Supplementary Material for Nanoscale
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Electronic Supplementary Information

Preparation, Stability and Cytocompatibility of Magnetic/PLA-PEG Hybrids

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The FT-IR spectrum of the $MagC_{18}$ derivative in Fig. S1 displays characteristic bands ascribed to bonds from chemical groups of the oleate molecules, as well as to the Fe-O bond of the γ-Fe_2O_3 lattice. Specifically the band at 3008 cm^{-1} arises from the C-H vibrations in which carbon atoms participate in the double bond of the oleate alkyl chain and bands between 3000-2800 to the C-H vibrations in which carbon atoms participate in the single bonds. The band at 1630 cm^{-1} is mainly ascribed to the H_2O presence from the KBr. The bands from 1550 to 1414 cm^{-1} are attributed to the carboxylate group, into which the carboxylic group of the oleic acid has been transformed to after the interactions with the surface Fe ions of the magnetic nanoparticles. The shoulder at 1706 cm^{-1} indicates the

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presence of traces of free oleic acid which could not been removed during the purification of the $MagC_{18}$ nanoparticles, possibly because it has been physiosorbed in the oleate sheath forming an interdigitated bilayer. Finally the bands at 628 and 447 cm^{-1} are typical for the iron oxide lattice.[1-3]

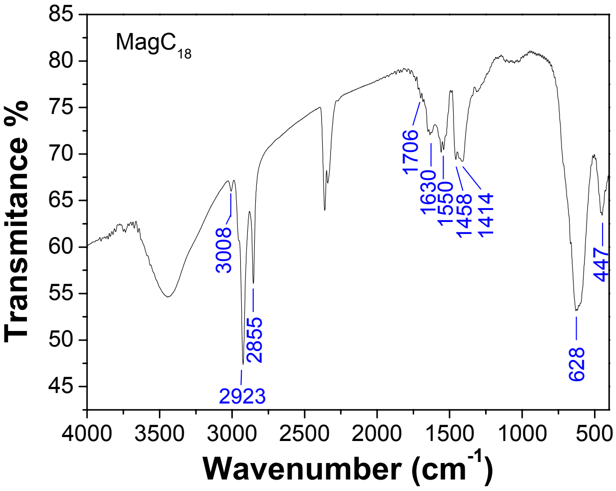

Fig. S1 FT-IR spectrum of the surface functionalized iron oxide nanoparticles with oleate units (MagC18).

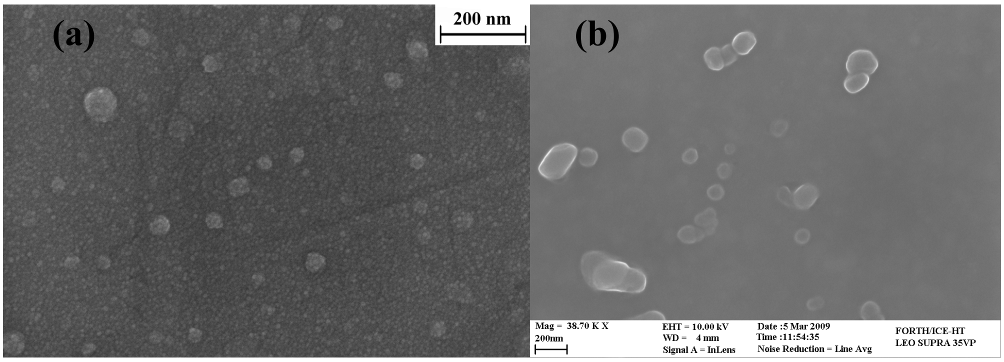

Fig. S2 SEM micrographs from **(a)** PLA-PEG nanospheres and **(b)** $MagC_{18}$/PLA-PEG without photo-enhancement.

