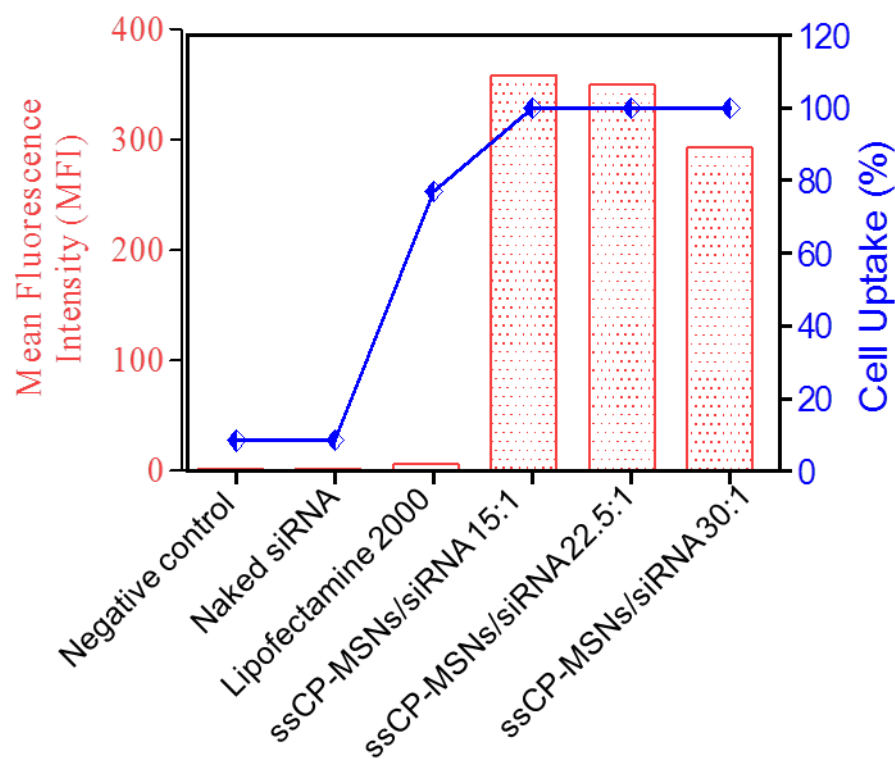
**Figure S1.** (a) BET nitrogen sorption isotherms of  $\text{MSN}_2$ ,  $\text{MSN}_{10}$  and ssCP-MSNs. (b) BJH pore size distribution of  $\text{MSN}_2$ ,  $\text{MSN}_{10}$  and ssCP-MSNs. (c) TEM images and (d) DLS study of ssCP-MSNs. (e) The stability of ssCP-MSNs in water before/after the sonication (80 W for 30 s).



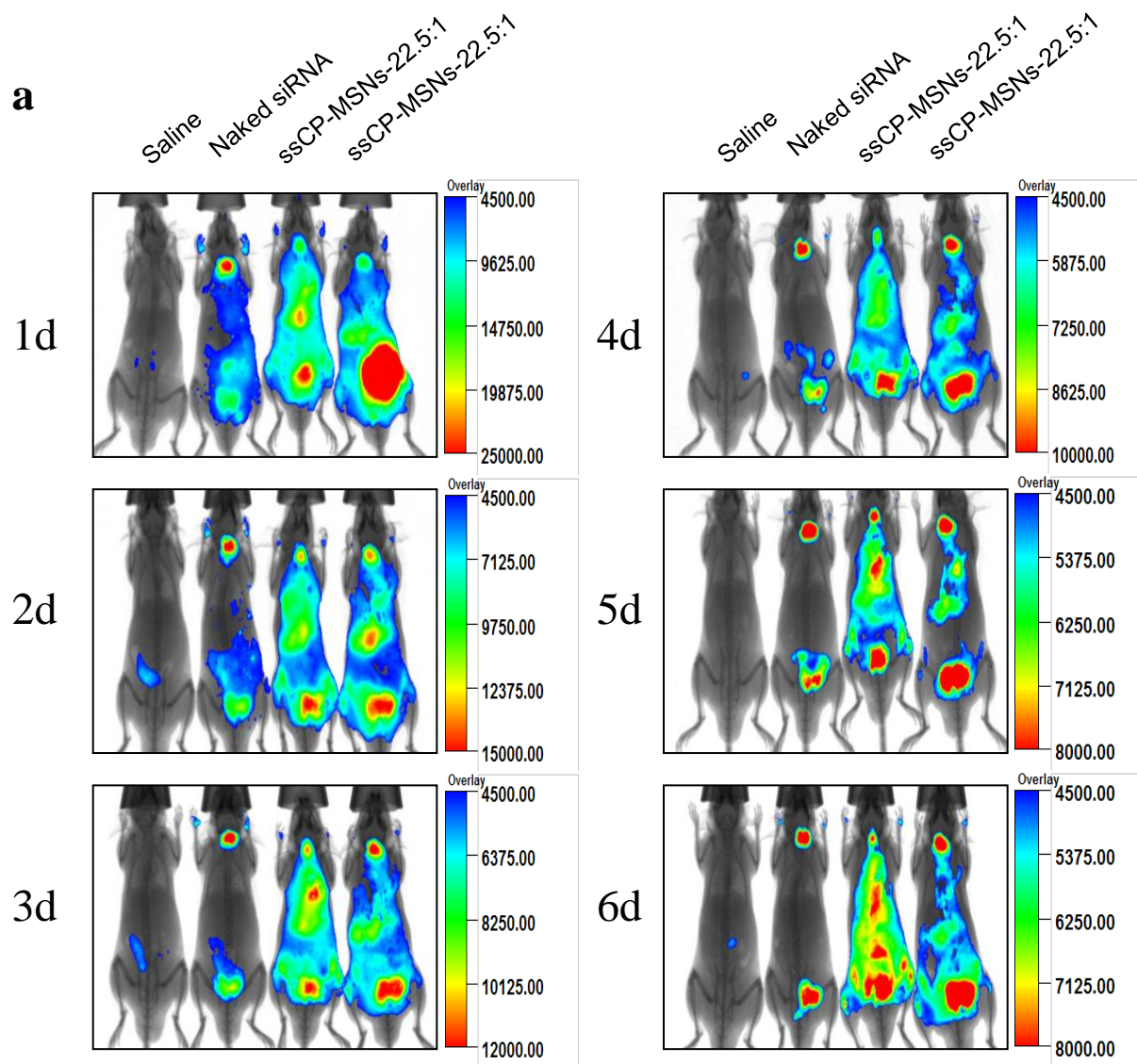
**Figure S2.** (a) zeta-potential of ssCP-MSNs and ssCP-MSNs/siRNA complexes. (b) Agarose gel electrophoresis retardation assay of ssCP-MSNs/siRNA complexes at different w/w ratios of ssCP-MSNs to siRNA. (c) Agarose gel electrophoresis of ssCP-MSNs with blocked pores/siRNA at different w/w ratios of ssCP-MSNs to siRNA. The weight of ssCP-MSNs/RhB was converted to the weight of ssCP-MSNs according to the RhB loading ratio of ssCP-MSNs (25  $\mu\text{mol/g}$ ).



