

## Supporting Information

# Sorafenib-loaded Silica-containing Redox Nanoparticle Decreases Tumorigenic Potential of Lewis Lung Carcinoma

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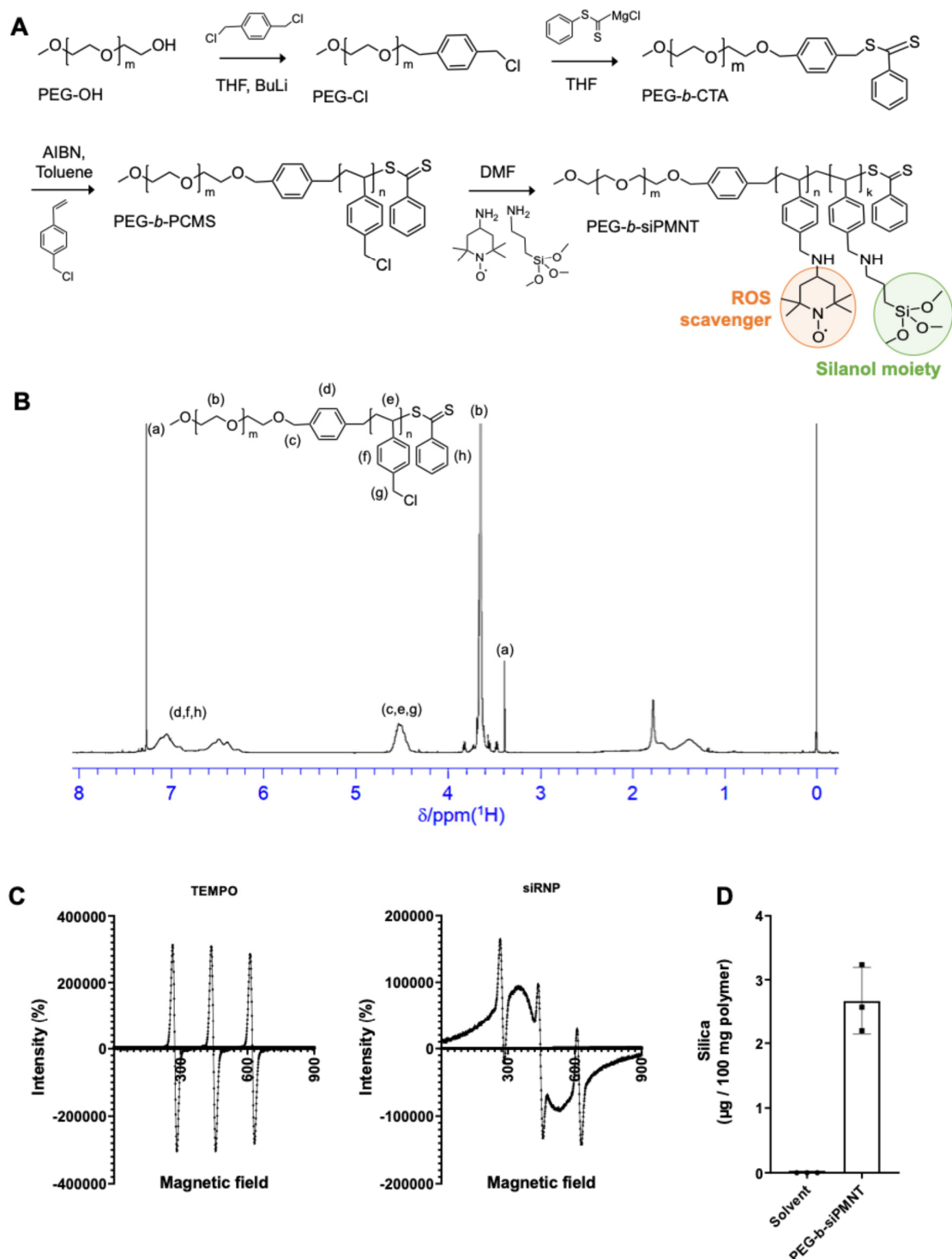
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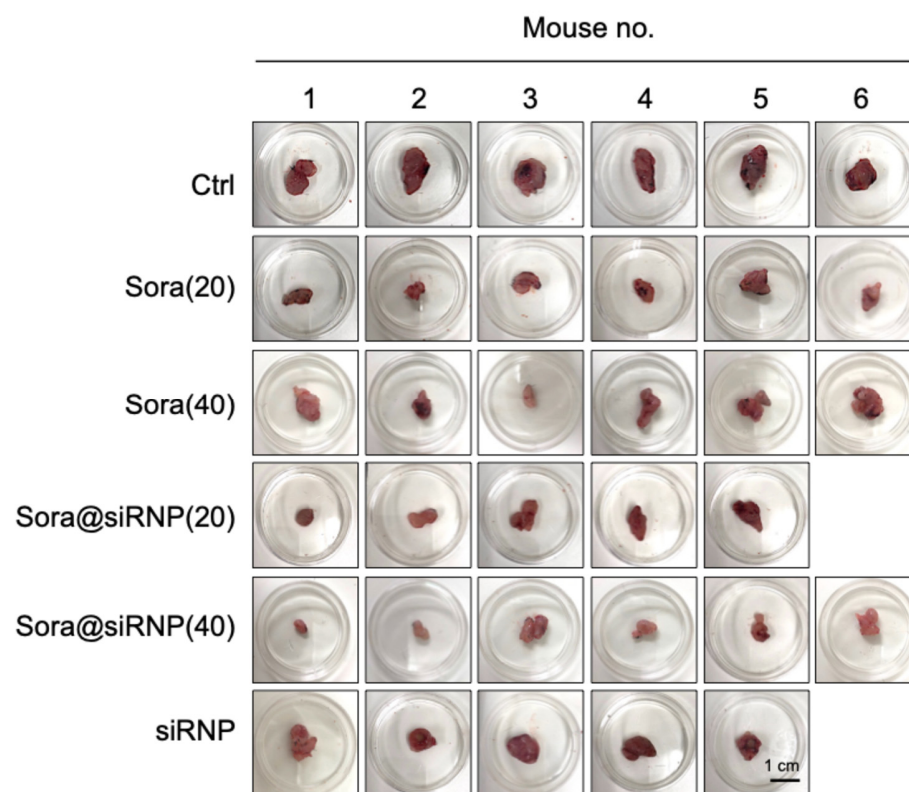
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### *Synthesis of block copolymers PEG-*b*-siPMNT*

