**Supporting Information**

## Materials and methods

### General procedures

Transmission electron micrograph (TEM) images were recorded with JEOL 1200 EXII microscope and with Titan G2 80-300 CT from FEI company (Hillsboro, OR) which was equipped with a post-column energy filter of model GIF tridium 863 from Gatan-Inc. For the purpose of TEM analysis, the sample particles were dispersed in ethanol and then dropped onto copper grids with porous carbon films. BET analyses were performed using a gas adsorption analyzer instrument. The specific area and pore structure parameters of the studied NPs were determined from the measurements of nitrogen adsorption-desorption at 77 K, the sample was degassed under vacuum at 353 K for 8 h. Absorption spectra were recorded on a Hewlett-Packard 8453 spectrophotometer The organization of the porous framework is controlled by XRD and performed with a PANalytical X'Pert MPD (Philips 1710) diffractometer.

### Materials

Absolute ethanol, cetyltrimethylammonium bromide (CTAB), sodium hydroxide, ammonium nitrate, Potassium bromide, bis(triethoxysilyl)ethane, (3-aminopropyl)triethoxysilane and bis[3-(triethoxysilyl)propyl] tetrasulfide were purchased from Sigma-Aldrich. Trisodium citrate dihydrate and hydrogen tetrachloroaurate (III) hydrate from Alfa Aesar. Gemcitabine monophosphate was purchased from Toronto Research Chemicals.

Synthesis of Au-TS nanoparticles.

Gold nanoparticles of 13 nm of diameter (Fig. S1) were obtained from the reported Frens method. 200 mL of solution of $HAuCl_4$ (1 mmol) heated at 110°C to boiling under reflux, then a 3 mL of $Na_3$-citrate (1 mmol) reducing agent was added under vigorous stirring for 30 minutes. The resulting solution was then cooled at room temperature.

For the synthesis of Au@E-TS, a solution of 5 mL of the previously proposed solution of Au NPs was diluted in 10 mL of water. Then 100 µL of APTES was added to stabilize the Au NPs. Note that, the addition of 100 µl of APTES was carried out in five times and under sonication.

Then, 62 mg of CTAB and 200 µL of sodium hydroxide (2M) mixed in 25 mL of ultra pure water stirred at 50°C in three neck bottom flask. After 30 minutes, 15 mL of the solution of gold NPs previously sonicated for 30 second, was added quickly under stirring at 1300 rpm. Then, a solution of 1, 2-bis (triethoxysilyl) ethane (43.2 µL) and bis [3-(triethoxysilyl)propyl] tetrasulfide (50.4 µL) was added. The condensation process was conducted for 2h. Afterwards, the solution was cooled at room temperature and collected by centrifugation for 25 minutes

at 12 Krpm. The sample was then extracted three times with an alcoholic solution of ammonium nitrate (6 g. $L^{-1}$) and washed three times with ethanol. Each extraction involved a sonication step of 30 minutes in order to remove the CTAB surfactant. The as-prepared material was dried for few hours under vacuum.