**Figure S3.** Cell viabilities of ssCP-MSNs/siRNA complexes at different w/w ratios *in vitro* were evaluated using (a) HepG2 cells and (b) 293A cells.

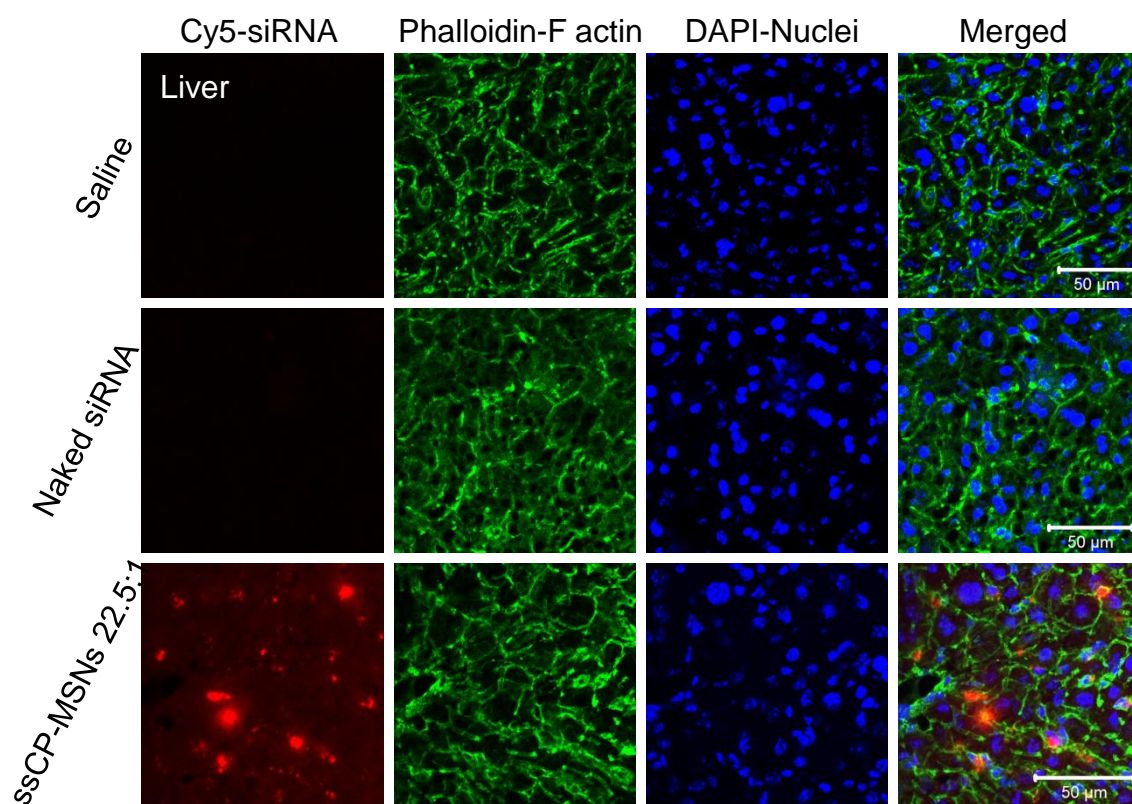


**Figure S4.** Percentages of cellular uptake and mean fluorescence intensity of ssCP-MSNs/ FAM-siRNA complexes. Negative control was the group without any treatment.

