Electronic Supplementary Material (ESI) for ChemComm.

Supporting information

Material and methods:

All chemicals were purchased from Sigma-Aldrich (St. Louis, MO) and used as received. Chemicals were of analytical grade and were used without further purification. Poly(D,L-lactide–co–glycolide) (50/50) with carboxylic acid end group (PLGA-COOH, inherent viscosity 0.12 dL/g, MW~7 kDa) was purchased from Lakeshore Biomaterials (Birmingham, AL, USA). Polyethylene glycol with amino and carboxylic acid end groups (NH_2-PEG-COOH, MW~3 kDa) was purchased from Rapp Polymere GmbH (Tübingen, Germany). All aqueous solutions were prepared with deionized water obtained using an ultrafiltration system (Milli-Q, Millipore) with a measured resistivity above 18 MΩ/cm. CH_2Cl_2 and $CHCl_3$ were passed through basic alumina prior to use. Transmission Electron Microscopy (TEM) was conducted on a Jeol JEM 2010 at 200 keV. Samples for TEM analyses were prepared by spreading a small drop of the nanoparticle dispersion on amorphous carbon-coated copper grids (Formvar carbon 400 mesh grids) followed by air-drying. Fourier transform infrared (FTIR) spectra were recorded on a Perkin-Elmer Spectrum 2000. DLS measurements were performed on a Malvern Zetasizernano-S working with a 532 nm laser beam. ζ potential measurements were conducted in DTS1060C-Clear disposable zeta cells at 25°C. Magnesium concentrations of the samples were measured at the inductively coupled plasma emission spectrometry (ICP-AES, Varian Liberty 51) after dissolution of the samples in concentrated nitric acid, the measurement were carried out by solution nebulization, instrumental sensitivity is 0.0013 ppm (mg/L). The crystalline structure of the samples was identified from X-Ray diffraction (XRD) patterns recorded in the 2θ range 10–70° with a scan step of $0.05°(2\theta)$ for 5s on a Philips X'pert pro diffractometer (Cu K α radiation). The crystallite size was determined from the (311) diffraction peak by using the Scherrer method. Scanning transmission electron microscopy (STEM) were performed with a Zeiss Supra 40, 20 keV Scanning transmission electron microscopy (STEM) were performed with a Zeiss Supra 40, 20 keV. Energy dispersive X-ray spectroscopy (EDX) was performed with INCA x-sight, OXFORD instruments., Thermogravimetric analysis (TGA) was performed using a TA Instruments TGA-SDT 2960 on sample sizes from 1 to 3 mg, and the mass was recorded as a function of temperature..

1. Synthesis

Synthesis of MgNPs:

The fabrication of nanometer sized magnesium crystals was achieved via a modified version of the particles prepared from Song et al.[1] In particular naphthalene (192 mg, 1.5 mmol) and $MgCl_2$ (142 mg, 1.5 mmol) were dispersed in 10 mL of anhydrous tetrahydrofuran (THF) and lithium bars (37 mg, 5.4 mmol) were added. After 24 hours the nanoparticles were centrifuged (6000 rpm) and purified by washing 3 times with anhydrous THF in order to remove lithium-naphthalene complex, LiCl byproduct and unreacted $MgCl_2$. The so-obtained magnesium nanoparticles (MgNPs) was recovered as a black powder and were re-dispersed into 10 mL of anhydrous THF maintaining a constant argon flux.