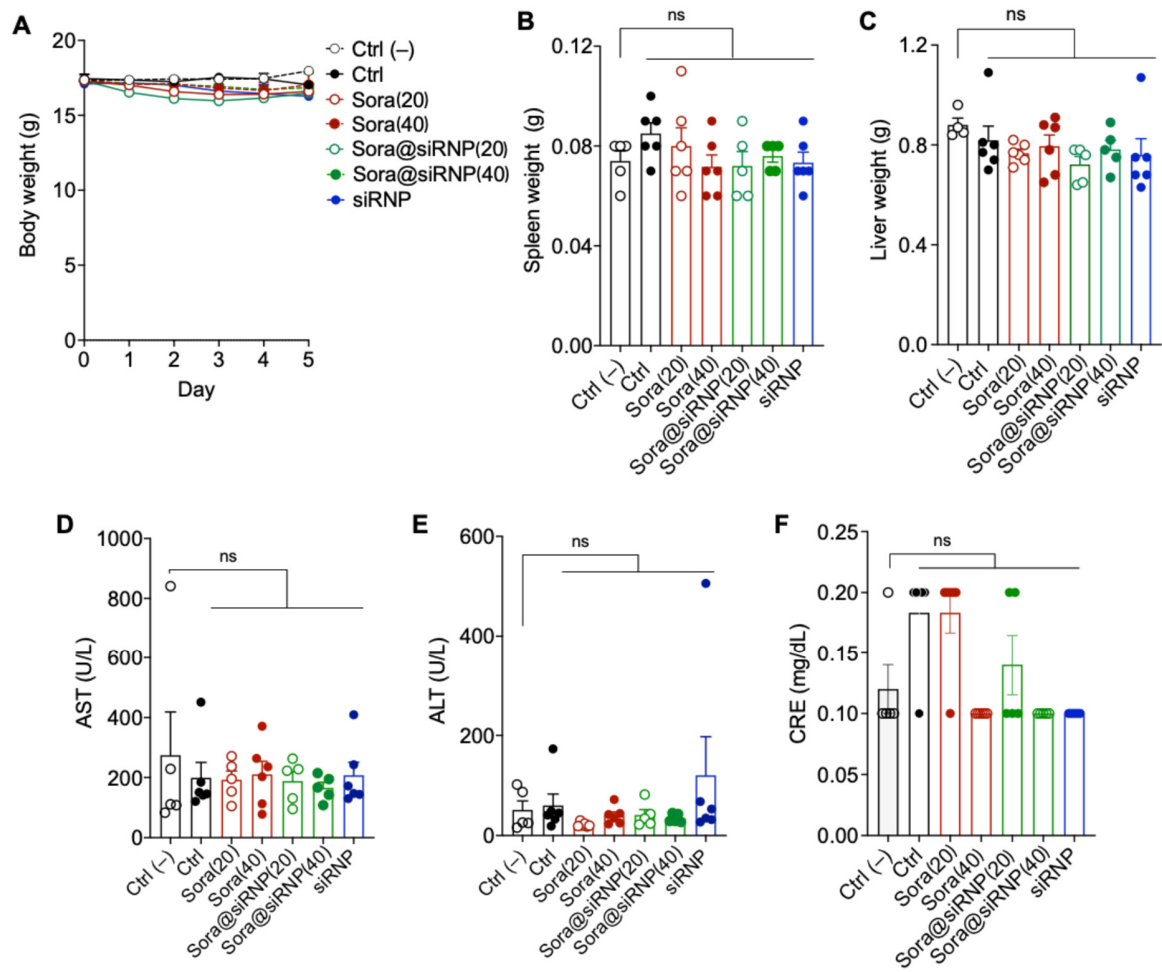
The target antioxidant block copolymer, PEG-*b*-siPMNT, was synthesized with some modifications to our previous reports [7,12]. Briefly, 3-aminopropyltrimethoxysilane (APTMS, 0.3 mL) and 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (4-amino-TEMPO, 2.5 g) in a molar ratio of 1:9 were added to a 4.8 g solution of PEG-*b*-PCMS in dimethylformamide. The mixture was incubated at 40 °C for 24 h to covalently conjugate the compounds to the PCMS segment of the block copolymer, resulting in the formation of PEG-*b*-siPMNT. A similar reaction was conducted without 4-amino-TEMPO to produce a non-antioxidant amphiphilic block copolymer, PEG-*b*-siPCMS.