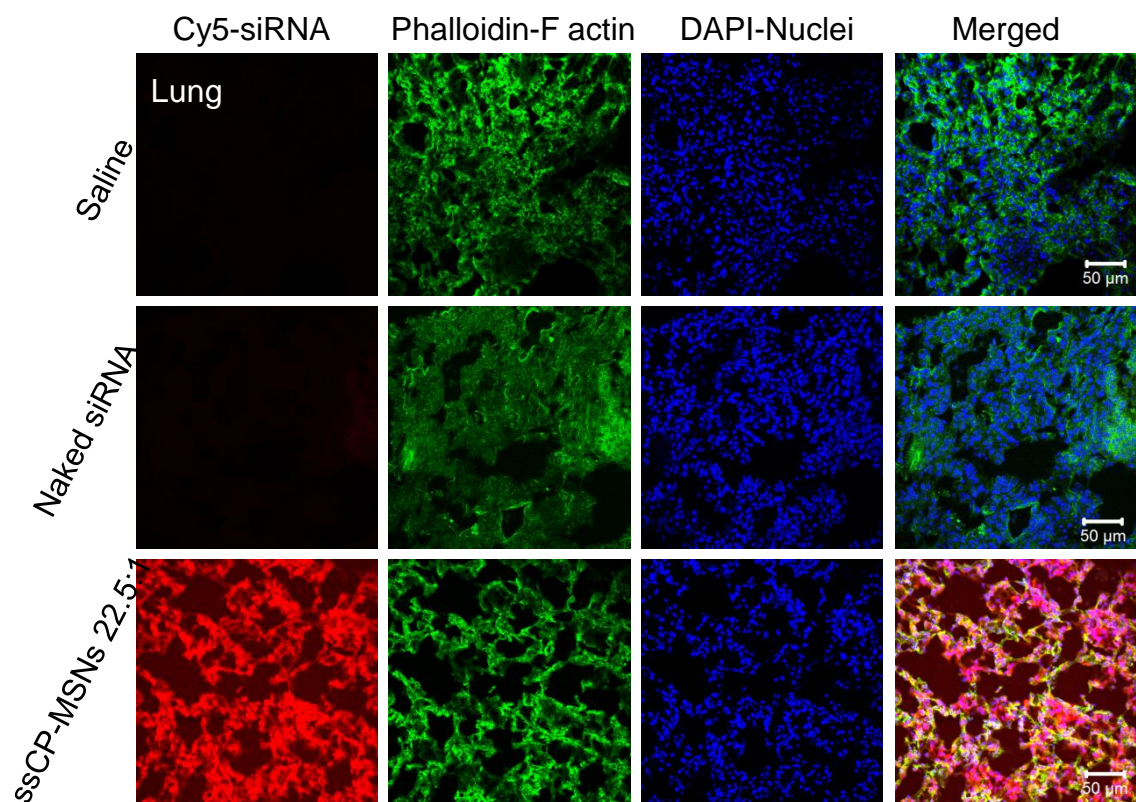


**Figure S5.** *In vivo* Cy5-siRNA distribution in mice at 6 days after intravenous injection of 50  $\mu\text{g}/\text{mouse}$  of Cy5-siRNA to C57 mice with ssCP-MSNs at the w/w = 22.5:1 (duplicate samples).



