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Supporting Information for

A Salt-Assisted Acid Etching Strategy to Hollow Mesoporous Silica/Organosilica for pH-Responsive Drug and Gene Co-Delivery

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A: Experimental Section

1. Materials

Tetraethyl orthosilicate (TEOS), ethanol, sodium carbonate (Na_2CO_3), ammonia solution (25-28%), hydrochloric acid (HCl), sulfuric acid (H_2SO_4), sodium chloride (NaCl), sodium sulfate (Na_2SO_4) were obtained from Sinopharm Chemical Reagent Co.. Octadecyltrimethoxysilane (C_{18}TMS) was purchased from Tokyo Chemical Industry Co. Ltd.. Cetyltrimethyl ammonium bromide (C_{16}TAB), Rhodamine B isothiocyanate (RITC), 1,4-bis(triethoxysilyl)benzene (BTEB) with R = phenylene group were purchased from Sigma-Aldrich. Phosphate buffer solution (PBS) and cell culture medium RPMI 1640 were purchased from Shanghai Runcheng Bio-Tech Co. Ltd. Fetal bovine serum (FBS) and Trypsin-EDTA were obtained from Gibco-BRL (Burlington, Canada). Lyso Tracker Green DND-26 were purchased from Invitrogen (Oregon, USA). Deionized water was used in all experiments. All chemicals were used as received without further purification.

2. Characterization

Transmission electron microscopy (TEM) images were acquired on a JEM-2100F electron microscope operated at 200 kV. Scanning electron microscopy (SEM) images/scanning transimission electron microscopy (STEM) images and corresponding element mapping / EDS spectrum were obtained on a field emission Maggellan 400 microscope (FEI Company). Nitrogen adsorption-desorption isotherms and pore size distribution at 77 K were tested on a Micrometitics Tristar 3000 system. All samples were pretreated for 4 h at 423 K under nitrogen before measurements. The pore size distributions were calculated from desorption branches of isotherms by the Barrett-Joyner-Halenda (BJH) method. Specific surface areas were calculated by the Brunauer_ Emmett_ Teller (BET) method. Ultraviolet / Visible (UV/Vis) spectra were recorded on a UV-3101PC Schimadzu spectroscope. Dynamic light scattering (DLS) measurement was conducted on Zetasizer Nanoseries (Nano ZS90). Inductively coupled plasma atomic emission spectrometry (ICP-AES) test was conducted on VISTA (Varian company, American). The CLSM images were obtained

in FV 1000, Olympus, Japan.

