Supporting Information

Mesoporous silica nanoparticles grafted with light-responsive protein shell for highly cytotoxic antitumoral therapy.

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Reagents.

Following compounds were purchased from Sigma-Aldrich Inc.: Avidin from egg white (powder, 10-15 U/mg protein (E1%/280), ≥98% (SDS-PAGE)), Streptavidin from *Streptomyces avidinii* (10 mM potassium phosphate, ≥13 U/mg protein), Biotin (≥99% (TLC)), Transferrin human (powder, suitable for cell culture), N,N'-Dicyclohexylcarbodiimide (DCC), N-hydroxysuccinimide (NHS), Doxorubicin hydrochloride (European Pharmacopoeia), Oxaliplatin, Tris(2,2´-bipyridyl)dichlororuthenium (II) ($[Ru(bipy)_3]Cl_2$), (+)-Biotin N-hydroxysuccinimide ester (NHS-B), aminopropyltriethoxysilane (APTES), ammonium nitrate, cetyltrimethylammonium bromide (CTAB), tetraethyl orthosilicate (TEOS). Fmoc-photolinker was purchased from abcr. All other chemicals (absolute ethanol, acetone, etc.) were of the best quality commercially available and they have been employed as received.

Characterization techniques.

Powder X-ray diffraction (XRD) experiments were performed with a Philips X'Pert diffractometer equipped with Cu Kα radiation (wavelength 1.5406 Å). XRD patterns were collected in the 2θ range between 0.6º and 8 with a step size of 0.02º and counting time of 5 s per step. Fourier transform infrared spectroscopy (FTIR) in a Thermo Nicolet nexus equipped with a Goldengate attenuated total reflectance device. The textural properties of the materials were determined by nitrogen sorption porosimetry by using a Micromeritics ASAP 2010. To perform the N_2 measurements, the samples were previously degassed under vacuum for 24 h at room temperature. Thermogravimetry analysis (TGA) were performed in a Perkin Elmer Pyris Diamond TG/DTA analyzer, with 5 ºC/min heating ramps, from room temperature to 600 ºC. The hydrodynamic size of mesoporous nanoparticles was measured by means of a Zetasizer Nano ZS (Malvern Instruments) equipped with a 633 nm "red" laser. Mass spectra were acquired with a Voyager DE-STR Biospectrometry MALDI-TOF mass spectrometer. Transmission electron microscopy (TEM) was carried out with a JEOL JEM 1010 instrument operated at 100 kV, equipped with a CCD camera (KeenView Camera). Sample preparation was performed by dispersing in distilled water and subsequent deposition onto carbon-coated copper grids. Scanning electron microscopy (SEM) analyses were made on a JEOL 6400-LINK AN10000 microscope (Electron Microscopy Centre, UCM). The samples underwent Au metallization previous to observation.

Calculation procedures.

The surface area was determined using the Brunauer-Emmett-Teller (BET) method and the pore volume, V_{pore} ($cm^3 \cdot g^{-1}$), was estimated from the amount of N_2 adsorbed at a relative pressure around 0.99. The pore size distribution between 0.5 and 40 nm was calculated from the desorption branch of the isotherm by means of the Barrett-Joyner-Halenda (BJH) method. The mesopore size, $Ø_{pore}$ (nm), was determined from the maximum of the pore size distribution curve.

