**Supplementary information**

**HA/PEI-coated Acridine Orange-loaded gold-core silica shell nanorods for cancer-targeted photothermal and chemotherapy**

**1. Methods**

**1.1. Photothermal conversion efficiency evaluation**

The AuMSS and AuMSS/PEI/HA nanoformulations’ photothermal conversion efficiency was calculated through the following equations:

η= (Equation S1)

*hS*= (Equation S2)

**Tmax** represents the maximum value of the temperature recorded in the medium; **Tamb** is the room temperature; **Qdis** corresponds to the heat dissipated from the light absorbed by the medium and container; **I** represent the intensity of the NIR laser (1.7), and **A808** is the absorbance of AuMSS nanoformulations at 808 nm. The value of ***hS*** was calculated from equation S2, where***h*** represents the heat transfer coefficient and ***S*** is the container’s surface area. **m** represents the water mass (0.2 g), **C** is the heat capacity of water (4.2 J/g °C) and the **s**is the sample system time constant that is calculated through the following equations:

s= - (Equation S3)

Ɵ= (Equation S4)

**t** represent the nanoparticles irradiation time (600 s) and **Ɵ** can be determined through the equation S4. **Tmax** represents the maximum value of the temperature recorded in the medium; **Tamb** is the room temperature (25°C).

**2. Results**

**2.1. Synthesis of PEI-TESPIC polymer**

The silane-modified PEI was obtained by promoting the TESPIC linkage to the PEI backbone through a hydrogen-transfer nucleophilic addition reaction between the amine groups of PEI and the isocyanate groups of TESPIC (Figure S1).



**Figure S1**: Schematic synthesis of PEI-TESPIC polymer.



**Figure S2**: FTIR spectrum of PEI-TESPIC polymer.

**2.2. Synthesis and characterization of AuMSS-based nanomaterials**

The chemical linkage of the PEI-TESPIC was performed by promoting its grafting on the AuMSS nanorods’ surface. Afterward, the linkage of HA to the obtained AuMSS/PEI nanoparticles was performed by promoting electrostatic interactions between the positively charged amine groups on PEI and negatively charged hydroxyl groups on HA.

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**Figure S3 –** Schematics of AuMSS functionalization’ approaches with the PEI and HA polymers.

**2.3. Evaluation of the photothermal properties of AuMSS-based nanomaterials**



**Figure S4 -** Photothermal conversion efficiency of AuMSS and AuMSS/PEI/HA nanorods. Data are presented as mean±s.d., n=3.

**2.4. Evaluation of AO cytotoxic effect in HeLa cells.**

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**Figure S5 -** Dose-response curve of AO in HeLa Cells.

**2.5. Hemocompatibility of AuMSS nanoformulations**



**Figure S6 -** Optical images of the blood supernatants and RBCs pellet recovered after AuMSS, AuMSS/PEI and AuMSS/PEI/HA nanorods incubation for 24h. PBS was used as negative control (K-) and Triton-X 100 was used as a positive control for red blood cells’ lysis (K+).

**2.6. Evaluation of 2D therapeutic effect mediated AuMSS nanoformulations**

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**Figure S7 -** Analysis of the cytotoxic activity of AuMSS and AuMSS/PEI/HA (100 µg/mL), with or without AO encapsulation or NIR laser irradiation (5min). Negative control (K-): cells without nanoparticles incubation; NIR control (K NIR): cells without nanoparticles incubation and irradiated with NIR laser (808 nm, 1.7 W/cm2, 5 min). Data are presented as mean ± standard deviation, n=5.