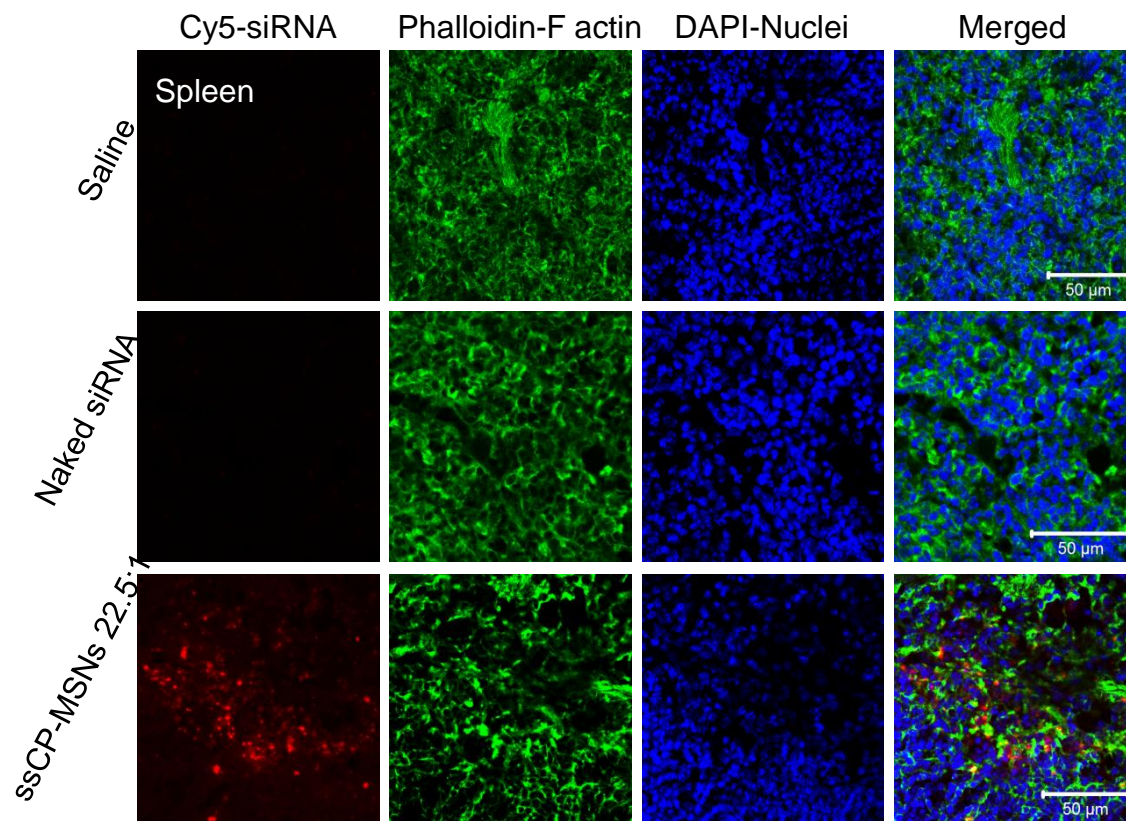


**Figure S6.** (a) *In vivo* siRNA distribution in liver at 4 h after intravenous injection determined by CLSM.

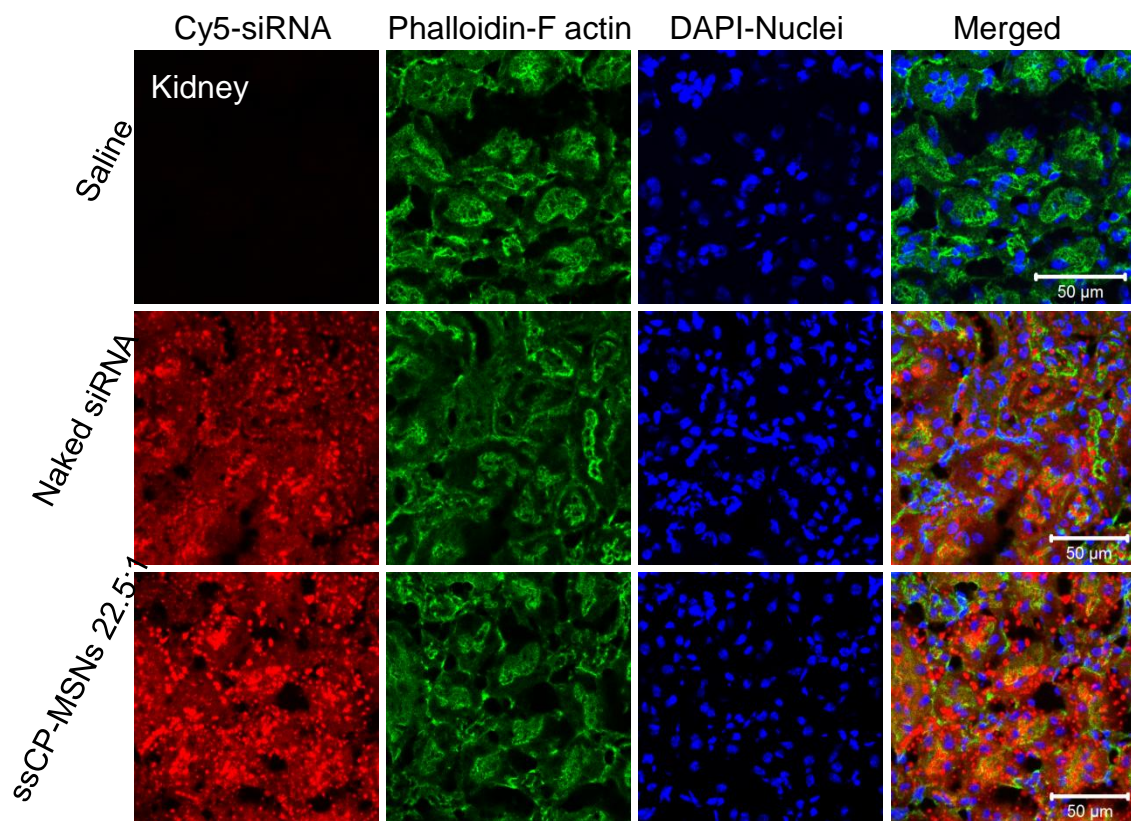


**Figure S6.** (b) *In vivo* siRNA distribution in lung at 4 h after intravenous injection determined by CLSM.

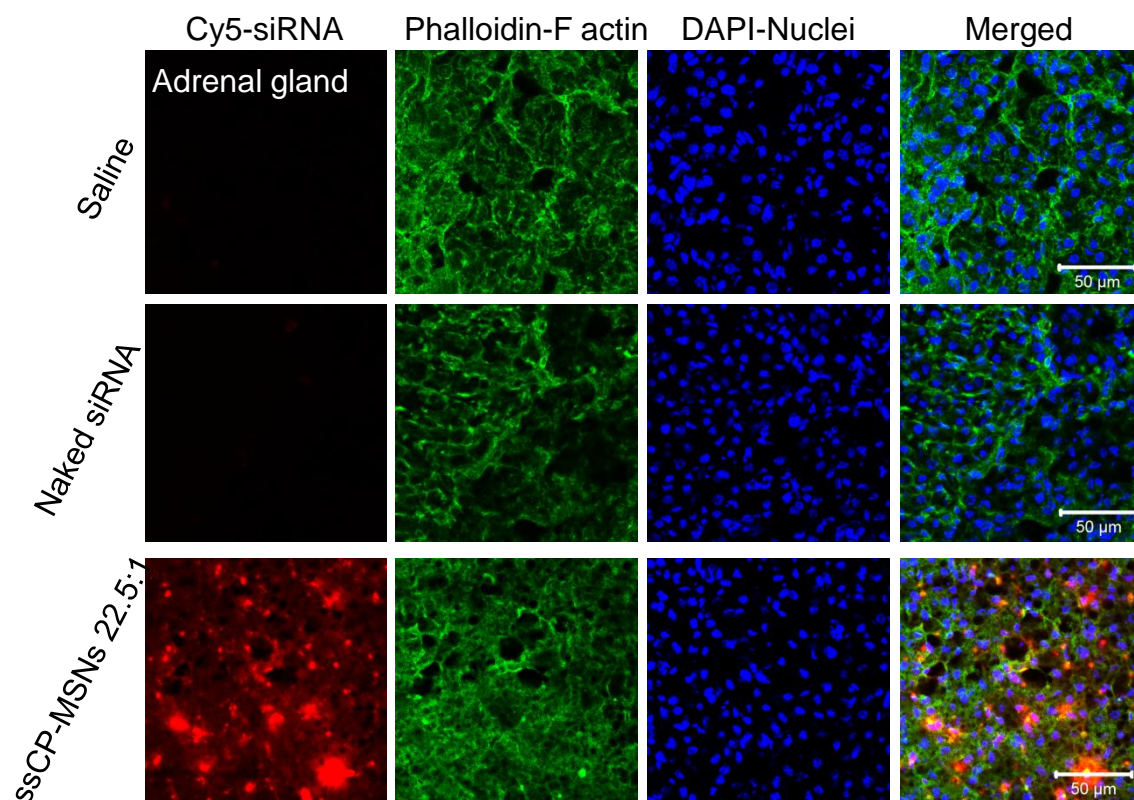