B: Supplementary figures

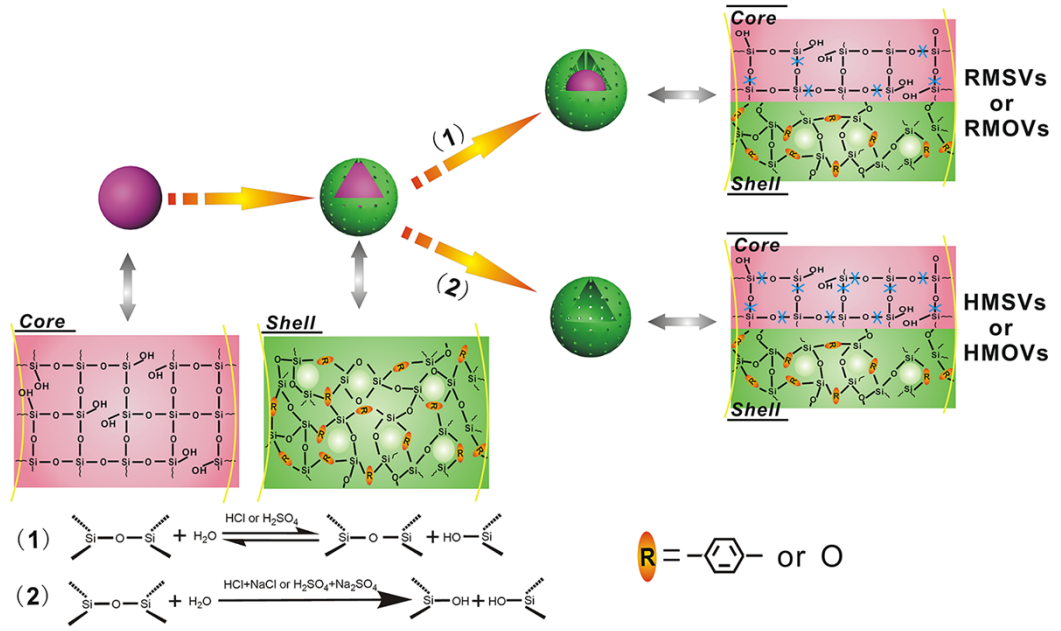

Figure S1. Schematic illustration of the synthetic procedure for R/HMSVs and R/HMOVs employing the acid etchants such as HCl, H_2SO_4 and NaCl, Na_2SO_4. The R moiety within the shell framework is phenylene (aromatic) group or oxygen.

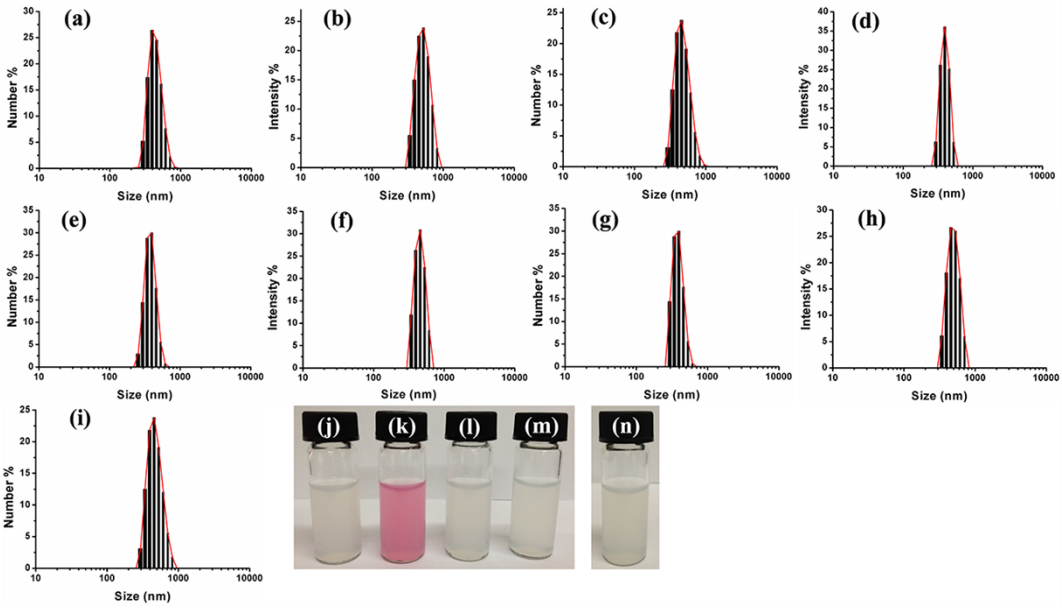

Figure S2. DLS particle size distribution of HMOVs dispersed in water (number-based data a), cell-culture media (intensity-based data b and number-based data c), phosphate buffer solution (PBS, intensity-based data d and number-based data e) and saline solution (intensity-based data f and number-based data g). DLS particle size distribution of HMOVs in water after one month storage (intensity-based data h and number-based data i). The photos j, k, l, m and n are the corresponding nanoparticles dispersions in water, cell-culture media, PBS, saline solution and water after one month storage.