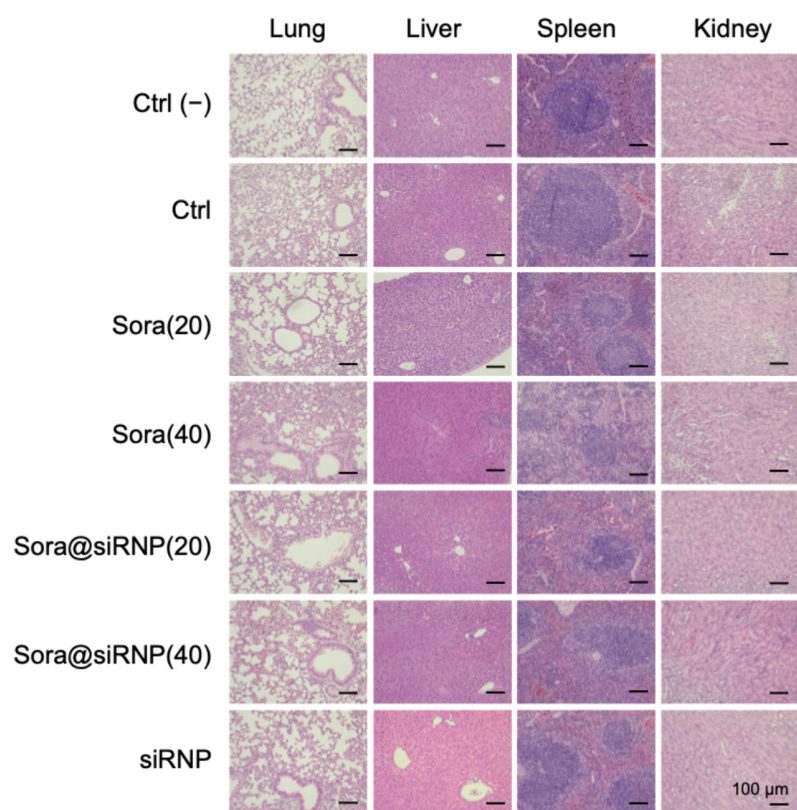
**Figure S1.** Scheme of PEG-*b*-siPMNT synthesis and characterization of siRNP. **(A)** Scheme of PEG-*b*-siPMNT synthesis. **(B)**  $^1\text{H}$ -NMR of pre-polymer PEG-*b*-PCMS dissolved in deuterated chloroform solvent. **(C)** Nitroxide radical signal of TEMPO before and after conjugated to block co-polymer PEG-*b*-PCMS of siRNP. **(D)** The amount of silica in siRNP after dialysis. Values expressed as mean  $\pm$  SD.