**Figure S6.** (c) *In vivo* siRNA distribution in spleen at 4 h after intravenous injection determined by CLSM.

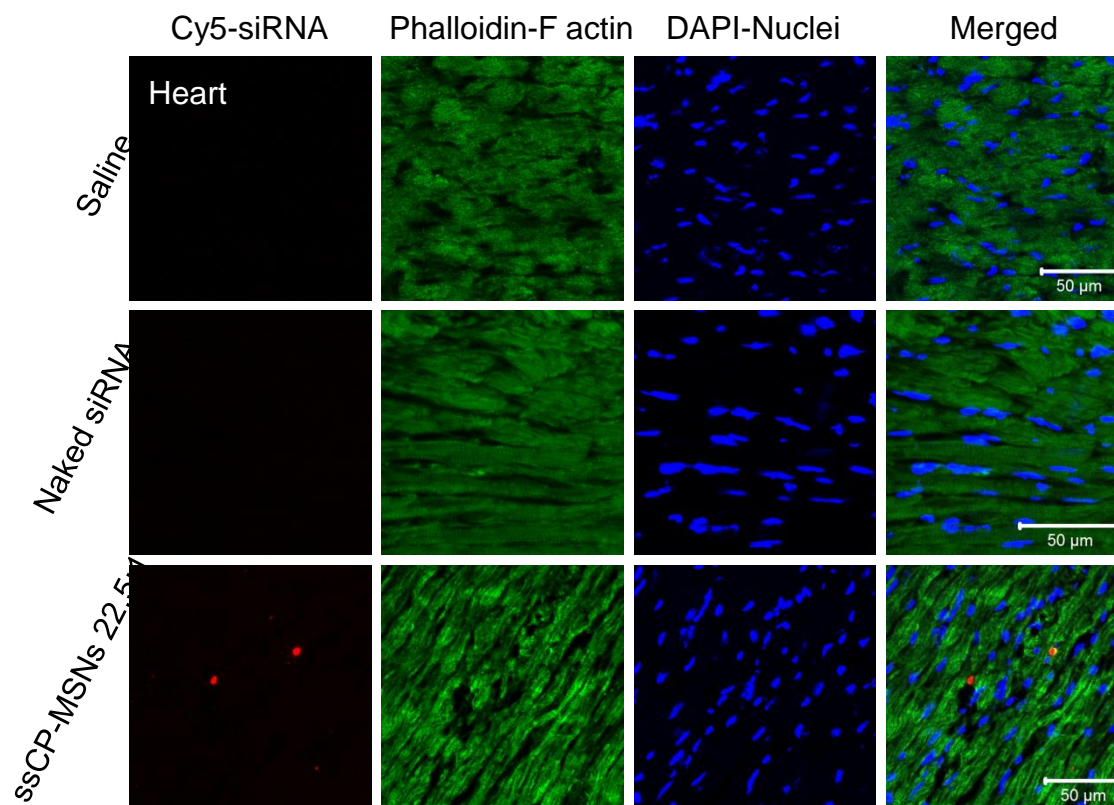


**Figure S6.** (d) *In vivo* siRNA distribution in kidney at 4 h after intravenous injection determined by CLSM.

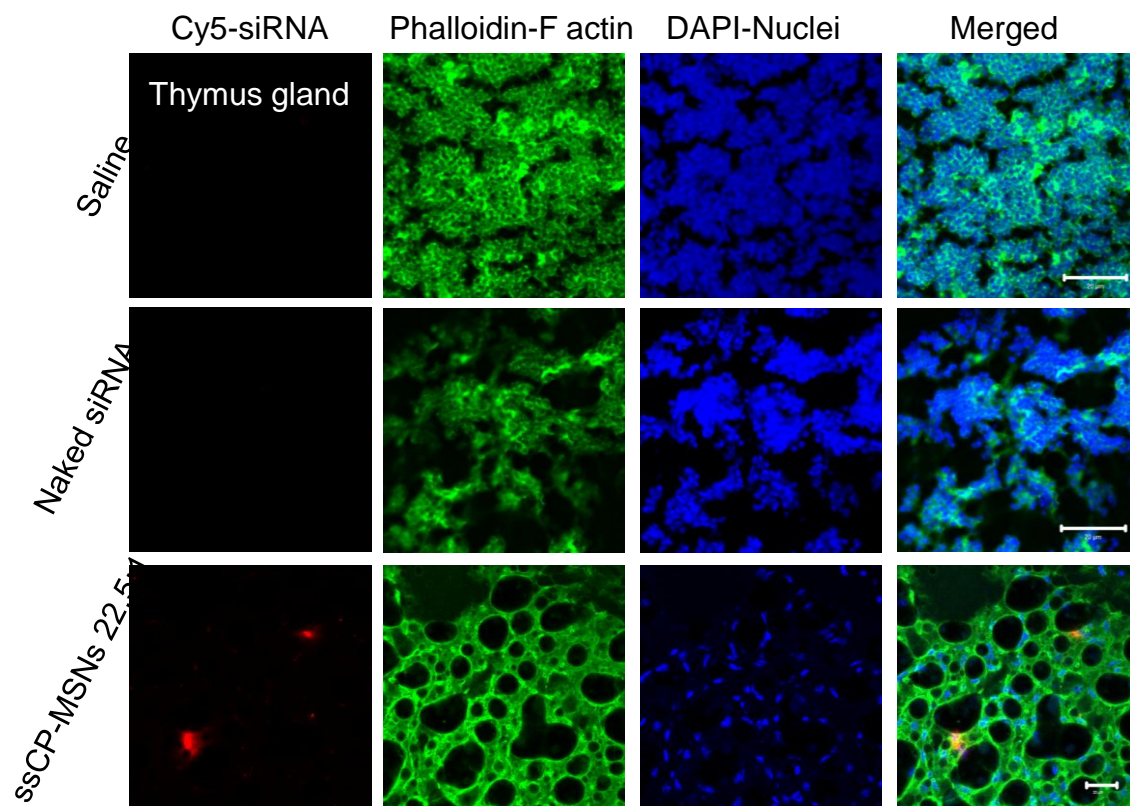


