Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

for

Integrated Pipeline for Ultrasensitive Protein Detection in Cancer Nanomedicine

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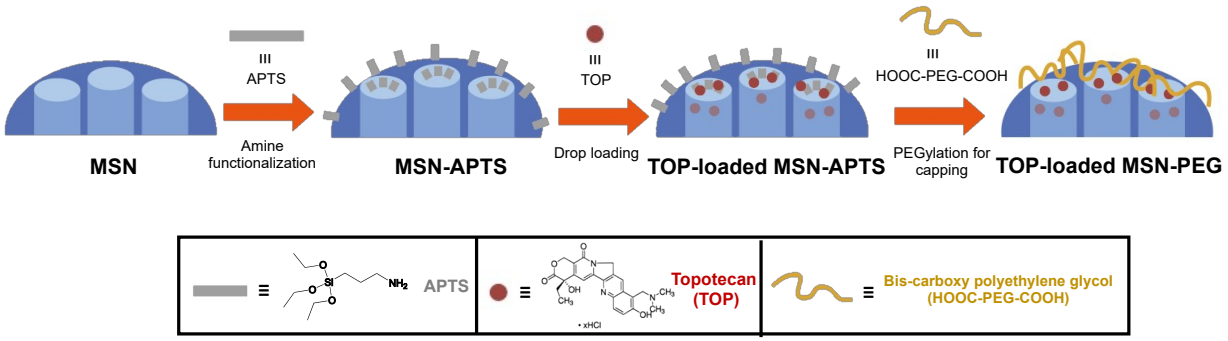
Table of Contents

I. Supporting scheme



Scheme S1: Synthesis of ultrasound-responsive PEGylated mesoporous silica nanoparticles (MSN-PEG)

II. Supporting figures

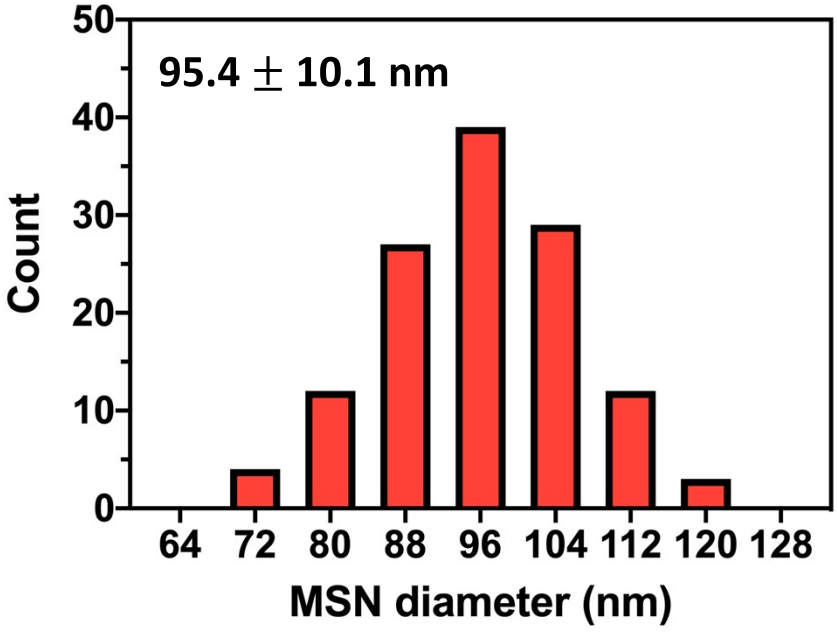


Figure S1. Size distribution of 95.4 ± 10.1 nm mesoporous silica nanoparticle (MSN) calculated from TEM images.

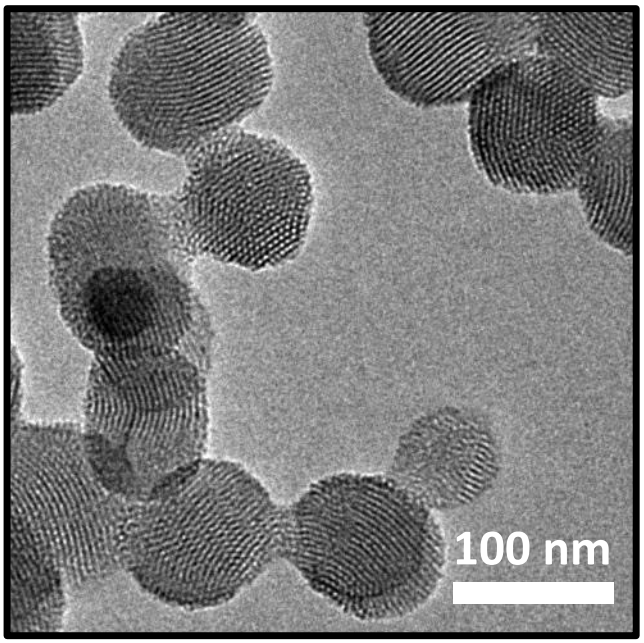


Figure S2. TEM image of MSN-PEG after ultrasound treatment and heating at 50 °C for 30 min.