FIGURES

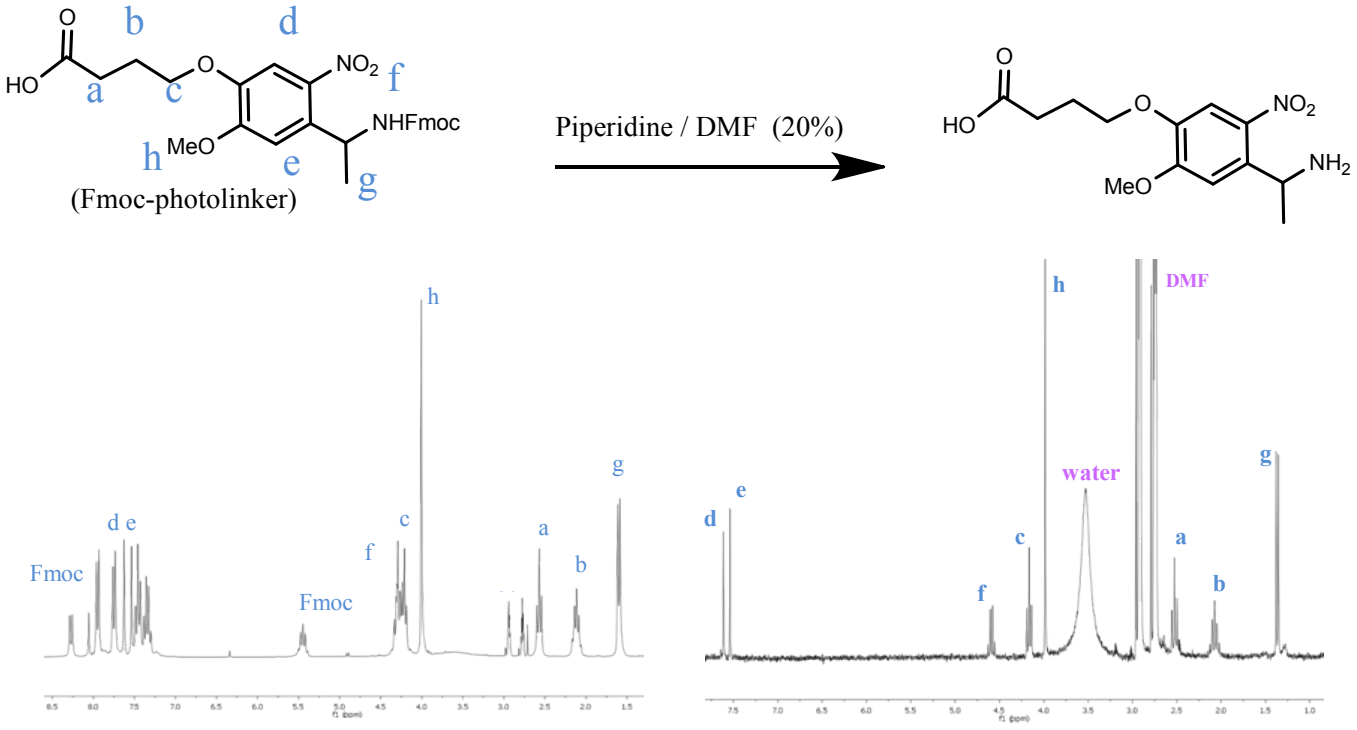

Figure S1. ^{1}H-RMN of Fmoc-photolinker and photolinker deprotected (PhoL1)

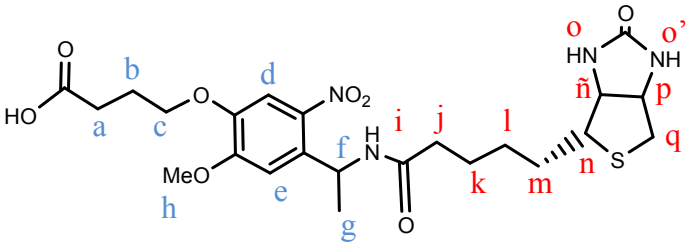

Figure S2. ^{1}H-RMN of the biotin-photolinker (PhoL2)

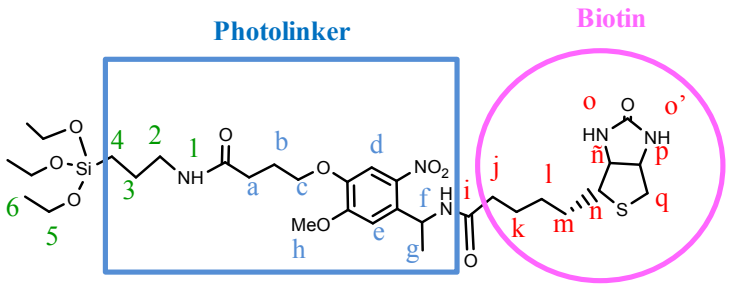

Figure S3. ^{1}H-RMN of the silated biotin-photolinker (PhoL3)