**Figure S6.** (e) *In vivo* siRNA distribution in adrenaline at 4 h after intravenous injection determined by CLSM.



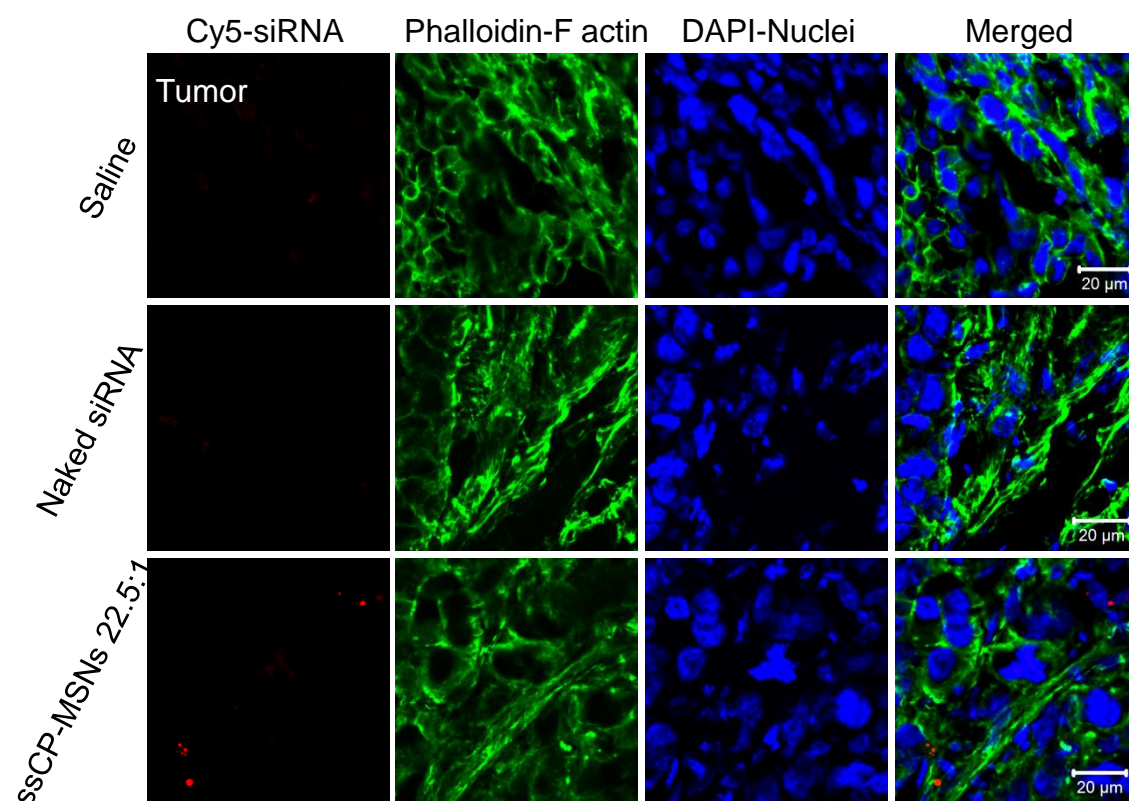


**Figure S6.** (f) *In vivo* siRNA distribution in heart at 4 h after intravenous injection determined by CLSM.

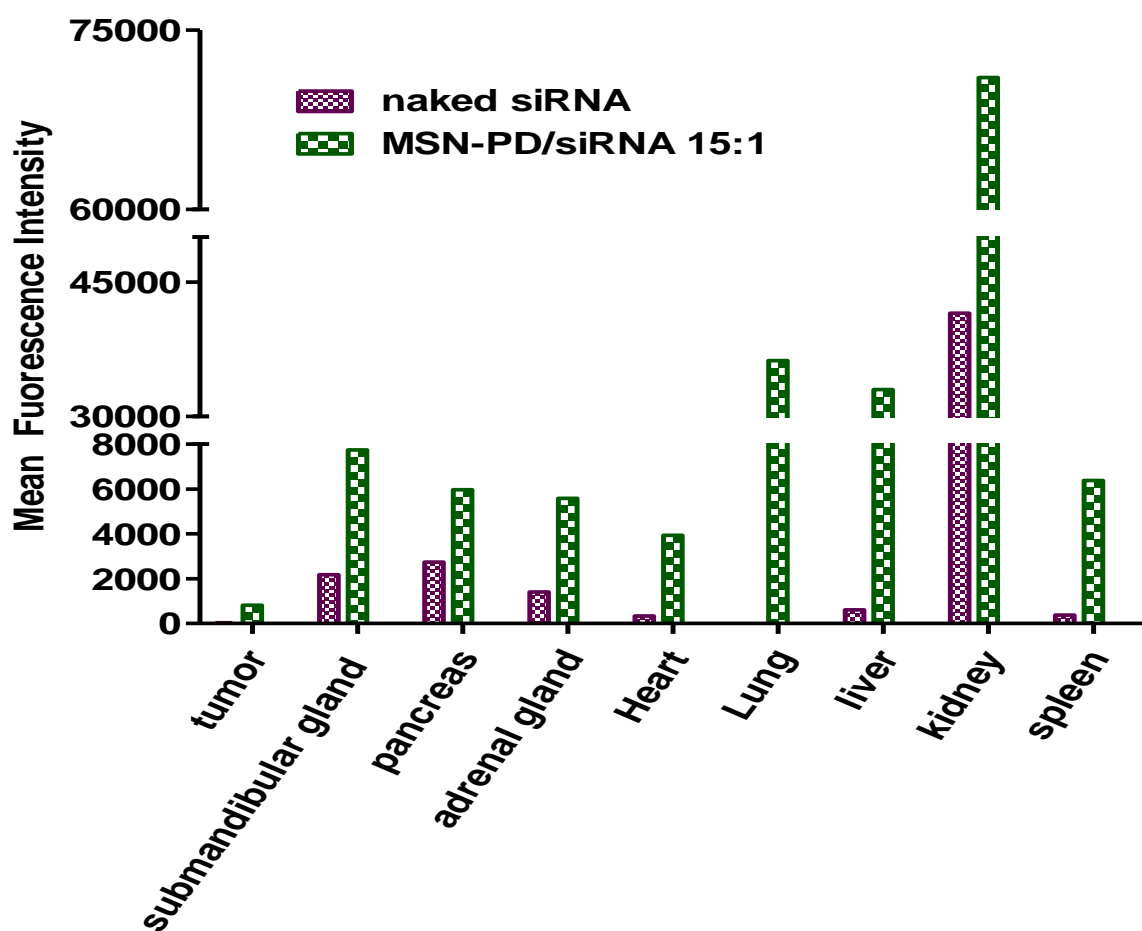


**Figure S6.