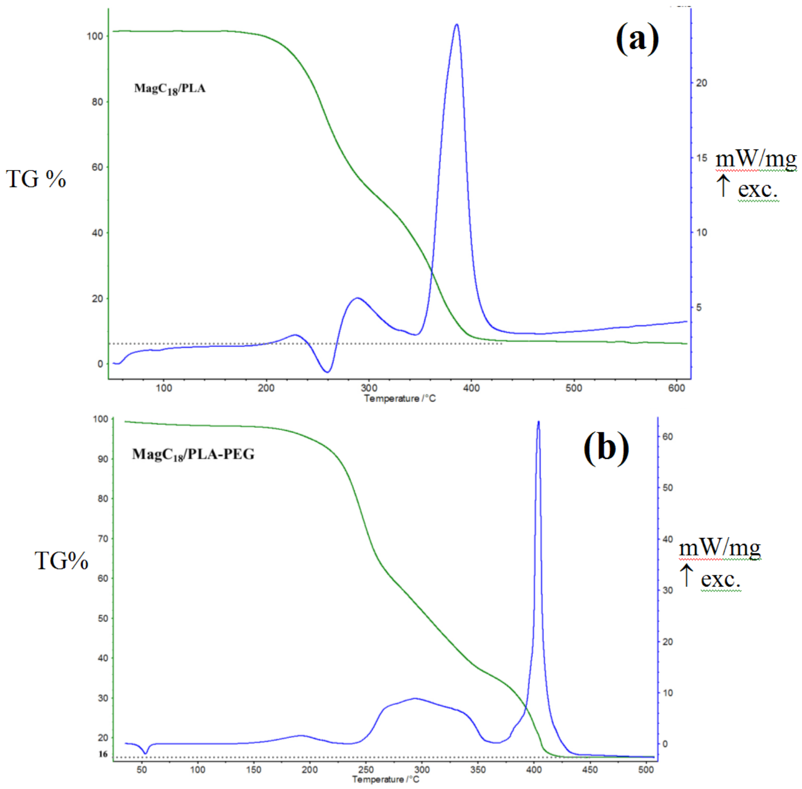

Fig. S3 Thermogravimetric diagrams from MagC$_{18}$/PLA and MagC$_{18}$/PLA-PEG, according to which solid residues of 7.5 % w/w and 15.3% w/w were estimated corresponding to the γ-Fe_2O_3 inorganic fraction.

The determination of the critical micelle concentration (CMC) of the MagC$_{18}$/PLA-PEG hybrid nanoassemblies, was attempted with the pyrene method. Nevertheless, magnetic iron oxide nanoparticles absorb light strongly below the wavelength of ~500 nm, as it has been previously established.[4] Therefore, quenching of the pyrene emission bands resulted to spectra which were difficult to evaluate (increased scattering from the high refractive index hybrids may also take place). For this reason, the CMC was estimated for the plain PLA(10)-PEG(5) copolymer as described in the experimental part of the article. In Fig. S4a the emission spectra of pyrene in aqueous solutions of PLA-PEG of various concentrations are presented and in Fig. 4b a typical deconvolution is shown, performed for the estimation of the I / I' bands area ratio. In Fig. S5, the plot of the I / I' against PLA-PEG concentration indicates a CMC of approximately 0.3 mg/L (2×10^{-5} mM). For comparison the CMCs from a common charged surfactant (sodium dodecyl sulfate) and from a lipid (oleoyl lysophosphatidylcholine), estimated at 8.3 mM [5] and 5×10^{-3} mM [6] respectively, are provided. In the article an extrapolation is done, noting that the CMC of the MNP loaded PLA-PEG will be similarly low. In fact, this extrapolation is in favour for the studied product, since it is well known that addition of hydrophobic solutes decreases the CMC of a micellar system.[7] In addition, as explained in the same reference,[7] the high electrolyte concentration (which is the case for the blood compartment) further decreases the CMC of charged and neutral amphiphiles, such as PLA-PEG.

