Supplementary Information

A novel synthetic approach of cerium oxide nanoparticles with improved biomedical activity

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Figure S1. ¹*H-NMR surface characterization of C1*. *C1* ¹*H-NMR spectrum compared with Pluronic F127, TEMED spectra and C1-450 NPs.*



Figure S2. C1-450 Physico-chemical characterization. (*A*) XRD diffraction patterns and Miller indexes. (*B*) TEM image. (*C*) TGA curve. (*D*) FTIR absorbance spectra.



Figure S3. Ce (III)-EG coordination depends on pH. (*A*) ¹*H-NMR spectra of EG peak at 3.66 ppm varying the pH from 3 to 11. (B) Dependence of peak full width at half maximum (FWHM) on the pH.*



Figure S4. CNP dispersion properties. DLS analysis of C1, C1-450, C2, C3, and C4 at 200 μ g/mL in water (pH 7.4) and in RPMI media +10% fetal bovine serum (FBS). The hydrodynamic diameter distribution by volume is reported.



Figure S5. CNP precipitation analysis over time. Time dependent variation of CNPs UV-VIS supernatant spectra after 7 days (red curve) and 14 days (blue curve) compared with CNP spectra immediately after sonication (black curve). CNP nominal concentration was set at 50 µg/mL.







Figure S6. TEMPOL/TEMPONE ESR system. (A) Scheme of TEMPOL degradation by HO[•] producing diamagnetic products (reaction 1), and paramagnetic TEMPONE species (reaction 2). (B) Simulation of TEMPOL (blue curve) and TEMPONE (red curve) ESR spectra (TEMPOL: TEMPONE ratio 1:1). TEMPOL spectra is shifted to the right by 0.035 G. (C) ESR spectra of 100 μM TEMPOL after 525 s of continuous production of HO[•] ± (C1, C1-450, C2 and C3 samples) as described in Methods section. For each spectra the quantification of TEMPOL and TEMPONE signals are reported in the bottom right.

50 45 40 35 % Apoptosis 30 25 20 15 10 5 0 NPs C1 C1-450 C2 C3 C4 — VP16 ++++++

Protection from VP16 induced apoptosis

Figure S7. Redox active CNPs reduce redox dependent apoptosis. % of apoptosis detected 3 h after cell treatment with VP16 \pm CNPs. Values are the mean of \geq 3 independent experiments \pm SD; *p < 0.05 (ANOVA). Significance with respect to the control group is shown.