** (g) *In vivo* siRNA distribution in thymus at 4 h after intravenous injection determined by CLSM.

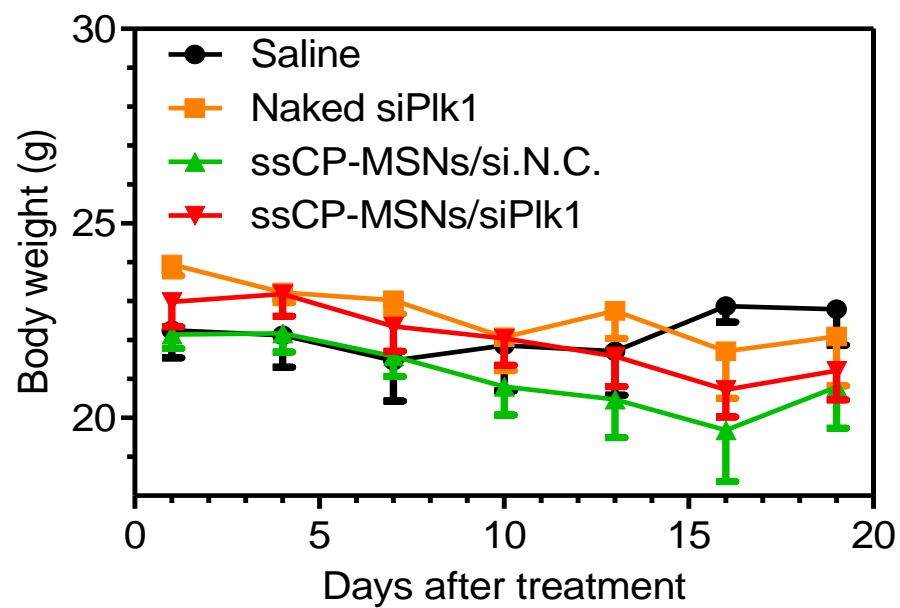
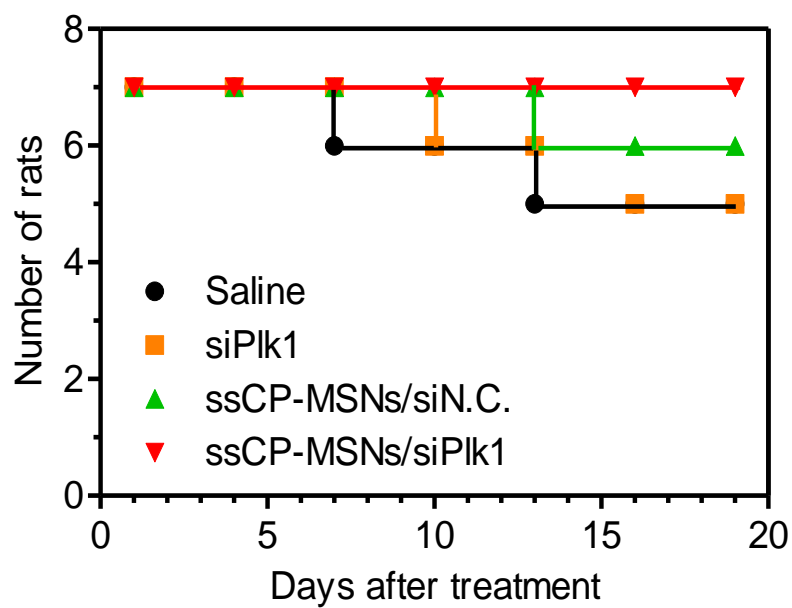




**Figure S7.** *In vivo* Cy5-siRNA distribution in tumors determined by CLSM, in tumor-bearing mice at 48 h after intravenous injection of 50  $\mu\text{g}/\text{mouse}$  of Cy5-siRNA to nude mice-bearing HeLa-Luc tumor.



**Figure S8.** Mean fluorescence intensities of ssCP-MSNs/Cy5-siRNA complexes in isolated organs, at 48 h after intravenous injection of 50  $\mu\text{g}/\text{mouse}$  of Cy5-siRNA to nude mice-bearing HeLa-Luc tumor.



**Figure S9.** The survival plots and body weight changes of mice after intravenous injection of ssCP-MSNs/siRNA.