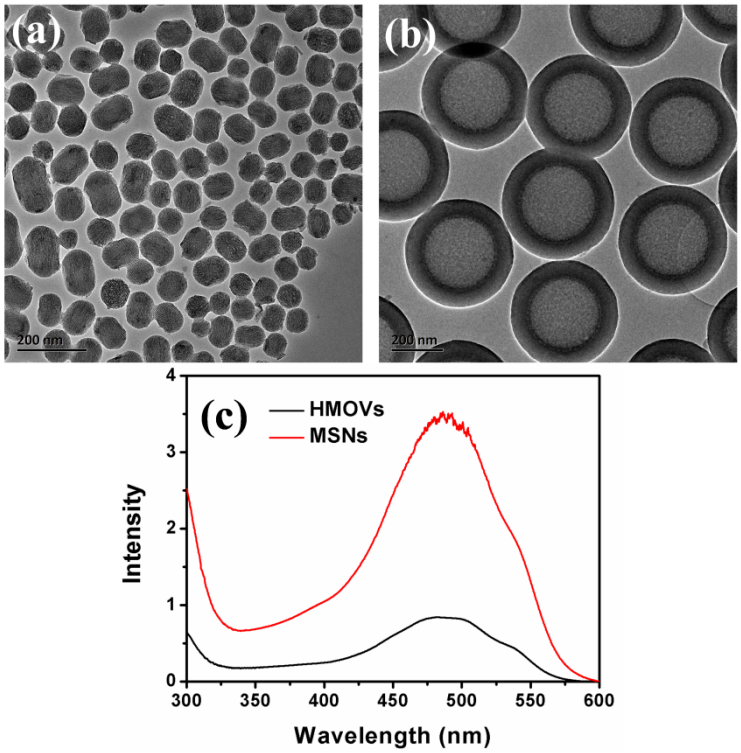

Figure S3. TEM images of MSNs (a) and HMOVs (b). UV-Vis spectra of DOX supernatant solution after loaded in MSNs (a) and HMOVs (b).

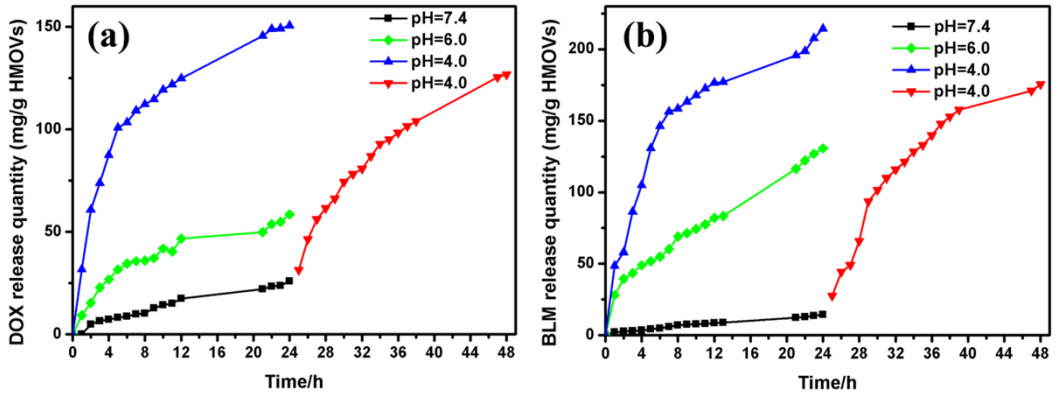

Figure S4. The releasing profiles of anticancer drug (a) DOX and (b) BLM from HMOVs nanosystems at different pH values (7.4, 6.0 and 4.0).

