Electronic Supplemental Information

**Synthesis of Au yolk/LDH shell nanoparticles as anticancer vehicles**

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Experimental Section

Materials. Hydrogen tetrachloroaurate(III) hydrate (Au≧47.8%), sodium citrate dihydrate (99%), Methotrexate (medical grade), tetraethyl orthosilicate (TEOS), 2-propanol (99.7%), NH₃·H₂O (AR grade, 25-28% w/w) were used without further purification.

Synthesis of Au NPs. Au NPs were synthesized using a seed growth method. Briefly, 200 mL of sodium citrate solution in Milli-Q water (2.2 mM) was heated to boiling, 3 mL of HAuCl₄ (24.3 mM) was added. The color of the solution changed from yellow to purple in the period of 15 min. For seed growth progress, immediately after the synthesis of the Au seeds and in the same vessel, the reaction was cooled to 90 °C. Then, 3 mL of sodium citrate (60 mM) and subsequently 3 mL solution of HAuCl₄ (24.3 mM) were sequentially added and recated for another 1 h.

Synthesis of Au@SiO₂. The synthesis was carried out following a modified Stöber method. 0.4 g MTX dissolved by 2 mL ammonia solution and added to the 200 mL resultant citrate-stabilized Au solution under vigorous stirring and gently stirred 24 h. Then the solution is filtered by 0.22 μm film and keep at 4 °C. It should be noted that filter used in MTX-stabilized Au NPs solution is almost clean, while the citrate-stabilized Au NPs’ is dark purple that indicate lots of Au-cit NPs are left on the filter. For SiO₂ coating, 3 mL of the above solution was concentrated (9000 rpm, 15min) to 200 μL to remove excess MTX and citrate. Netx, the complexes were re-dispersed in 4 mL water and added into a mixture of ammonia (0.5 mL) and 2-propanol (20 ml) under vigorous stirring (300 rpm). Finally, various amounts of TEOS (5, 10, 15 μL) in 3 mL 2-propanol were consecutively added to the reaction mixture in 10 min. The
reaction was allowed to proceed for 17 h at room temperature under continuous stirring (200 rpm). After that, the product was isolated by centrifugation and rinsed with ethanol for two times. And then re-dispersed in 10 mL ethanol for further study. Throughout the entire process, the color of the solution remained red, indicating the non-aggregated state of the Au NPs.

**Dissolution of Au@SiO$_2$.** 10 mL attained Au@SiO$_2$ (80 nm in diameter, prepared by 10 μL TEOS) ethanol solution is added to 30 mL PVP (60mg) solution. NaOH adjust the pH value to 10.5 and 11, then the solution is heated to 90 °C for 9 h.

**Synthesis of Au@LDH-MTX.** 10 mL attained previous Au@SiO$_2$ ethanol solution is added to a 25 mL solution containing PVP (60mg), MTX (30mg, dissolved by 0.5 mL 0.1M NaOH). Then 4 ml 0.3 mM Mg(NO$_3$)$_2$ and 0.15 mM Al(NO$_3$)$_3$ mixed solution is added along with the 0.1 M NaOH keeping the pH value at 10.5 and 11, respectively. At last, the solution is reacted at room temperature for 0.5 h and heated to 90 °C for 9 h.

**Synthesis of LDH-MTX.** A mixed salt solution, containing 0.032 mol/L Mg$^{2+}$ and 0.016 mol/L Al$^{3+}$ with ethanol/water (volume ratio of 1:3) as solvent, was first prepared. MTX was dissolved into 15 mL 10% NH$_3$·H$_2$O to obtain a 0.05 mol/L solution. Then, the mixed salt solution was added to the MTX solution at a constant rate of 3 mL/min, and the final solution was adjusted to pH 9.5 by adding a certain amount of 10% NH$_3$·H$_2$O. Followed by vigorous stirring for 1 h at 60 °C, the products were washed several times with deionized water and ethanol. Finally, the product was transferred into a Telfon-lined stainless steel autoclave with 80 °C hydrothermal
treatment for 24 h.

**In vitro bioassay** Cells were routinely cultured at 37 °C in a humidified atmosphere with 5% CO₂ in 75 cm² flasks containing 10 mL of Dubecco’s modified eagle medium (DMEM) supplemented with 10% fetal bovine serum (FBS), and 100 U/mL penicillin and 100 mg/mL streptomycin. When the cells were grown to 80-90% cellular confluence, the fault culture cells were differentiated with trypsin-EDTA and then washed twice with PBS (pH=7.4), which was previously prepared. Then, the cells were diluted with a volume of DMEM containing 10% FBS. For cell proliferation and viability studies, the cells were seeded onto 96-well plates and were incubated overnight at 37 °C under a 5% CO₂ atmosphere. After that, the medium in the wells was replaced with fresh medium containing Au@LDH-MTX, MTX and LDH-MTX and further incubated for 24 or 48 h. The effect of the nanoparticles on cell proliferation was determined using an MTT (a yellow tetrazole) assay. Briefly, after the supernatant was removed, 10 μL of MTT (5 mg·mL⁻¹ in PBS, pH=7.4) stock solution and 90 μL DMEM with no FBS were added into each well and further incubated for 4 h at 37 °C. During the incubation, MTT was reduced to insoluble purple formazan by mitochondrial reductase in the living cells. Afterwards, the product was dissolved with 100 μL of dimethylsulfoxide (DMSO). Absorbance was recorded at 570 nm on a microplate reader (Thermo MK3, USA).
**Fig. S1** The chemical structure of MTX.

**Fig. S2** TEM image of the resultant materials using Au-cit NPs for SiO₂ coating.

**Fig. S3** TEM image of the prepared LDH-MTX.