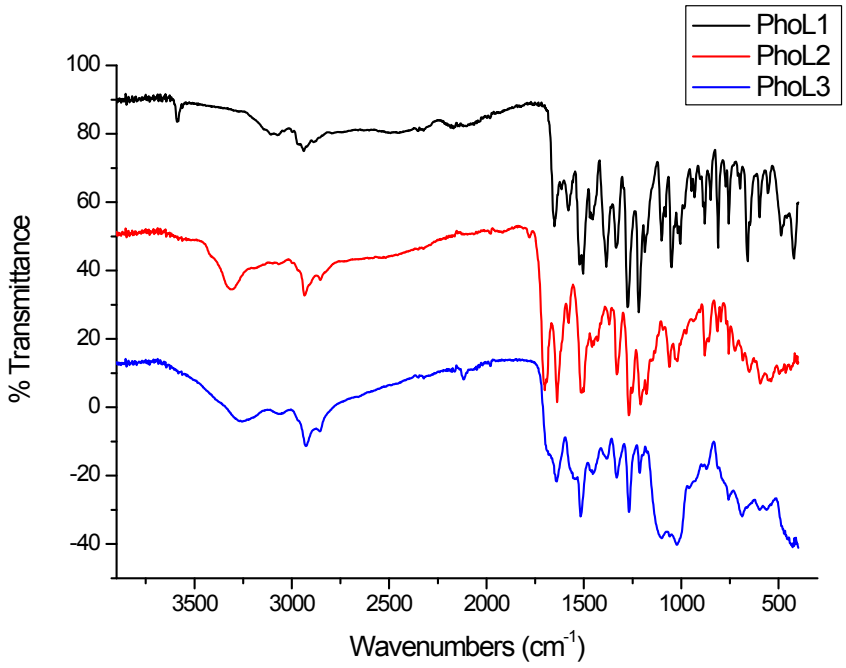

Figure S4. IR spectrum of PhoLX

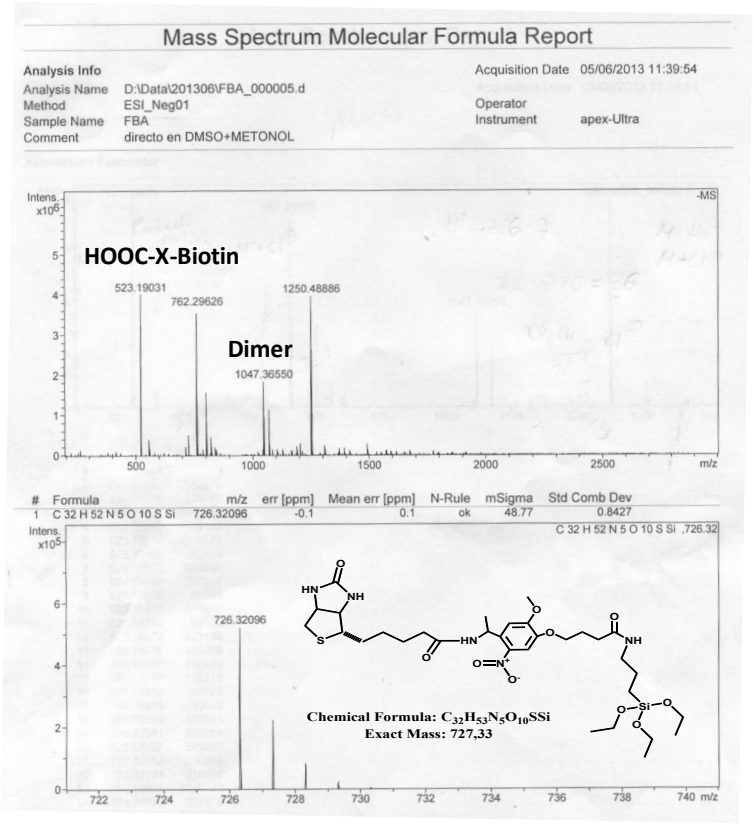

Figure S5. Mass Spectrum of PhoL3

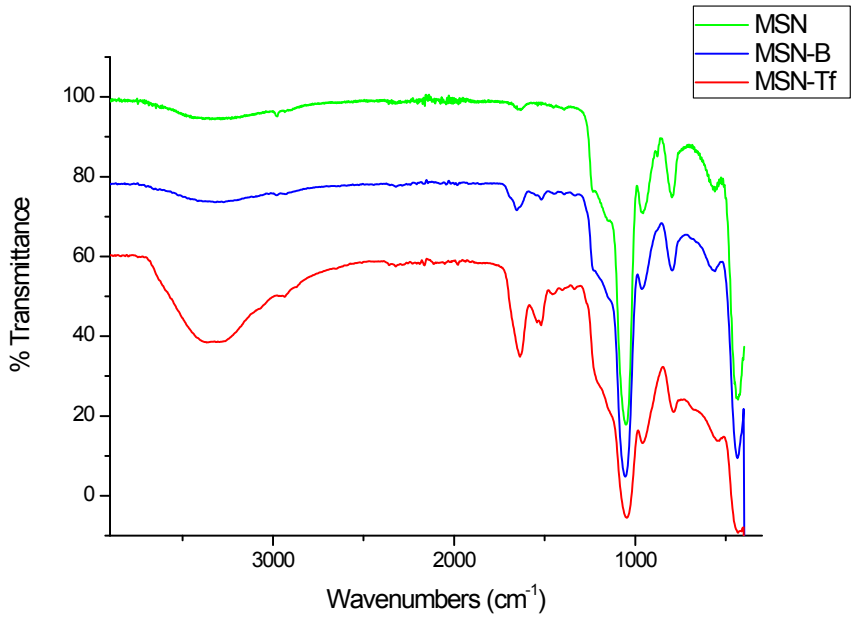

Figure S6. IR spectrum of MSN materials

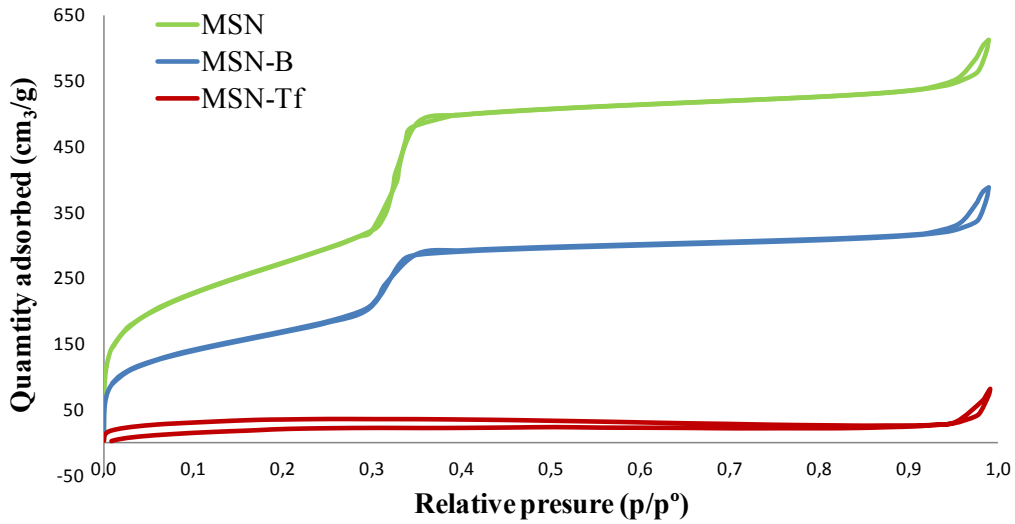

Figure S7. Isotherm linear plot of MSN materials

Sample	BET Surface ($m^2 \cdot g^{-1}$)	V_{pore} ($cm^3 \cdot g^{-1}$)	Φ_{pore} (nm)
MSN	**951.82**	**0.863**	**2.4**
MSN-B	**580.60**	**0.516**	**2.4**
MSN-Tf	**120.73**	**0.061**	**-**