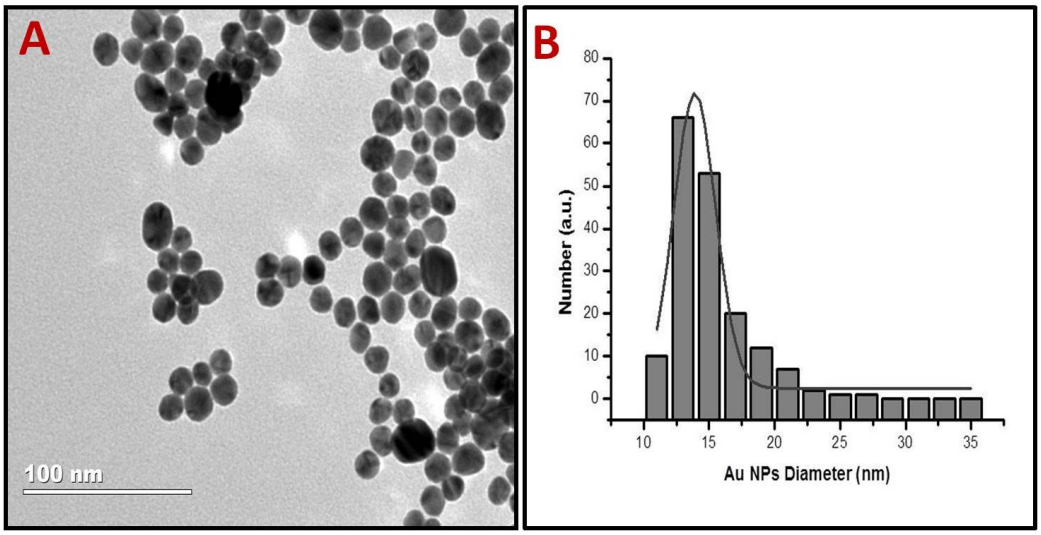


**Figure S 1.** TEM images (A) and size distribution of gold nanoparticles (B)

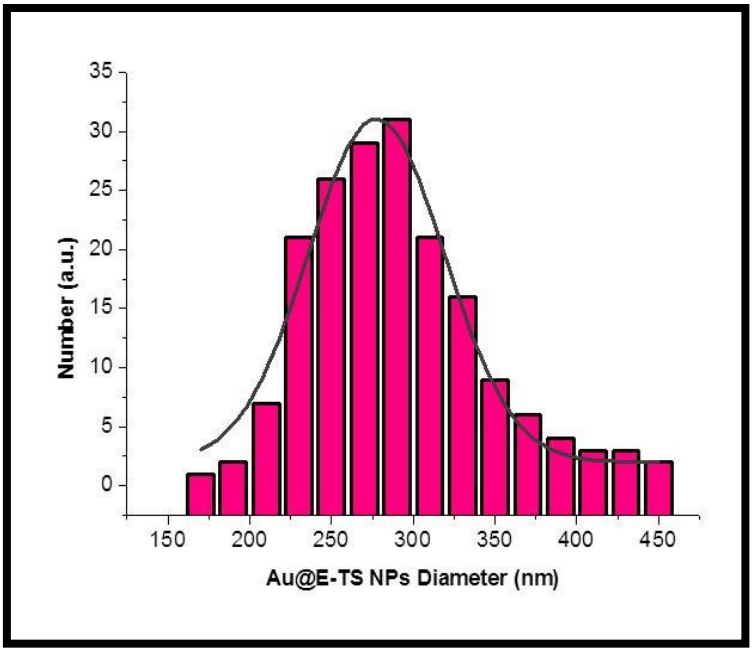


**Figure S 2.** Distribution size of Au@E-TS NPs

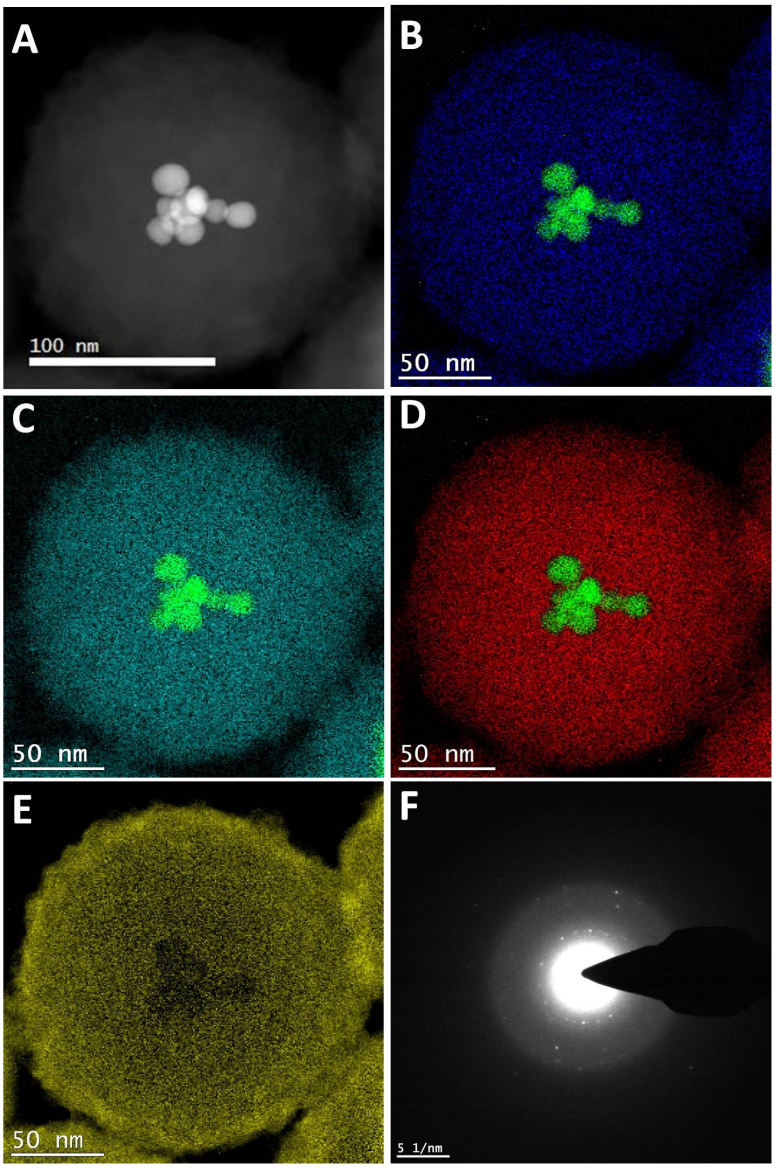


**Figure S 3.** TEM (DF-STEM) (A), Elemental mapping of oxygen (B), carbon (C), sulfur (D) and silicon (E). Fast Fourier transform (FFT) of the SI image (F)

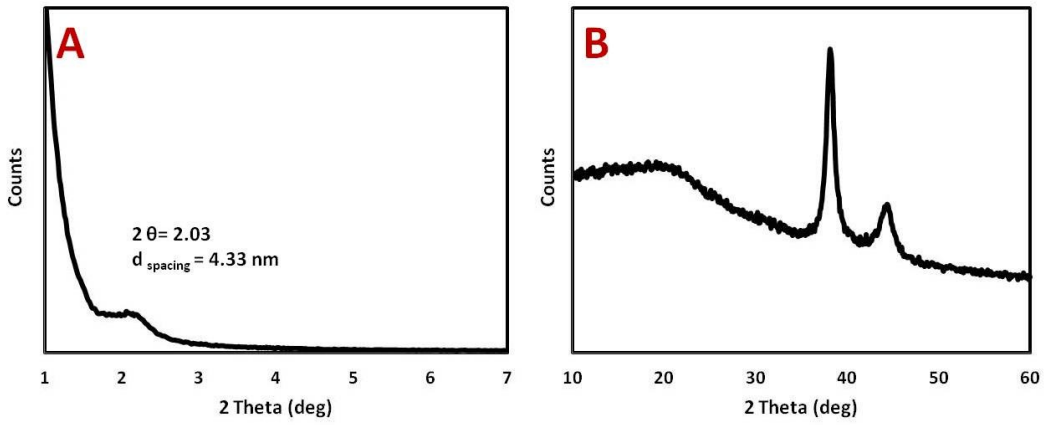


**Figure S 4.** XRD pattern of Au@E-TS nanoparticles at low (A) and wide angles (B)

## Gemcitabine monophosphate (GMP) loading of Au@E-TS NPs.

A mixture of Au@E-TS nanoparticles (7.5 mg), GMP (3 mg), and deionized water (2 mL) was prepared in tube, sonicated for 10 min. Then, the solution was stirred at room temperature for 48h. Finally, the Au@E-TS NPs were collected by centrifugation for 10 min at 12000 rpm and washed three times with water, and dried for few hours under vacuum.

The loading capacities were deduced by the titration of in the supernatant fractions.