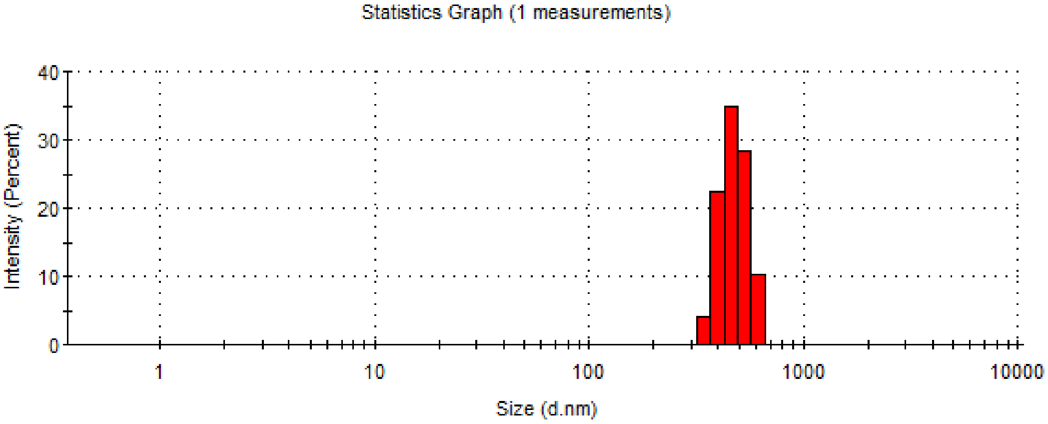

Figure S1: DLS analysis of MgNPs

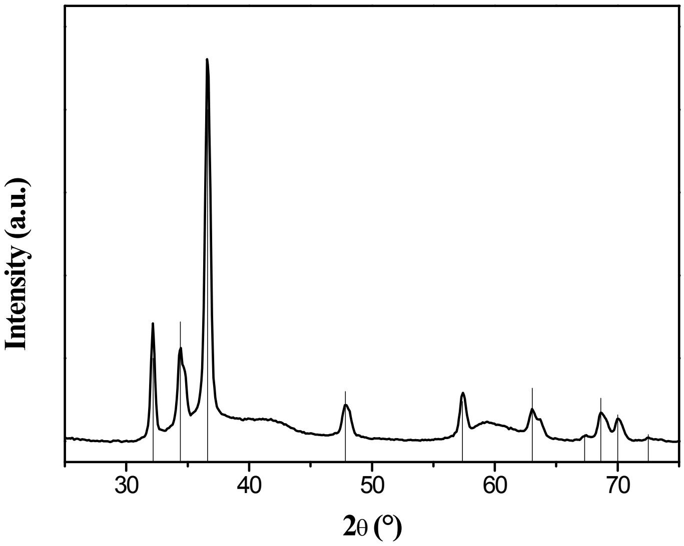

Figure S2: XRD analysis of MgNPs. The vertical lines correspond to hexagonal Mg pattern.