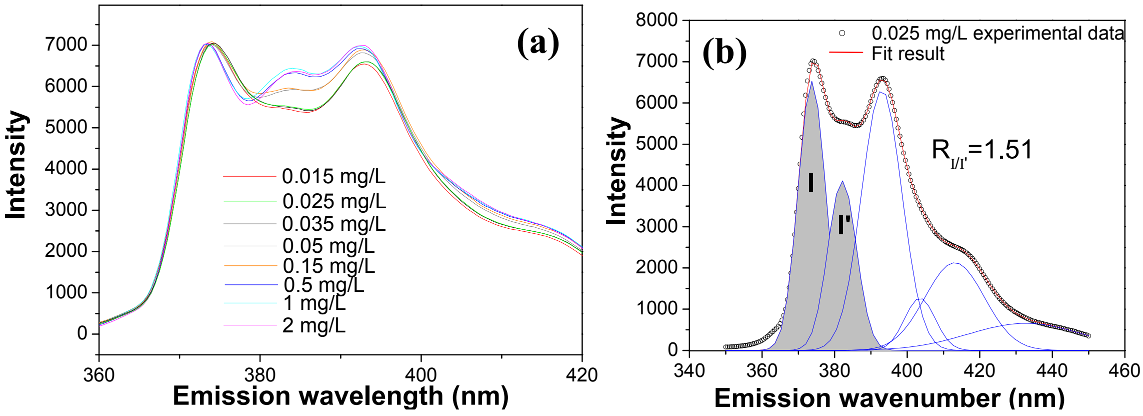

Fig. S4 (a) Emission spectra of various concentrations of PLA-PEG aqueous solutions in presence of pyrene 6×10^{-7} M). **(b)** A typical deconvoluted spectrum. All spectra were deconvoluted to the same number of bands.

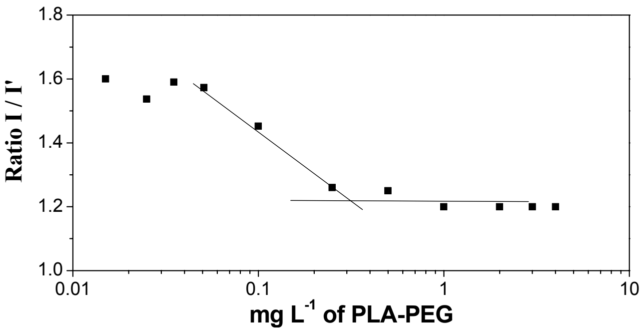

Fig. S5 The ratio of the areas of the I to I' bands as calculated after deconvolution of the spectra recorded from each micellar solution plotted against the concentration of the block-co-polymer.

The zeta potential (ζ_p) variation of the magnetic nanocolloids upon [NaCl] increase (available in ESI) provides another explanation for the observed differences in the colloidal properties of MagC$_{18}$/PLA and MagC$_{18}$/PLA-PEG hybrids. The ζ_p of the cholate-stabilized PLA system changes from very negative values, due to the cholates's carboxylate anionic group, to less negative values with increasing NaCl concentrations and the colloid starts to destabilize. On the other hand, the ζ_p values for the PLA-PEG systems are close to zero, as expected for the neutral hydrophilic shell of PEG segments. This difference on the electrokinetic properties of the MagC$_{18}$/PLA-PEG system in response to increasing NaCl concentrations provides further evidence for the core-shell (micellar) structure of the MagC$_{18}$/PLA-PEG hybrids.

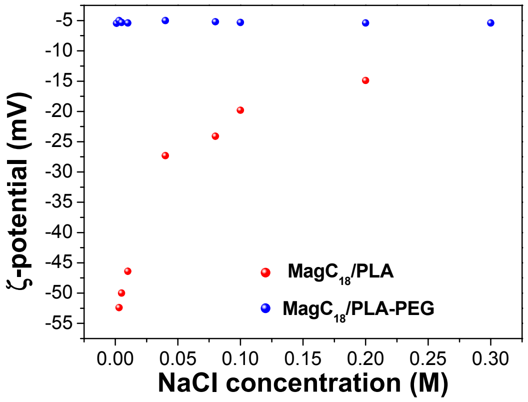

Fig. S6 Zeta potential variation upon [NaCl] increase for the hybrid polymeric nanospheres.