Loading Capacity (wt %) = [mass of loaded drug/ (mass of loaded drug+ mass of NPs)]* 100

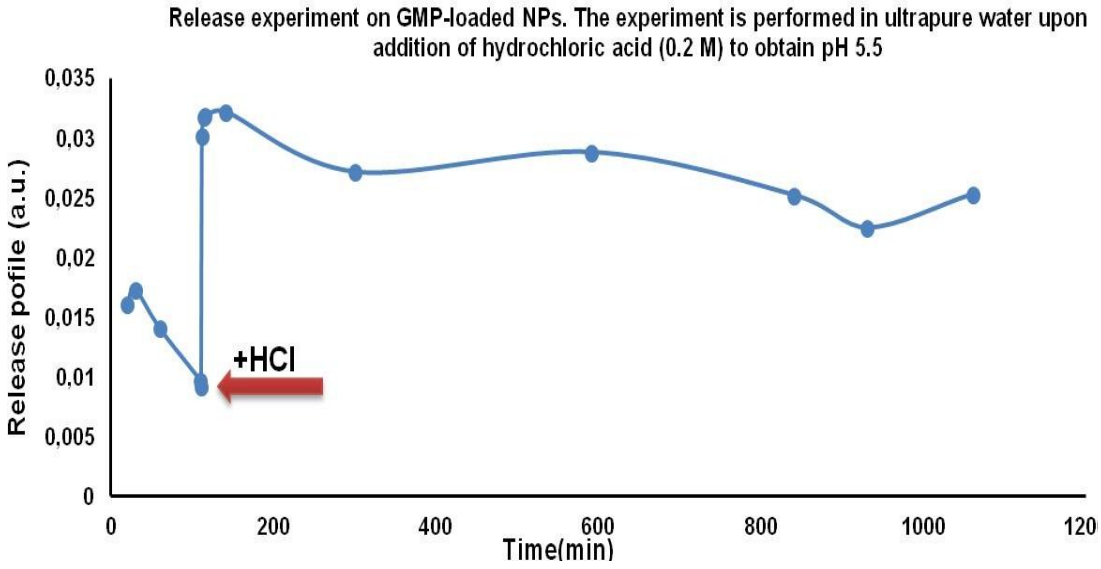


**Figure S 5.** Release experiment on GMP-loaded NPs monitored by absorbance of GMP at 270 nm.

## In vitro studies

### Cell culture

MDA-MB-231 were purchased from ATCC (American Type Culture Collection, Manassas, VA). Cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM-F12) supplemented with 10% foetal bovine serum and 50 $\mu g.mL^{-1}$ gentamycin. These cells were allowed to grow in humidified atmosphere at 37°C under 5% CO2.

### Cytotoxic study

MDA-MB-231 cancer cells were seeded into 96-well plates at 500 cells per well in 200 µL culture medium and allowed to grow for 24 h. Increasing concentrations of POR-organosilica NPs with or without Gemcitabine were added in culture medium of MDA-MB-231 cells. Three days after treatment, a MTT assay was performed to determine the drug delivery potential of the nanoparticles. Briefly, cells were incubated for 4 h with 0.5 $mg.mL^{-1}$ of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; Promega) in media. The MTT/media solution was then removed and the precipitated crystals were dissolved in EtOH/DMSO (v/v). The solution absorbance was read at 540 nm in a microplate reader.

#### TPE- Imaging

MDA-MB-231 cancer cells were plated onto bottom glass dishes (World Precision Instrument, Stevenage, UK) at a density of $10^6$ $cells.cm^{-2}$. Twenty four hours after seeding, cells were then washed once and incubated in 1 mL culture medium containing Au@E-TS NPs at a concentration of 80 $\mu g.mL^{-1}$ for 24 h. Fifteen min before the end of incubation, cells were loaded with CellMask™ plasma membrane stain (Invitrogen, Cergy Pontoise, France) at a final concentration of 5 $\mu g.mL^{-1}$. Prior the observation, cells were washed gently with phenol red-free DMEM. Cells were then visualized with a LSM 780 LIVE confocal microscope (Carl Zeiss, Le Pecq, France), at 750 nm using a high magnification (63x/1.4 OIL DIC Plan-Apo).