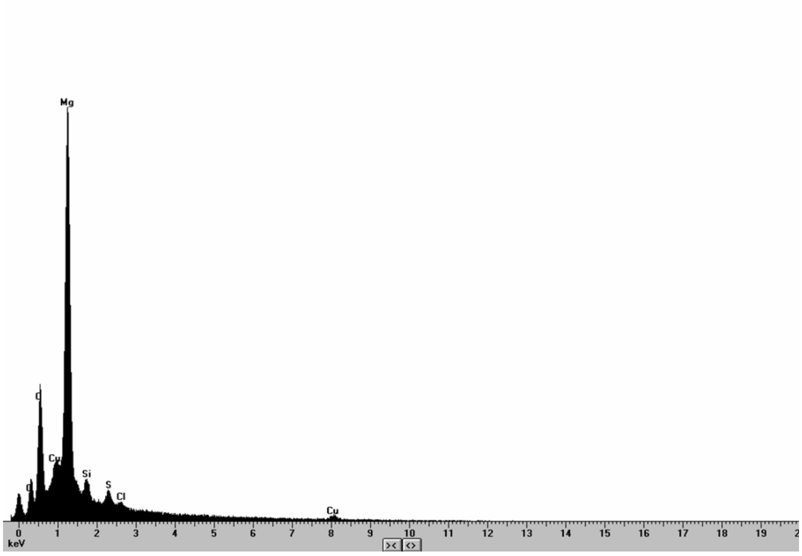

Figure S3: EDX analysis of MgNPs

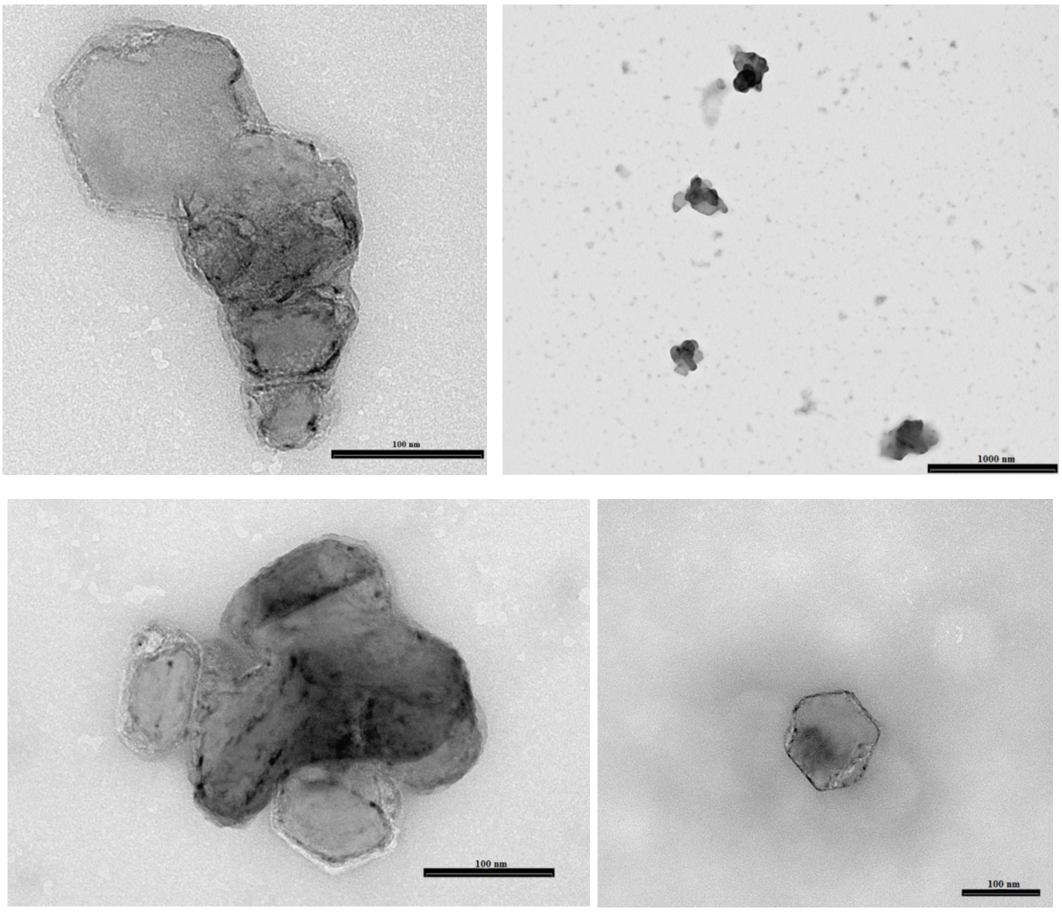

Figure S4: TEM figures of MgNPs

***Ripening of MgNPs**:*

The ripening process was performed as previously described by Kalidindi et al.[2] MgNPs dispersed in anhydrous THF (10 mL) were incubated with the selected aliphatic amine (0.5 mmol) under sonication for 3 hours then under mechanical stirring for 24 hours. After that MgNPs were centrifuged (6000 rpm) and purified by washing 3 times with anhydrous THF and redispersed into 10 mL of the same solvent.

	hexadecylamine	decylamine	octylamine	butylamine
d (nm)	849.4	481.5	438.1	321.6
PDI	0.43	0.28	0.38	0.29

Table S1: MgNPs diameter obtained after ripening with different amines.

Coating of MgNPs with ligand 1:

Ligand **1** was obtained following the procedure described.[3] For the coating of nanoparticles a solution of MgNPs in anhydrous THF (10 mL) was incubated with the ligand **1** (200 mg, 0.73 mmol) under argon: for the first hour the mixture was sonicated in an ultrasound bath while for the following 24 hours it was mechanical stirred at room temperature. Upon reaction the so-obtained MgNPs-**1** were collected by centrifugation (6000 rpm), purified by washing 3 times with THF in order to remove the unreacted ligand then finally easily redispersed into 10 mL of dichloromethane.

