Electronic Supplementary Information

Tuning sub-10 nm single-phase $NaMnF_3$ upconversion nanocrystals as ultrasensitive hosts for pure intense fluorescence and excellentT_1magnetic resonance imaging

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Experimental Details:

Materials: $MnCl_2$ (99%), $Yb(NO_3)_3{\cdot}5H_2O$ (99.99%), $Er(NO_3)_3{\cdot}6H_2O$ (99.9%), $Tm(NO_3)_3{\cdot}6H_2O$ (99.99%), NaF (99%), 1-octadecene (90%), oleic acid (90%), octadecene (90%), poly(maleic anhydride-alt-1-octadecene) (99%), poly(ethylene glycol) methyl ether (99%) were purchased from Sigma-Aldrich. The solvents, such as hexane, ethanol, chloroform, diethyl ether are provided by Aik Moh, Singapore. All the chemicals were used without further purification.

Synthesis of the Lanthanide-doped $NaMnF_3$ Nanocrystals (NCs): $MnCl_2$, $Yb(NO_3)_3{\cdot}5H_2O$ and $Er(NO_3)_3{\cdot}6H_2O$ or $Tm(NO_3)_3{\cdot}\ 6H_2O$ were added to a flask containing the mixture of 1-octadecene (10 ml) and oleic acid (10 ml) under vigorous stirring at room temperature (the ratio varies according to the experiment requirements). The resulting mixture was then heated to 160 ^{o}C for 0.5 h, at which time the solution turned from colorless to brownish. After the solution was cooled to room temperature, a methanolic solution (10 ml) of NaF (5 mmol) was injected into the flask. The mixture was stirred at 60 ^{o}C for 30 min and then purged by N_2 at 100 ^{o}C for 20 min. Subsequently, the temperature was raised to 300 ^{o}C and kept for 45 min under nitrogen.

Finally, the reaction was cooled to room temperature. The as-prepared NCs were collected by centrifugation, washed with ethanol and hexane for several times, and finally re-dispersed in chloroform for further modification.

Surface modification of the $NaMnF_3$ NCs:

Synthesis of PMAO-PEG polymer: Amphiphilic PMAO-PEG was synthesized following Yu et al protocol with modifications.[1] In a typical synthesis, 1g of poly(maleic anhydride-alt-1-octadecene) (PMAO) and 1.5 g of poly(ethylene glycol) methyl ether (PEG-OH) were dissolved in 10 ml chloroform. 50 ul of concentrated H_2SO_4 was added to it. The mixture was refluxed at 60 ^{0}C overnight. The mixture was then neutralized using 1M NaOH followed by centrifugation to remove salt and water. The clear dispersion of PMAO-PEG in chloroform was later added dropwise into 250 ml diethylether to precipitate the polymer. The precipitated polymer was filtered, washed with ether, dried and subsequently lyophilized.

Surface modification of $NaMnF_3$ NCs: PMAO-PEG (100 mg) was dissolved in 9 ml chloroform and the $NaMnF_3$ NCs dispersion in chloroform (1 ml) was added to it and the solution was stirred overnight at room temperature. Then, chloroform was removed slowly using a rotary evaporator at room temperature, leaving a waxy layer in the flask. About 15 ml of distilled water was then added to the waxy liquid and dispersed well by sonication for 15 min. The flask was mounted back to the rotary evaporator and removed the remaining chloroform. The NCs were then collected using centrifuge. The collected pellet was redispersed in 10 ml distilled water. The NCs dispersion in water was used for relaxivity measurements and phantom imaging.

Characterization:

Transmission Electron Microscopy (TEM): TEM images were acquired using a JEOL JEM-2100F microscope operating at 200 kV. Two drops of NC dispersion were placed onto a carbon film supported on a 200 mesh copper grid (3 mm in diameter) and dried in air at room temperature. The carbon grid with NCs sample was then mounted into the vacuum chamber for imaging.

Energy-dispersive X-ray spectroscopy (EDX): EDX spectroscopy was done using a high resolution transmission electron microscope (JEOL, JEM-2100F) operating at 200 kV and EDS (EDAX, AMETEK, USA, system resolution: 135 eV). A few drops of NCs dispersion were put onto a holey carbon film supported on a 200 mesh copper grid (3 mm in diameter) and dried in air at room temperature. The carbon grid with sample

was then mounted into the vacuum chamber for elemental compositional analysis.