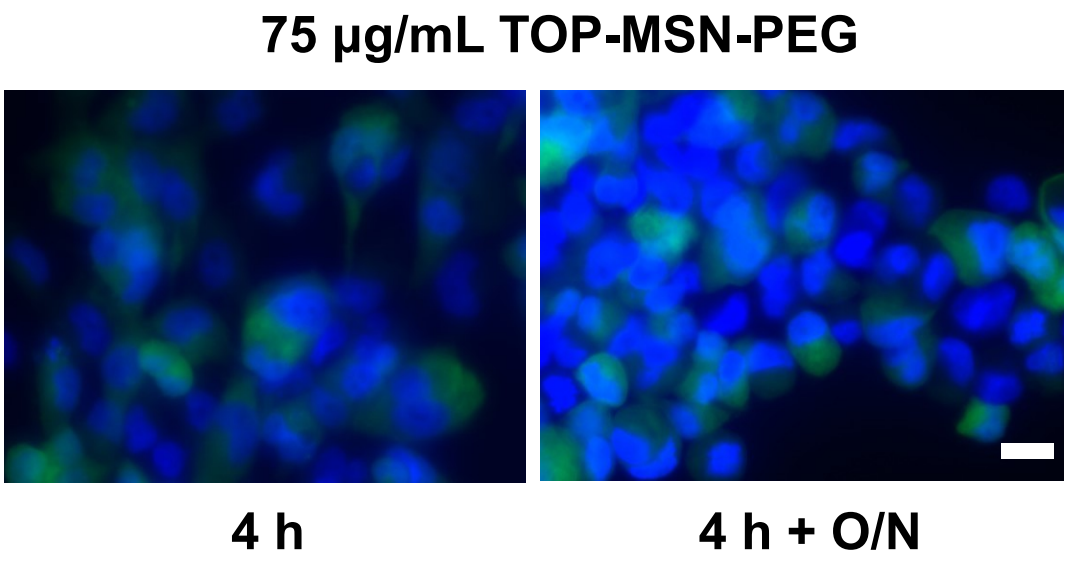


Figure S3. Fluorescence microscope images of OVCAR-3 cells after 4 h treatment of 75 µg/mL TOP-MSN-PEG with and without an additional 20 h of incubation. In the merged images, the blue fluorescence was emitted from Hoechst 33342, which stained the cell nucleus, and the green fluorescence was emitted from TOP molecules carried by TOP-MSN-PEG. The scale bar is 20 µm.

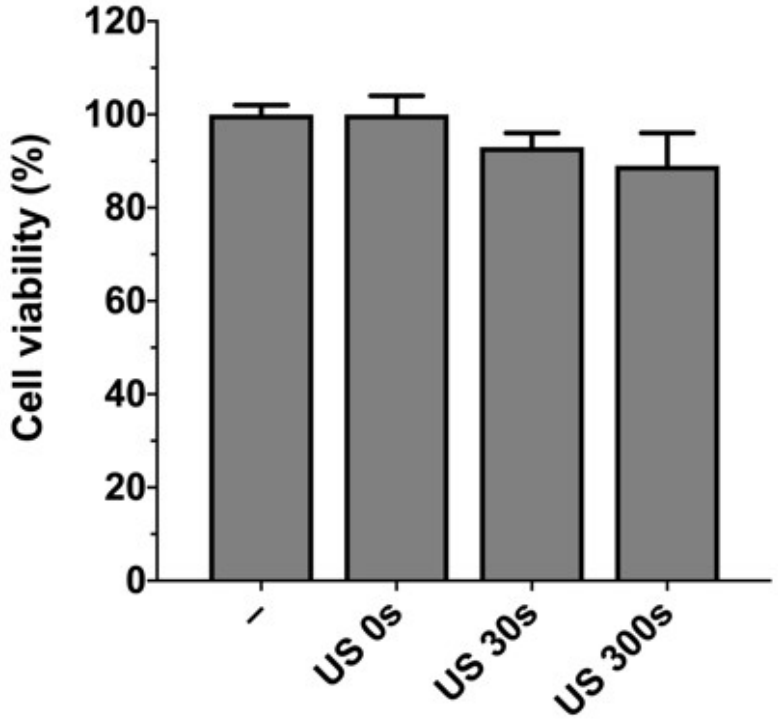


Figure ~~S3~~ S4. Cytotoxicity of the cells incubated with the supernatant obtained from ultrasound-stimulated TOP-loaded MSN-PEG solution. Cell viability was determined by a CCK-8 assay and normalized to the cells without any treatment (control). Data are displayed as the mean (color bar) ± standard deviation (SD) (black brackets) of three independent experiments.

III. Supporting tables

	MSN	MSN-PEG
BET surface area (m^2/g)	1123	142
Pore volume (cc/g)	1.21	0.32
Average pore diameter (nm)	2.4	N/A

Table S1. Brunauer-Emmett-Teller (BET) surface area, total pore volume, and average pore diameter of MSNs and MSNs-PEG analyzed from the N_2 adsorption/desorption isotherms.

Ultrasound parameters (power density; stimulation duration)	Temperature increase (℃)	Cell viability (%)
0 W/cm^2; 0s	0	100
37.5 W/cm^2; 15s	0	100
56.3 W/cm^2; 15s	0	99
56.3 W/cm^2; 30s	1	N/A
56.3 W/cm^2; 60s	2	N/A
75 W/cm^2; 15s	1	93
75 W/cm^2; 30s	2	90
75 W/cm^2; 60s	5	72
75 W/cm^2; 120s	10	59

Table S2. Summary of the temperature increase of the cell supernatant and the cell viability post ultrasound treatments with various ultrasound parameters (power densities and stimulation durations). The initial temperature of the solution was 22ºC.