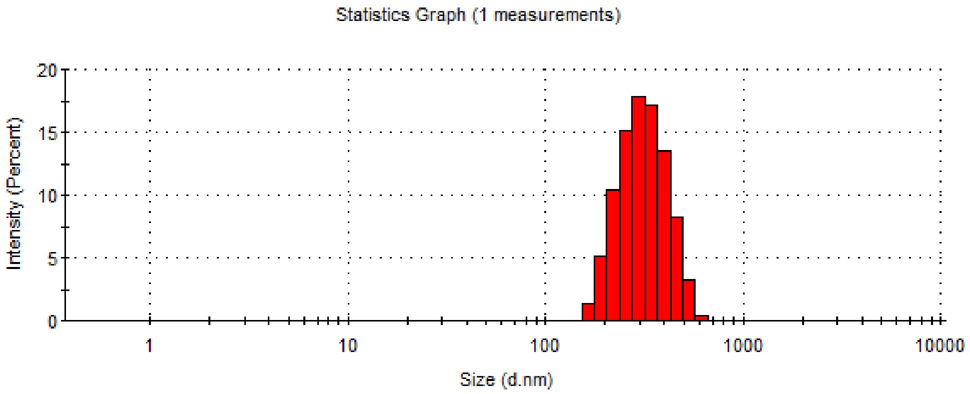

Figure S5: DLS analysis of MgNPs-**1**

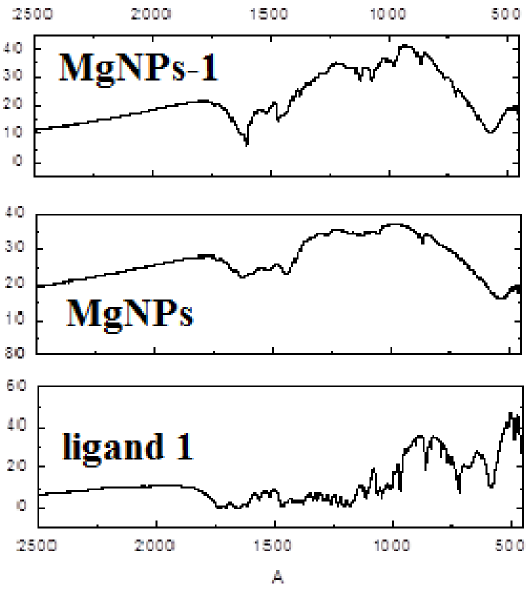

Figure S6: IR comparison between MgNPs, ligand **1** and MgNPs-**1**.