X-ray Diffraction Analysis (XRD): Approximately 50 mg of the NCs sample was pressed gently in an agate mortar to break up lumps. The powdery samples were then spread evenly onto a zero background holder. Step-scan X-ray powder diffraction data were collected over the range of 2θ range of 10-80° on a D8 Advance Bruker powder X-ray diffractometer with Cu Kα radiation. The scanning step size was 0.02° with a counting time of 1s per step.

Photoluminescence Spectra (PL): NCs were dispersed in chloroform in a standard quartz cuvette at room temperature and their fluorescence properties were studied using a Fluoromax-4, Horiba Jobin Yvon Spectrofluorometer, which employs a photon-counting detection system, for detecting fluorescence emission. To obtain the emission spectra, sample excitation was accomplished using a diode laser, BWF-2 (980 nm, P_{max} = 1.0 W at 3.0A, B&W TEK Inc.) coupled to a 100 μm (core) optical fiber.

Fourier Transform Infrared Spectroscopy (FTIR): A few milligrams of finely ground sample were mixed with KBr powder with a mass molecular ratio of about 1:100. The mixture was then palletized before the measurement. The measurement was conducted in a Digilab FTS 3100 instrument by collecting 64 scans with a resolution of $4cm^{-1}$.

Magnetic Resonance Imaging (MRI): The T_1-weighted image was obtained on a 7 T Bruker ClinScan MRI system. All samples were dissolved in double distilled water. Other relevant acquisition parameters are: number of acquisitions = 16, field of view = 39 mm, slice thickness = 1 mm. All experiments were performed in 1% agarose medium.

Cell Viability Study: To evaluate the cytotoxicity of the nanocrystals, A-5RT3 cells were incubated with nanocrystals as a function of nanocrystal concentration and incubation time. Data are presented as mean ± standard deviation for three independent experiments. A-5RT3 cells were plated in 96-well plates with a cell density of 10^4 cells per well and allowed to grow into full confluence. And then, the medium were replaced by refresh ones with nanocrystals of different concentrations and the cells were incubated for 24 h, 48 h or 72 h, separately. alamarBlue assays (Invitrogen) were performed at each time point. The cytotoxicity was expressed as the percentage of cell viability compared to that of untreated control cells.

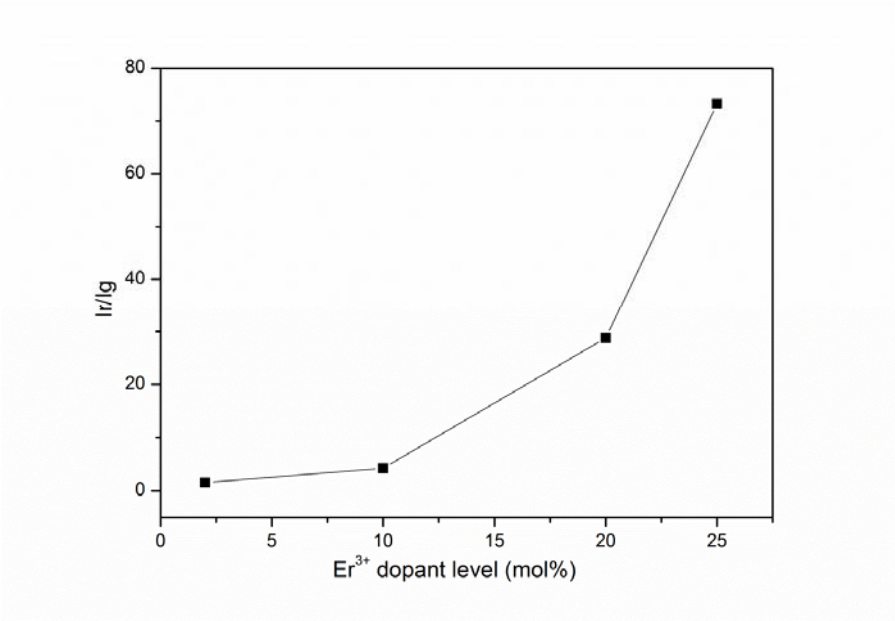

Fig. S1. Red to green emission intensity ratio (I_R/I_G) versus dopant concentration of Er^{3+} ions.