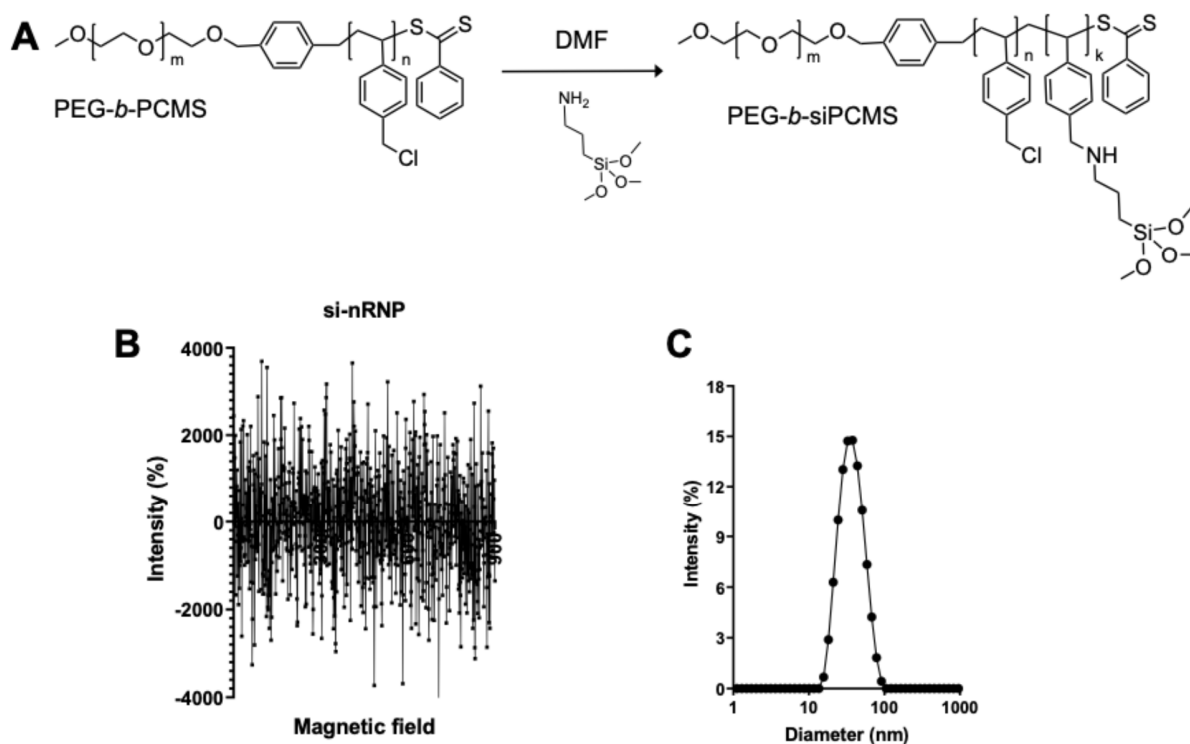
**Figure S2.** Images of extracted tumors from individual mice after treatment with sorafenib and sora@siRNP (n = 5-6 mice/group), scale bar = 1 cm.