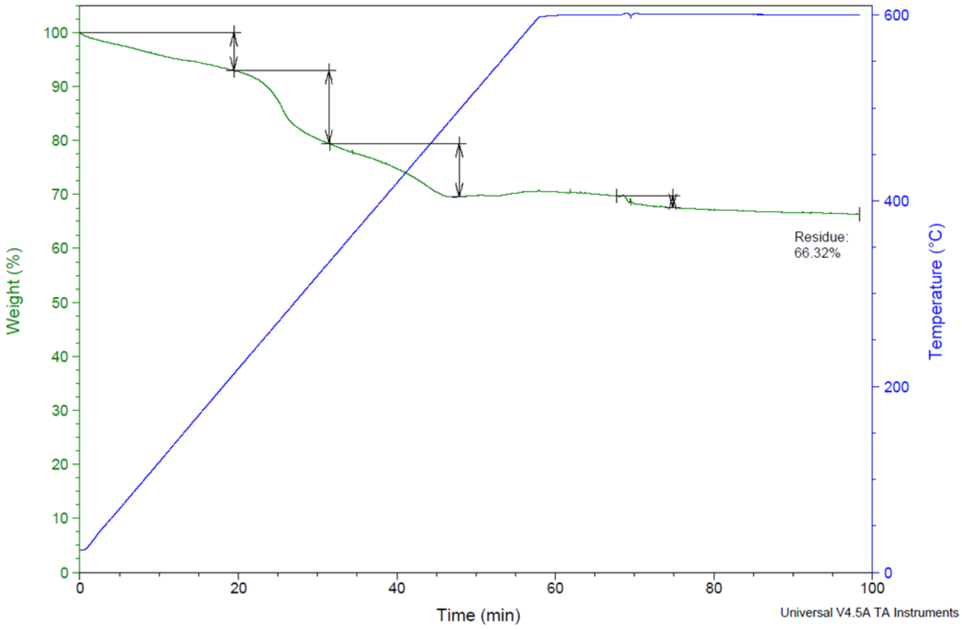

Figure S7: TGA analysis of MgNPs-**1**: r.t.-600 °C under nitrogen then 600 °C constant in air

Preparation of micelles:

PLGA-*b*-PEG-COOH (10 kDa, 100 mg, 0.01 mmol) was dissolved in 10 mL of dichloromethane already containing MgNPs-**1**. 100 mL of ultrapure water were carefully poured on the organic phase. The two phases were ultrasonicated at 50% power for 2 minutes with a tip probe sonicator while cooling down the container in an ice bath. The organic solvent was then completely evaporated under smooth reduced pressure. The so-obtained MgNPs-**1**@PMs were purified by washing with water and meanwhile concentrated using a tangential flow filter (Pellicon XL filter device, Biomax membrane with 500.000 NMWL, Millipore, USA) to obtain a final volume of 10 mL.