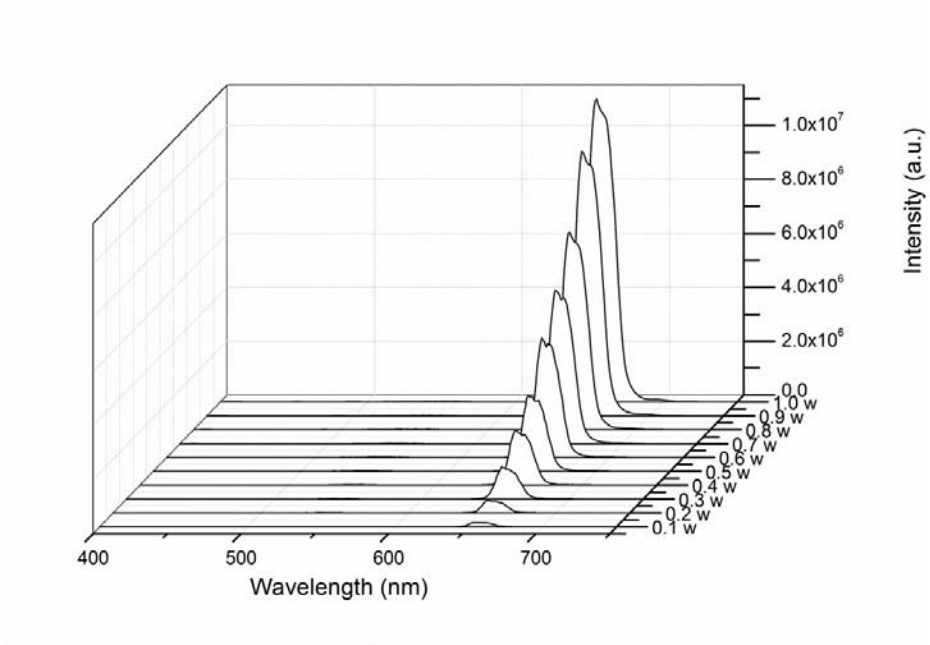

Fig. S2. Room temperature UC emission spectra of $NaMnF_3$: Yb^{3+}, Er^{3+} NCs under different 980 nm laser power excitation when Mn^{2+} ratio is fixed at 50 mol%. All samples were dispersed in chloroform (1 mg/ml).

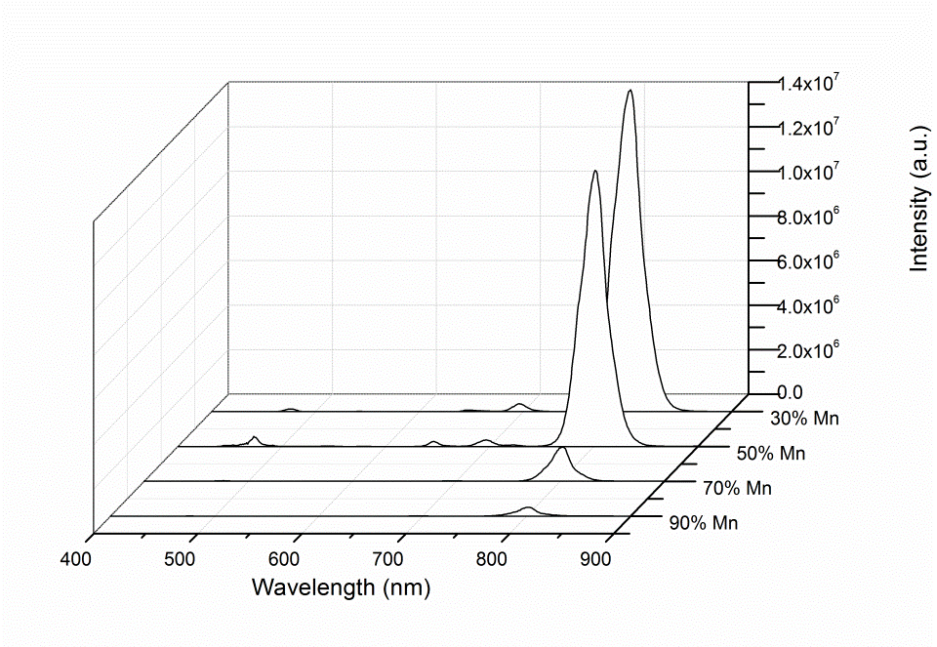

Fig. S3. Room temperature UC emission spectra of $NaMnF_3$: Yb^{3+}, Tm^{3+} NCs with different Mn^{2+} ions concentration when Tm^{3+} dopant is fixed at 0.02 mol%. All samples were dispersed in chloroform (1 mg/ml), spectra were recorded at a power of 1 w.