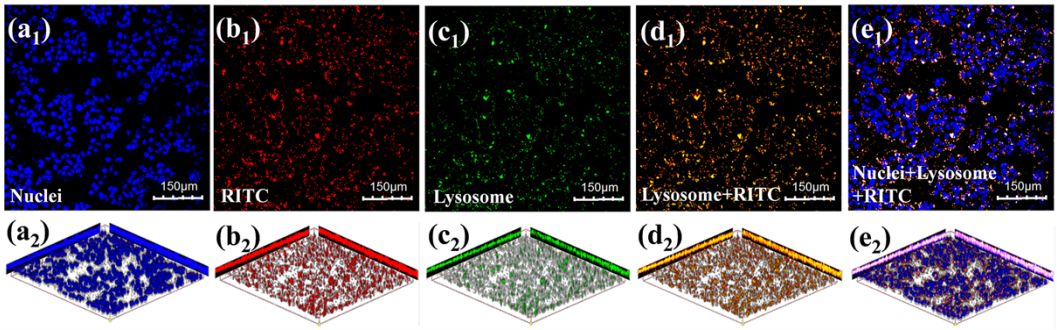

Figure S5. CLSM images of MCF-7/ADR cancer cells after co-incubation with RITC-HMOVs (50 μg/mL) for 4 h. After incubation, the cell nuclei were stained with DAPI and lysosomes were stained with Lyso Tracker Green DND-26, and three-dimensional confocal fluorescence reconstruction images of RITC-HMOVs endocytosed by MCF-7/ADR cancer cells to demonstrate the internalization and intracellular location of nanoparticles within cancer cells (nuclei (a_1 and a_2): blue fluorescence of DAPI staining; HMOVs (b_1 and b_2): red fluorescence of RITC grafting; Lysosomes (c_1 and c_2): green fluorescence of Lyso Tracker Green DND-26 staining); Merged images of red and green fluorescence (d_1 and d_2); merged images of blue, red and green fluorescence (e_1 and e_2).

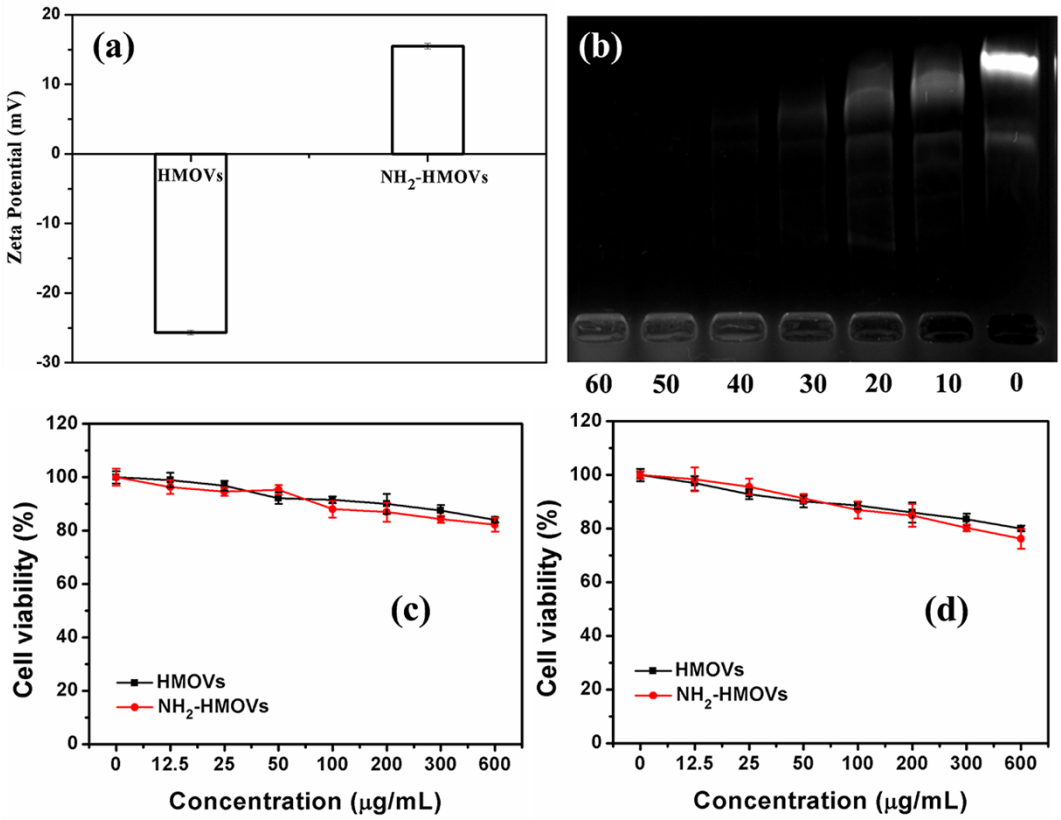

Figure S6. (a) Zeta potentials of HMOVs and NH_2-HMOVs. (b) Gel retardation electrophoresis assay demonstrating the shRNA-nanoparticle complexation at different mass ratio (MR) of NH_2-HMOVs to shRNA (MR=0, 10 , 20, 30, 40, 50 and 60). Cell viabilities of HMOVs and NH_2-HMOVs against MCF-7/ADR cancer cells at different concentrations in 24 h (c) and 48 h (d) of incubation.