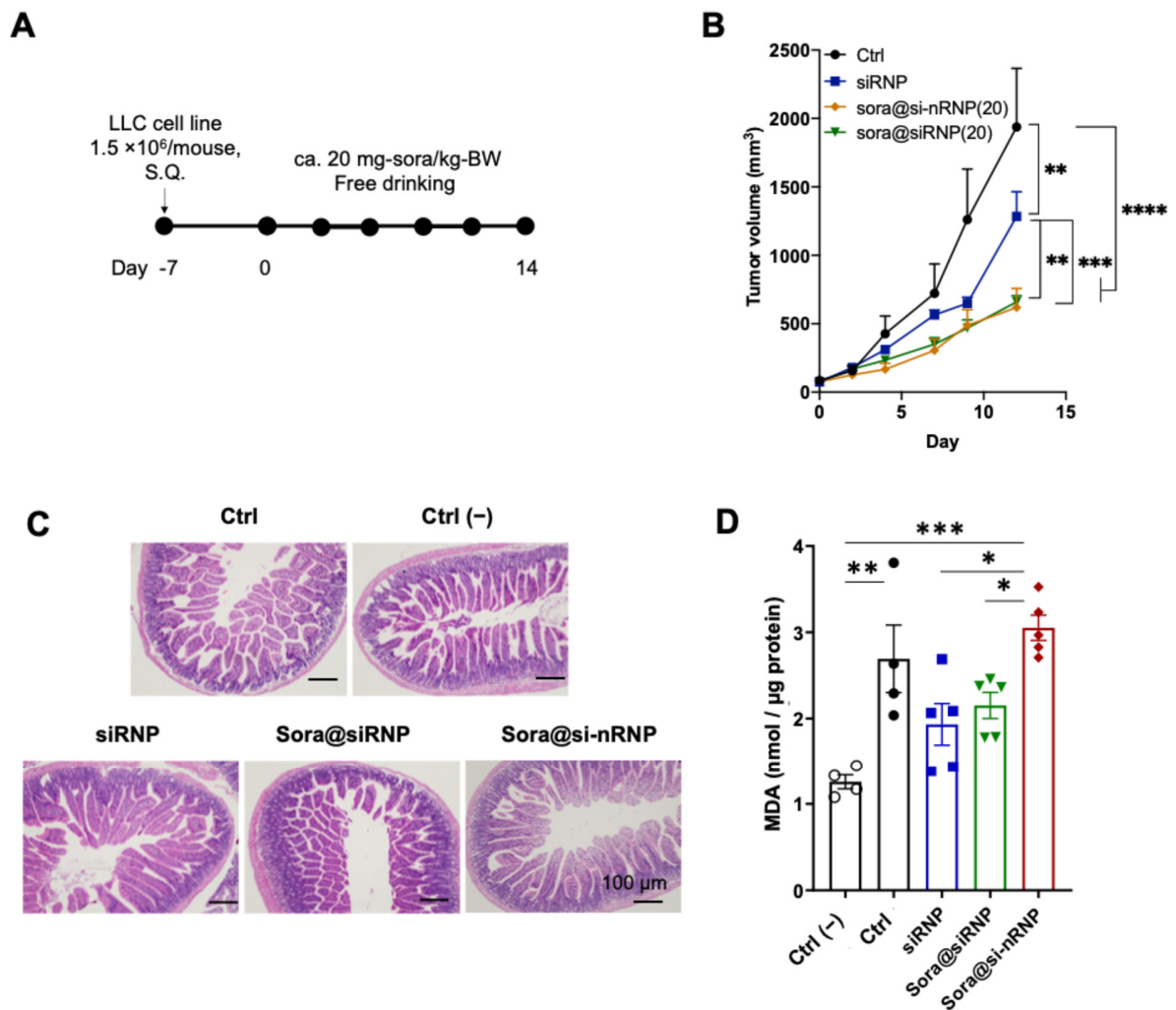
**Figure S3.** Safety evaluation of treatments in LLC-tumor-bearing mice. **(A)** Body weight profile during treatment. Weight of vital organs; **(B)** spleen and **(C)** liver. Plasma organ damage markers; **(D)** AST, **(E)** ALT, and **(F)** CRE. Values expressed as mean  $\pm$  SEM. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , Tukey's Post Hoc test.