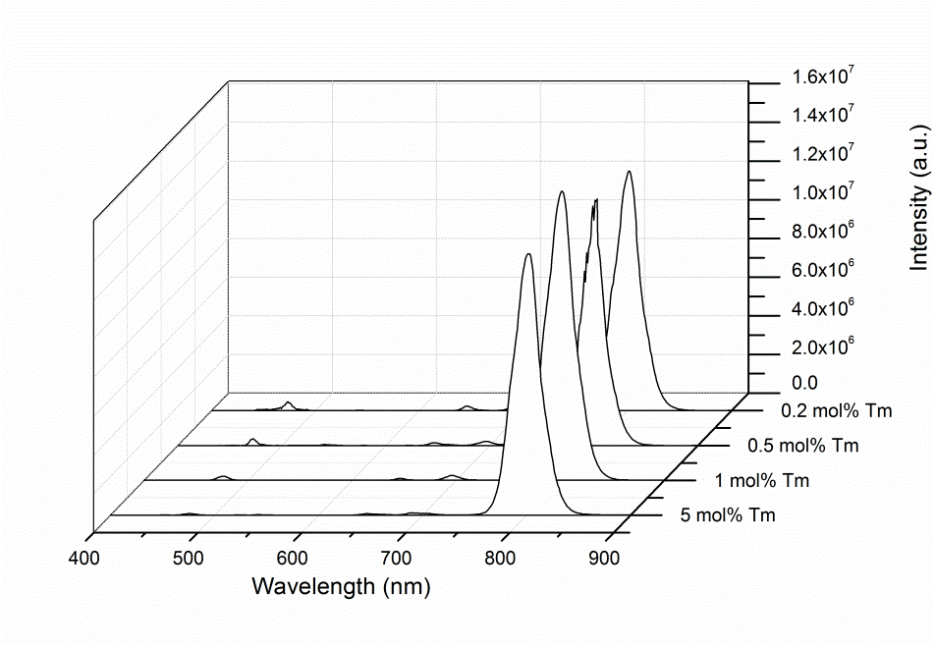

Fig. S4. Room temperature UC emission spectra of $NaMnF_3$: Yb^{3+}, Tm^{3+} NPs with different Tm^{3+} ions dopant concentration when Mn^{2+} dopant is fixed at 50 mol%. All samples were dispersed in chloroform (1mg/ml), spectra were recorded at a power of 1 w.

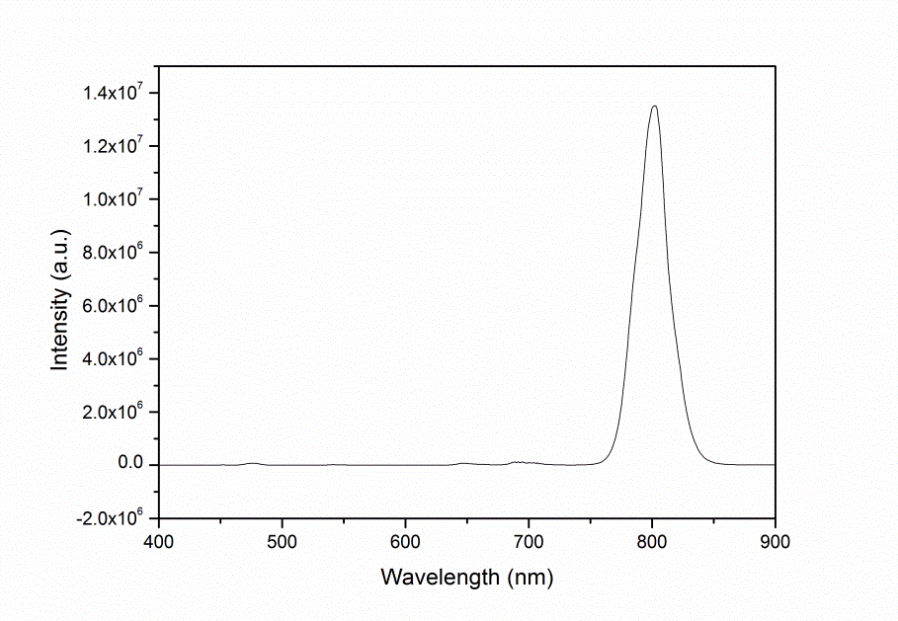

Fig. S5. Room temperature UC emission spectrum of $NaMnF_3$: Yb^{3+}, Tm^{3+} NPs (50/45/5 mol%) dispersed in chloroform (1mg/ml), spectrum was recorded at a power of 1 w. Pure NIR-NIR emission was achieved.