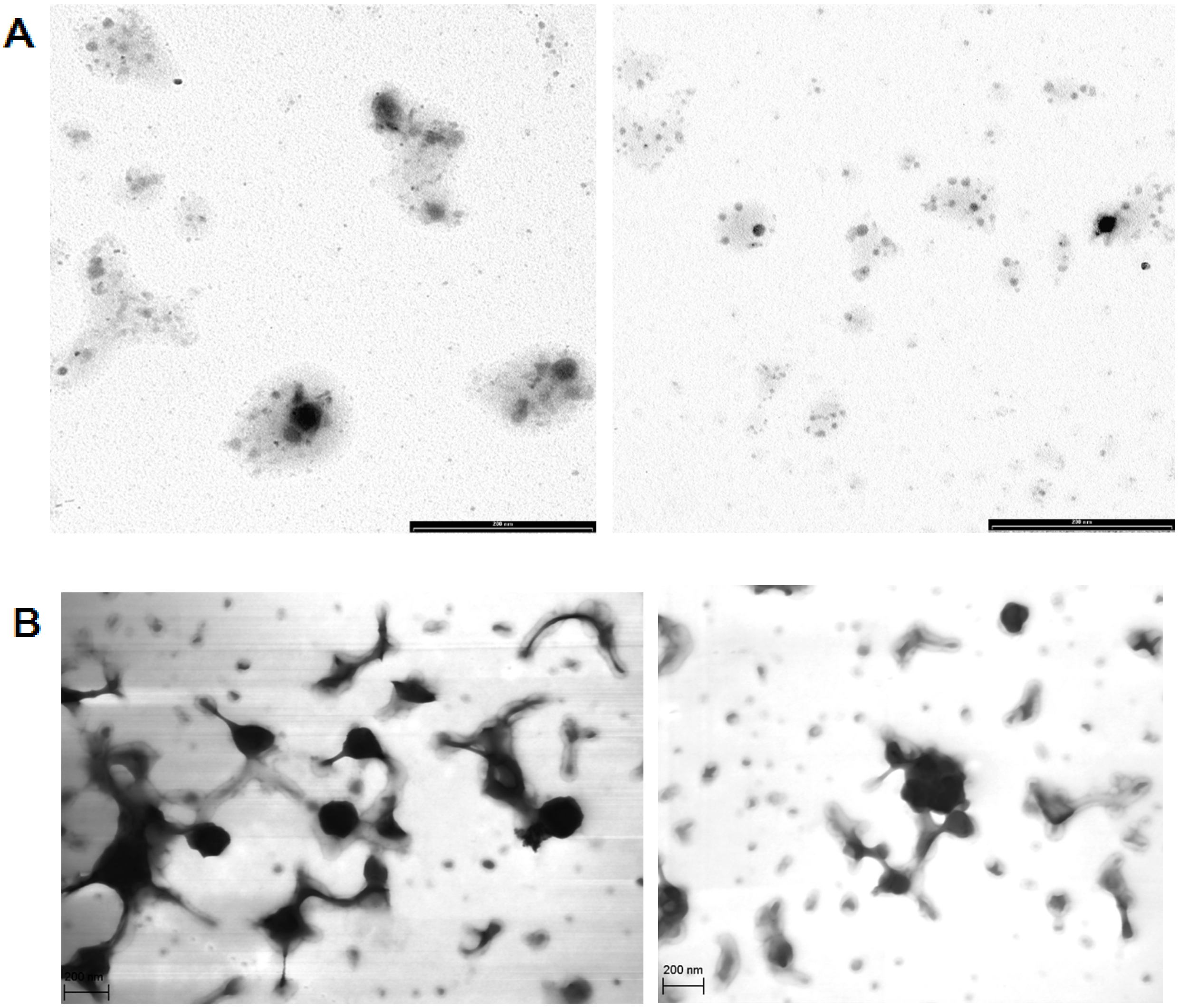

Figure S8: A) TEM figures and B) STEM figures of MgNPs-**1**@PMs. In all the figures scale bar is 200 nm

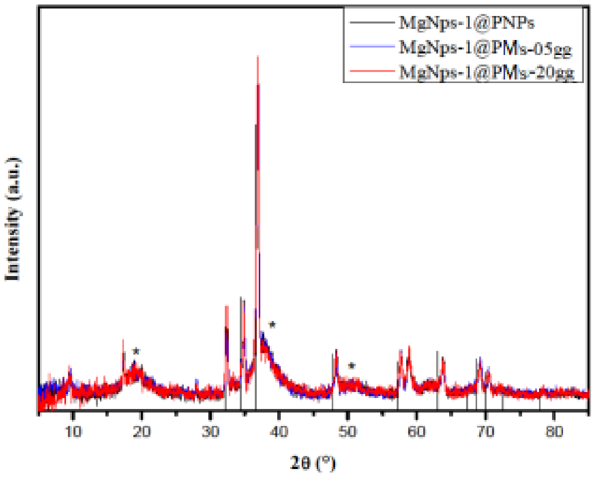

Figure S9: XRD analysis of MgNPs-**1**@PMs after 0, 5, and 20 days upon synthesis. The vertical lines correspond to hexagonal Mg pattern. (*) marks the peaks due to the surface MgOH layer.

2. Photothermal effects

Laser setup:

The laser experiments on nanoparticle samples were performed with a bench setup consisting of a 810 nm AlGaAs diode laser (El.En S.p.A.) coupled with a 600-µm-core optical fiber.[4] In a preferred configuration, 50 µL amounts of particle samples were introduced into 96-weel polystyrene petri dishes lying on a stage positioned 20 mm above the fiberoptic tip and finally irradiated with laser light. The temperature profiles were measured by an infrared thermocamera (Thermovision A20 FLIR Systems Inc.) with a ± 0.15 °C temperature sensitivity and the transmitted laser power was monitored with a power meter (Ophir, Model PD2A). Maximum temperature values reached within the irradiated areas were collected during the laser illumination.