Table S1. Textural parameters of MSN materials

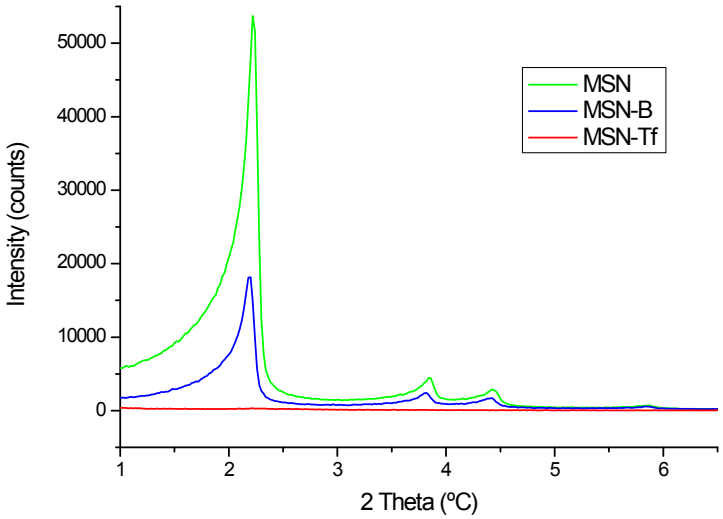

Figure S8. Small-angle XRD pattern of MSN materials

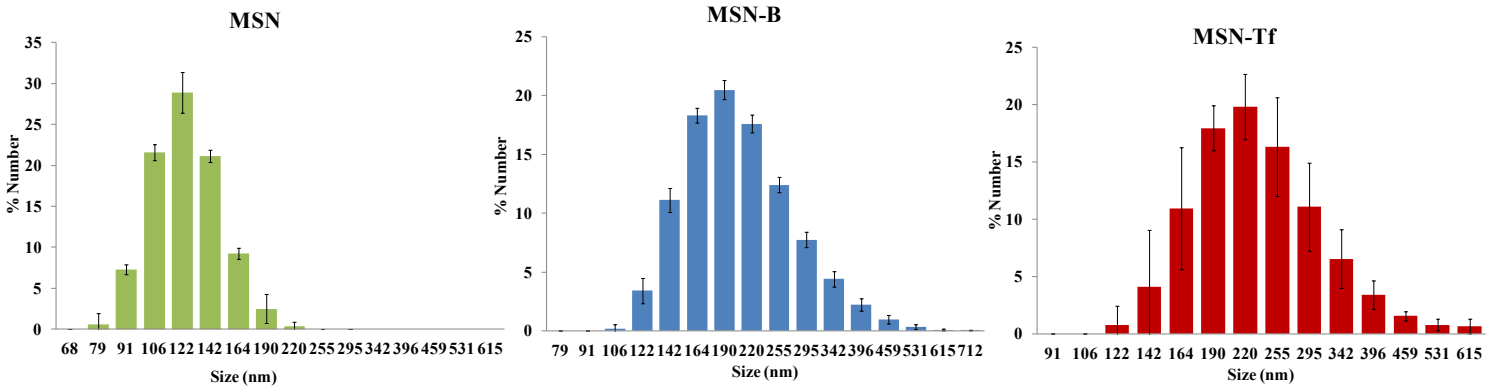

Figure S9. DLS measurements of MSN materials.

Sample	M	$\bar{x}$	σ	PDI
MSN	122	125	22.6	0.03
MSN-B	190	213	64.5	0.09
MSN-Tf	220	245	84.0	0.12

Table S2. Sadistic parameters calculated from DLS measurements.

The **mode** (M) is the value that appears most often in a set of data.

Arithmetic mean; $$\bar{x} = \frac{1}{n}\sum_{i=1}^{n} xi$$

Standard deviation; $$\sigma = \sqrt{\frac{\sum_{i-1}^{n}(xi-\bar{x})^2 fi}{N}}$$

Polydispersity index; $\text{PDI} = \left(\frac{\sigma}{\bar{x}}\right)^2$

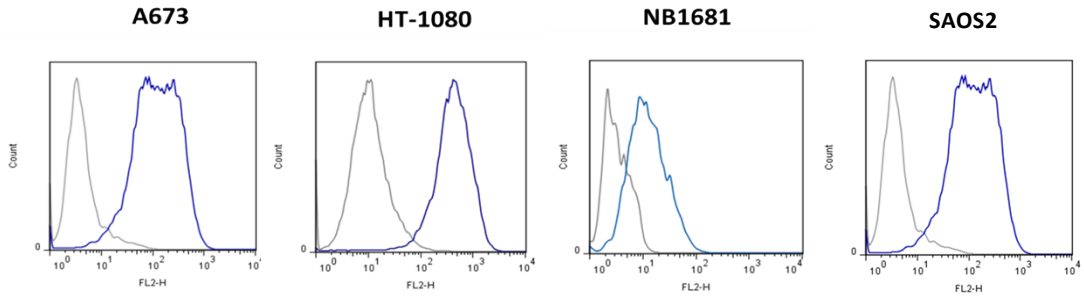

Figure S10. Flow cytometry of A673, HT1080, NB1681 and SAOS2 cells marked with an anti-transferrin receptor antibody (blue) or isotype antibody control (grey)