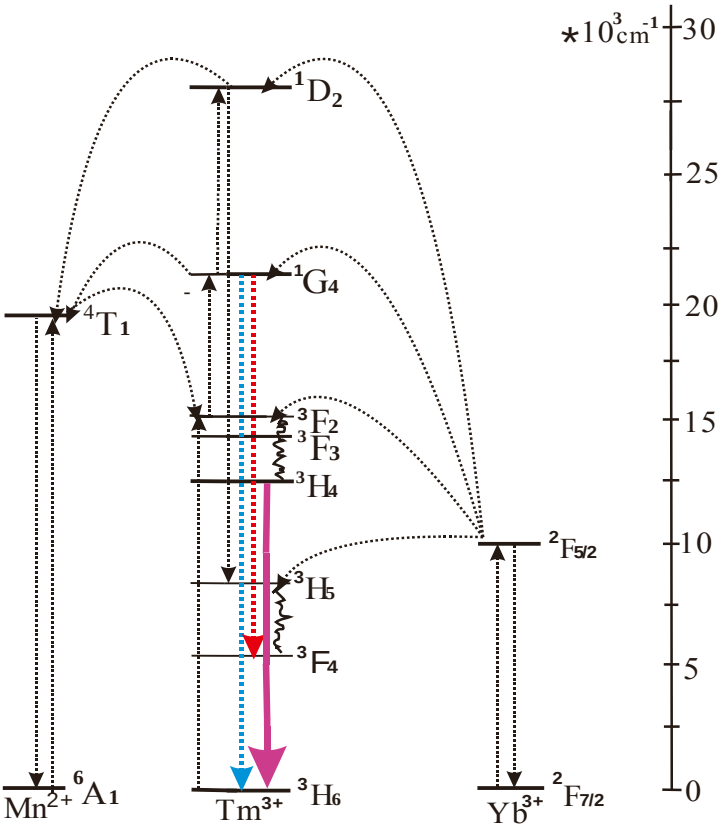

Fig. S6. Proposed energy transfer mechanisms of $NaMnF_3$: Yb^{3+}, Tm^{3+} NCs. Blue and red emissions at 475 nm and 650 nm correspond to the transition $^1G_4$-$^3H_6$ and $^1G_4$ -$^3F_4$ of Tm^{3+} ions, respectively. A strong NIR emission centered at 800 nm was attributed to the transition from $^3H_4$-$^3H_6$. A single narrow-band NIR emission at 800 nm was observed which was ascribed to nonradiative energy transfer from the $^1D_2$ and $^1G_4$ levels of Tm^{3+} to the $^4T_1$ level of Mn^{2+}, followed by back-energy transfer to the $^3F_2$ level of Tm^{3+}.

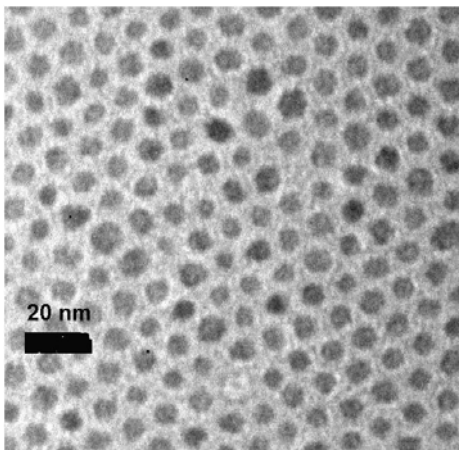

Fig. S7. TEM image of $NaGdF_4$: Yb^{3+}, Er^{3+} NCs.

