Supporting Information

Multi-Step Encapsulation of Chemotherapy and Gene Silencing Agents in Functionalized Mesoporous Silica Nanoparticles

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AUTHOR INFORMATION

The authors declare no competing financial interest.

All authors have given approval to the final version of this manuscript.

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Supporting Video 1. Intravital microscopy video of cyclodextrin-grafted polyethyleniminemesoporous silica nanoparticles (CP-MSNP) loaded with doxorubicin (DOX) and small interfering RNA (siRNA)^{FAM} (yellow) in an MDA-MB-231 orthotopic breast cancer tumor. The video was captured 0.5 h post-injection of particles (siRNA, 15 μ g). Tumor blood vessels are shown in blue (bovine serum albumin Alexa Fluor 647 conjugate).



Figure S1. Transmission electron microscopy (TEM) images of mesoporous silica nanoparticles MSNP-OH.



Figure S2. CP-MSNP@DOX-mediated protection of small interfering RNA (siRNA) in serum. Particles were incubated with 50% fetal bovine serum (FBS) at 37 °C for 30 min, 6 h, 12 h, 24 h, 48 h, or 60 h. Samples were run on a 2% agarose gel and stained with ethidium bromide. siRNA, 200 ng.



Figure S3. Viability of MDA-MB-231 breast cancer cells exposed CP-MSNP (20-100 μ g/mL) and CP-MSNP/scrambled siRNA (10-100 nM) for 72 h. Results are presented as mean \pm s.d. of triplicates. PBS, phosphate buffered saline.



Figure S4. Levels of adenosine triphosphate (ATP) in MDA-MB-231 cells exposed CP-MSNP and CP-MSNP/siRNA for 48 h. Scrambled siRNA (Scr) and pyruvate kinase M2 siRNA (PKM2) were used at a dose of 50 nM. Results are presented as mean \pm s.d. of triplicates.



Figure S5. Intravital microscopy image of tumor blood vessels in an MDA-MB-231 orthotopic breast cancer model.



Figure S6. Immunohistochemical staining of PKM2, Ki67, and terminal deoxynucleotidyl transferase mediated dUTP nick end-labeling (TUNEL) in orthotopic MDA-MB-231 breast cancer tumors from athymic nude mice. Mice received weekly intravenous injections of particles for four weeks. Scale bar, $100 \mu m$.



Figure S7. Body weights of mice bearing orthotopic MDA-MB-231 breast cancer tumors. Mice received weekly intravenous injections of PBS, CP-MSNP, CP-MSNP@DOX, CP-MSNP@DOX/Scr, or CP-MSNP@DOX/PKM2 for four weeks. Results are presented as mean \pm s.d. (*n* = 3).



Figure S8. Hematoxylin and eosin (H&E) staining of major organs (heart, liver, spleen, kidney, lungs, and brain). Athymic nude mice bearing orthotopic MDA-MB-231 breast cancer tumors received weekly intravenous injections of CP-MSNP or CP-MSNP@DOX/PKM2 siRNA for four weeks. Scale bar, 100 µm.