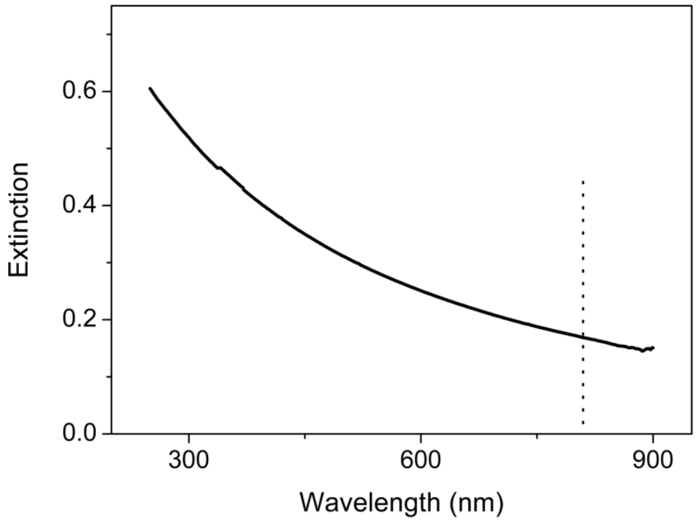

Figure S10: Extinction spectrum of MgNPs-**1**@PMs. The emission line of the 810 nm diode laser used for hyperthermia experiments is indicated with a dashed line.

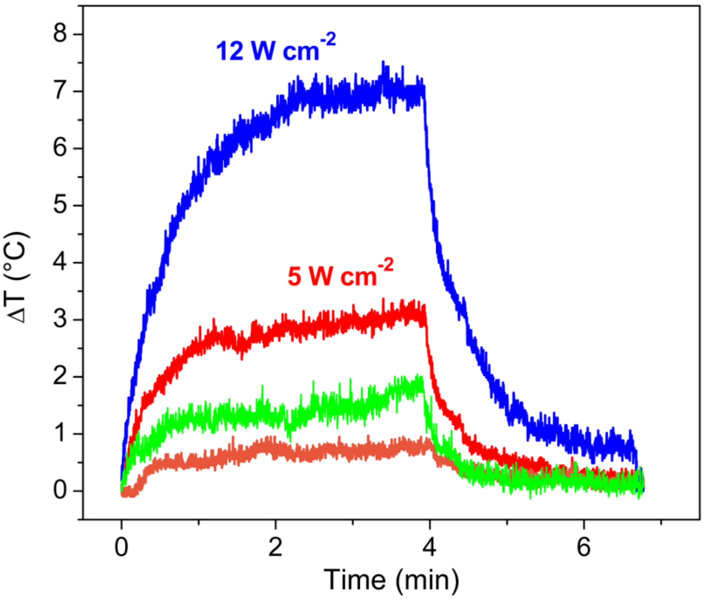

Figure S11: Comparison between the temperature profiles produced by illuminating a MgNPs-**1**@PMs sample containing 5.3 mM Mg with a 12 (blue) or a 5 (red) W cm^{-2} laser radiation for t_{irr} = 4 min and an analogue particle sample lacking the Mg core (green and brown, for 12 and 5 W cm^{-2}, respectively).

3. Biological studies

Cell culture:

HN13 head and neck cancer cell line was maintained in Dulbecco's modified Eagle's medium (PAA) supplemented with 10% fetal bovine serum (Euroclone), 2mM L-glutamine (Euroclone) and 100 units/ml penicillin/streptomycin (Euroclone) in a humidified incubator at 37 °C under 5% CO_2 atmosphere.

Cytotoxicity assay:

Cells were seeded at $2x10^4$ cells/well in 24-well plate and cultured overnight. MgNPs-**1**@PMs were diluted in culture medium to the indicated concentrations and added to the cells. Cells were incubated for 24h with MgNPs-**1**@PMs, trypsinized and counted manually with a Burker chamber, using Trypan blue dye exclusion staining

References

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[1] M. R. Song, M. Chen, Z. J. Zhang, *Mater. Charact.,* 2008, **59**, 514.

[2] S. B. Kalidindi, B. R. Jagirdar, *Inorg. Chem.* 2009, **48**, 4524.

[3] M. Comes Franchini, G. Baldi, D. Bonacchi, D. Gentili, G. Giudetti, A. Lascialfari, M. Corti, P. Marmorato, J. Ponti, E. Micotti, U. Guerrini, L. Sironi, P. Gelosa, C. Ravagli, A. Ricci, *Small*, 2010, **6**(3), 366.

[4] P. Matteini, F. Tatini, L. Luconi, F. Ratto, F. Rossi, G. Giambastiani, R. Pini, *Angew Chem Int Ed*, **2013**, *52*, 5956-5960.