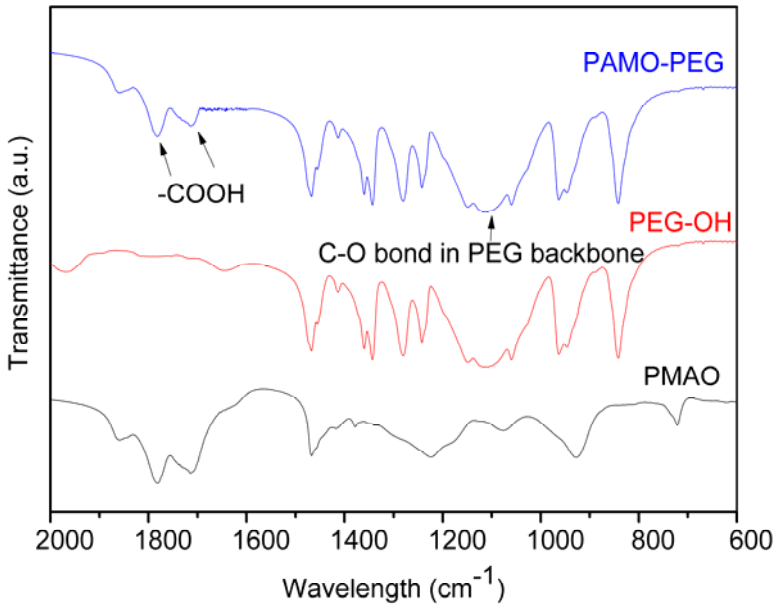

Fig. S8. FTIR spectra of functionalized $NaMnF_3$ NCs. The result shows that peak intensity at 1780 cm^{-1} decrease while peak intensity at 1720 cm^{-1} increase, which is ascribed to the reaction of the anhydride moieties and the formation of –COOH group, respectively. The strong peak at 1100 cm^{-1} corresponds to C-O bonds in the PEG backbone.

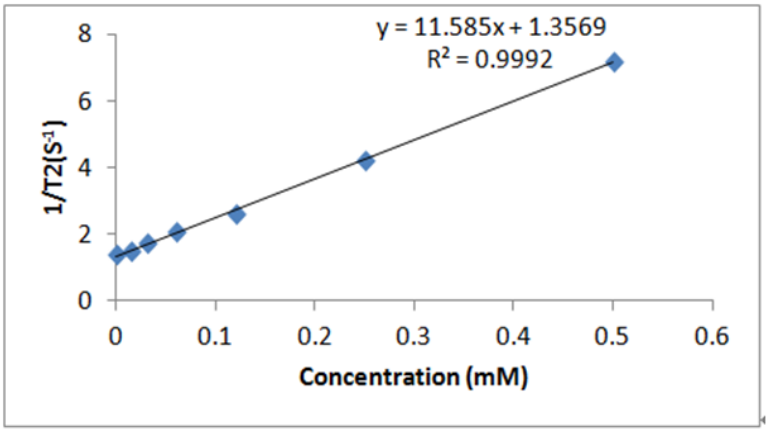

Fig. S9. Plot of relaxation rate ($1/T_2$) versus molar concentration of PEG-UC NCs suspension.

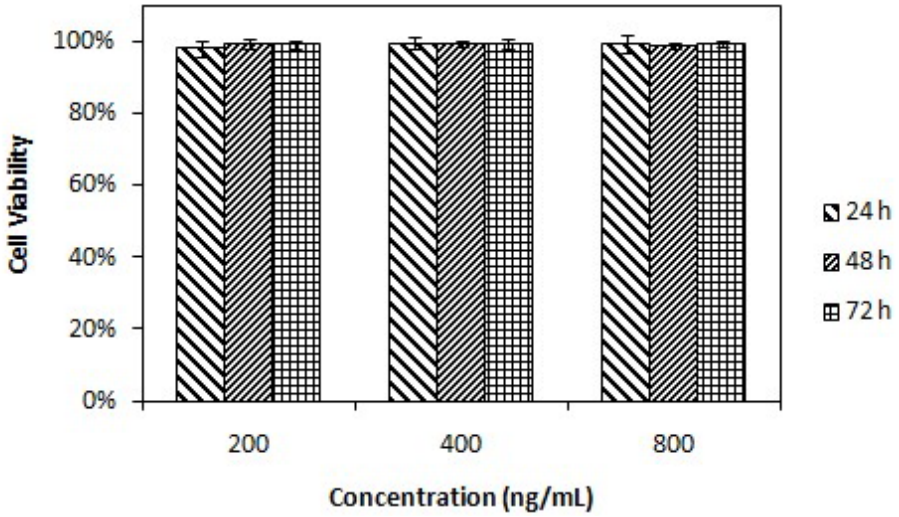

Fig. S10. The viability of A-5RT3 cells incubated with nanocrystals as a function of nanocrystal concentration and incubation time. NCs concentration of 800 ng/mL with cells incubated for 72 h is considered as the extreme condition in this study.

Reference:

1. W. W. Yu, E. Chang, J. C. Falkner, J. Zhang, A. M. Al-Somali, C. M. Sayes, J. Johns, R. Drezek and V. L. Colvin, *J. Am. Chem. Soc.*, 2007, **129**, 2871.