**Figure S4.** The HE-stained images of lung, liver, spleen, and kidney.

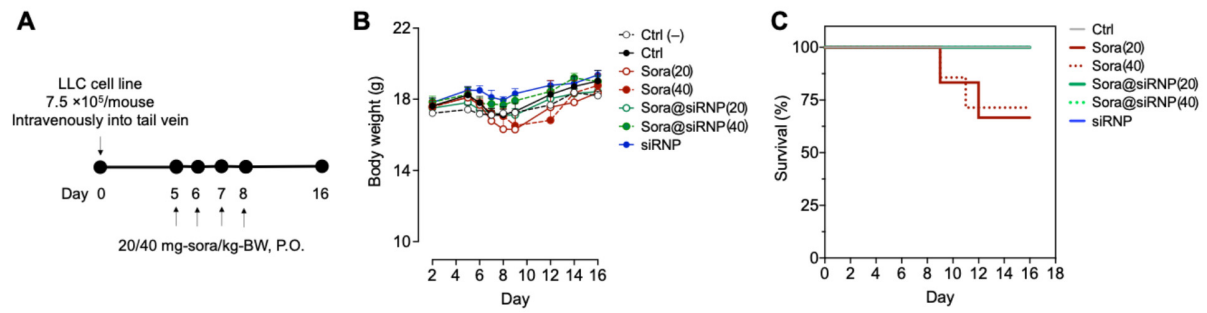


**Figure S5.** Synthesis scheme and characterization of non-antioxidant si-nRNP micelle (no nitroxide radical). **(A)** Scheme of PEG-*b*-siPCMS synthesis [7]. **(B)** ESR signal of obtained PEG-*b*-siPCMS polymer indicating no nitroxide radical in si-nRNP. **(C)** Size distribution of si-nRNP micelle after dialysis using DLS.



**Figure S6.** Efficiency of sora@siRNP treatment in LLC-tumor-bearing mouse model by free drinking (ca. 20 mg-sora/kg-BW). **(A)** The scheme of *in vivo* treatment efficiency of sora@siRNP(20) in LLC-tumor-bearing model. **(B)** The tumor volume of mice during treatment. **(C)** HE-stained sections of small intestine (jejunum). **(D)** Lipid peroxidation (MDA) analysis of small intestine. Values expressed as mean  $\pm$  SEM. \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ , Tukey's Post Hoc test.





**Figure S7.** Survival studies in an experimental metastasis mice model. **(A)** Animal study plan. **(B)** Body weight profile. **(C)** Kaplan–Meier survival curves of mice. Values expressed as mean  $\pm$  SEM.