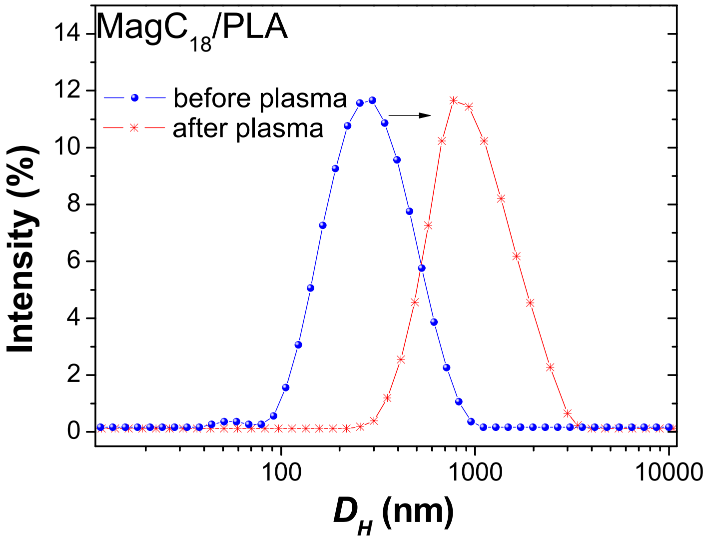

Fig S7 Effect of human blood plasma incubation on the D_h of the Mag/PLA hybrid colloid

Results from the ZFC and FC magnetization curves

The appearance of the maximum in the ZFC magnetization curves (red data) suggests that the assembly of the magnetic nanoparticles passes from the blocked state to the superparamagnetic regime as the temperature rises. Since the system exhibits a size distribution, the blocking temperature is related to the superparamagnetic transition of the nanoparticles with the most probable size, whereas the temperature of irreversibility corresponds to the superparamagnetic transition of the largest nanoparticles. In other words, the difference between the values of temperature of irreversibility (T_{irr}) and blocking temperature (T_b) is a quantitative measure of the size range of the magnetically-active nanoparticles present in the system. Since this difference is extremely low in both studied systems, we can conclude that magnetic nanoparticles exhibit nearly uniform size distribution. In addition, the monotonous increase of the FC magnetization curves for the temperatures below the particular blocking temperature confirms that the magnetic interparticle interactions are significantly suppressed in both samples with different iron oxides contents. It is experimentally well documented [8] that if some interparticle interactions exist in the nanoparticle system, they frequently manifest themselves by the change of the FC profile below the corresponding blocking temperature, which becomes nearly constant as the strength of the interparticle interactions increases.[9] Thus, the magnetization increase in FC curve below the blocking temperature observed in both investigated samples reflects the suppression of magnetic interactions among particles due to their encapsulation and oleate-functionalization.

Spectrophotometric determination of Fe ions.

The Fe_2O_3 content in the magnetic colloids was determined spectrophotometrically following the 1,10-phenanthroline method.[10] 20 μL from the colloid were mixed in an 1.5 mL microcentrifuge tube with 20 μL concentrated HCl 37% in order to dissolve Fe_2O_3 into ferric ions. After 30 min the sample had turned yellow and was transferred in a 10 mL volumetric flask. Hydroxylamine hydrochloride (NH_4 Cl) was added (0.1 mL, 1g L^{-1}) in order to reduce Fe^{+3} to Fe^{+2}. 1,10-phenanthroline (1 mL, 100g L^{-1}) and CH_3COONa (0.8 mL, 1.2

M) were then added and diluted up to the 10 mL mark. After ten min the absorbance at 510 nm was recorded and the concentration in ppm was calculated based on a previously prepared calibration curve spanning from 0.1 to 3.5 ppm.

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