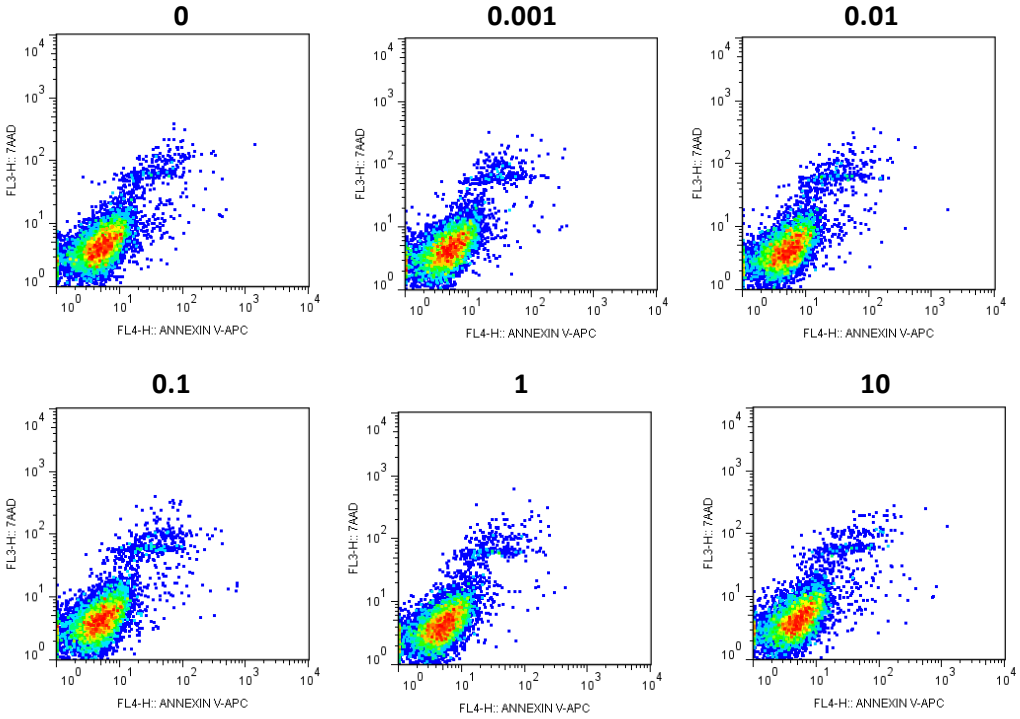

Figure S11. Flow cytometry of Oxalilplatin nanoparticles-treated HT1080 cells(without UV irradiation), stained with Annexin-V and 7-AAD. Doses of Oxalilplatin in µg/mL. These data indicate that incubation with nanoparticles but without UV irradiation has no effect over viability of tumoral cells.

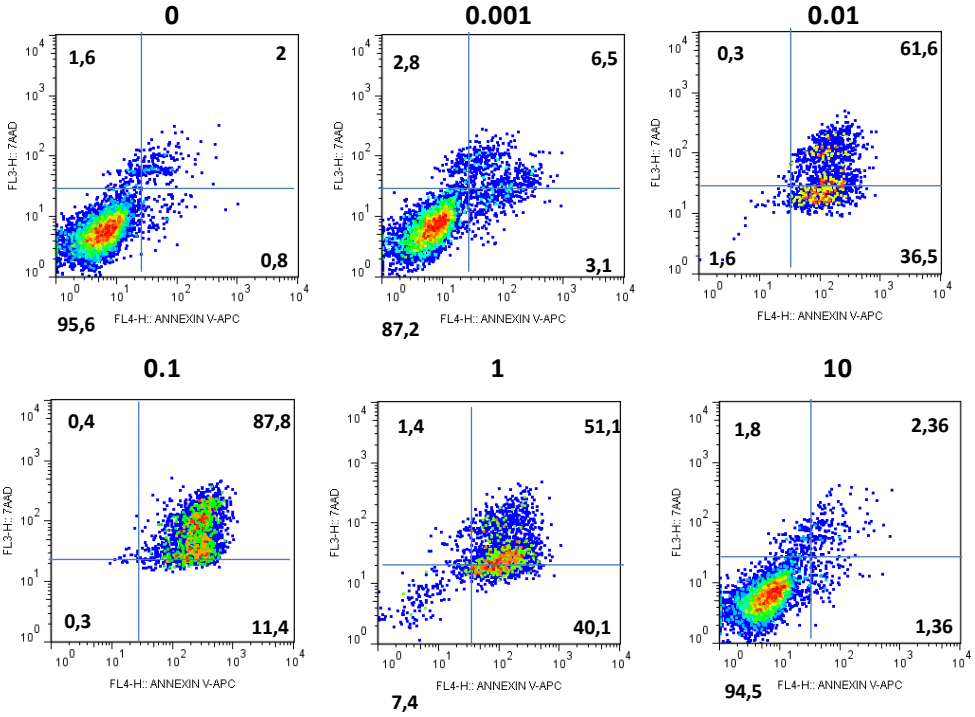

Figure S12. Flow cytometry of Oxalilplatin nanoparticles-treated and UV irradiated HT1080 cells, stained with Annexin-V and 7-AAD. Doses of Oxalilplatin in μg/mL. These data indicate that incubation with nanoparticles and UV irradiation has a high effect over viability of tumoral cells, with a 100% of apoptosis in doses so lower as 0.01μg/mL