Supporting Information for

Composition tunable ultrasmall manganese ferrite nanoparticles: an insight in the *in vivo* T_1 contrast efficacy

Yuqing Miao[1‡], Qian Xie[2‡], Huan Zhang[1], Jing Cai[3], Xiaoli Liu[1], Ju Jiao[4], Shanshuang Hu[5], Anujit Ghosal[1], Yu Yang[5], Haiming Fan[1]*

1. Key Laboratory of Synthetic and Natural Functional Molecule Chemistry of the Ministry of Education, College of Chemistry and Materials Science, Northwest University, Xi'an, Shaanxi 710069, China.
2. Division of nephrology, Peking University Third Hospital, Beijing, China.
3. State Key Laboratory of Oncology in South China, Sun Yat-sen University Cancer Center, Collaborative Innovation Center for Cancer Medicine, Guangzhou 510060, China.
4. Department of Nuclear Medicine, The Third Affiliated Hospital of Sun Yat-sen University, 600 Tianhe Road, Guangzhou, Guangdong 510630, China.
5. School of Life Sciences, National Engineering Research Center for Miniaturized Detection Systems, Northwest University, Xi'an, Shaanxi, China

‡Yuqing Miao and Qian Xie have equal contribution.

Corresponding author*: fanhm@nwu.edu.cn

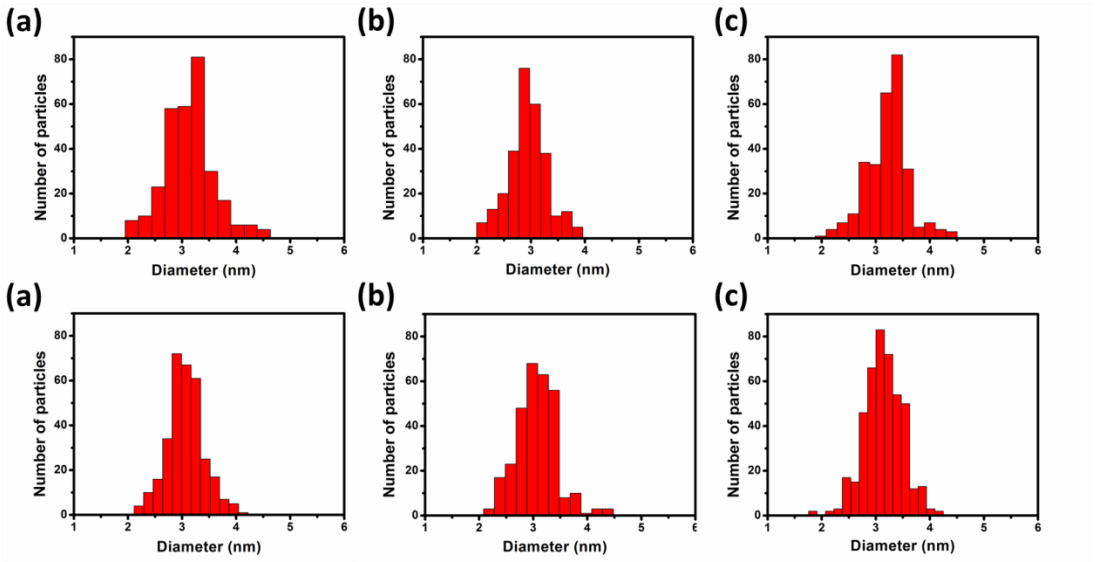

Figure S1. The diameter histograms of as-synthesized ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles measured from TEM images (Figure 1a-f) respectively.

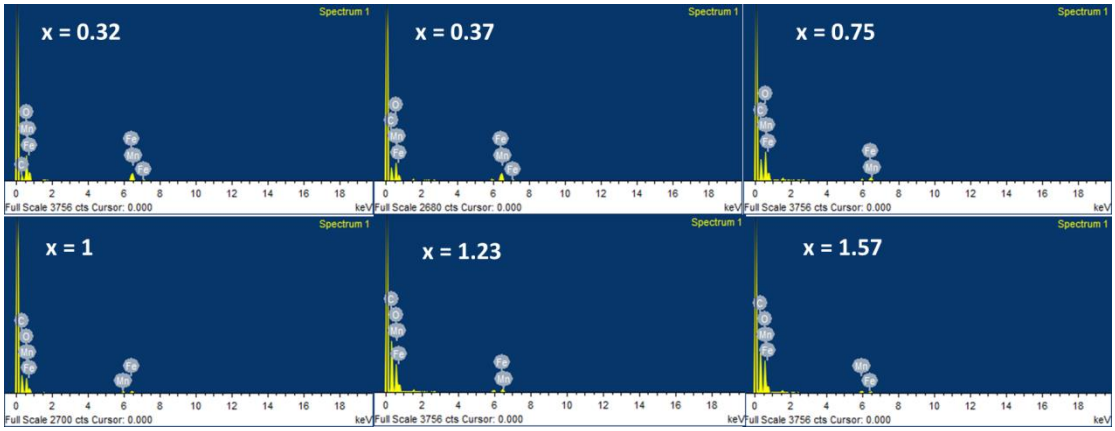

Figure S2. Energy dispersive X-ray spectroscopy (EDS) of ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles at different Mn doping level (x = 0.32, 0.37, 0.75, 1, 1.23, and 1.57).

Table S1. EDS and ICP measurements of ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles

	EDS	ICP
1	$Mn_{0.22}Fe_{2.78}O_4$	$Mn_{0.32}Fe_{2.68}O_4$
2	$Mn_{0.39}Fe_{2.61}O_4$	$Mn_{0.37}Fe_{2.63}O_4$
3	$Mn_{0.78}Fe_{2.22}O_4$	$Mn_{0.75}Fe_{2.25}O_4$
4	$MnFe_2O_4$	$MnFe_2O_4$
5	$Mn_{1.3}Fe_{1.7}O_4$	$Mn_{1.23}Fe_{1.77}O_4$
6	$Mn_{1.54}Fe_{1.46}O_4$	$Mn_{1.57}Fe_{1.43}O_4$

Table S2. Binding energies of ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles

	Fe $2p_{3/2}$	Fe $2p_{1/2}$	Mn $2p_{3/2}$	Mn $2p_{1/2}$
$Mn_{0.32}Fe_{2.68}O_4$	711.9	725.8	642.6	654.4
$Mn_{0.37}Fe_{2.63}O_4$	711.0	724.3	642.0	653.9
$Mn_{0.75}Fe_{2.25}O_4$	711.8	724.7	642.4	654.5
$MnFe_2O_4$	711.8	725.5	642.1	653.9
$Mn_{1.23}Fe_{1.77}O_4$	710.9	725.1	641.8	653.7
$Mn_{1.57}Fe_{1.43}O_4$	711.2	724.8	641.6	653.2

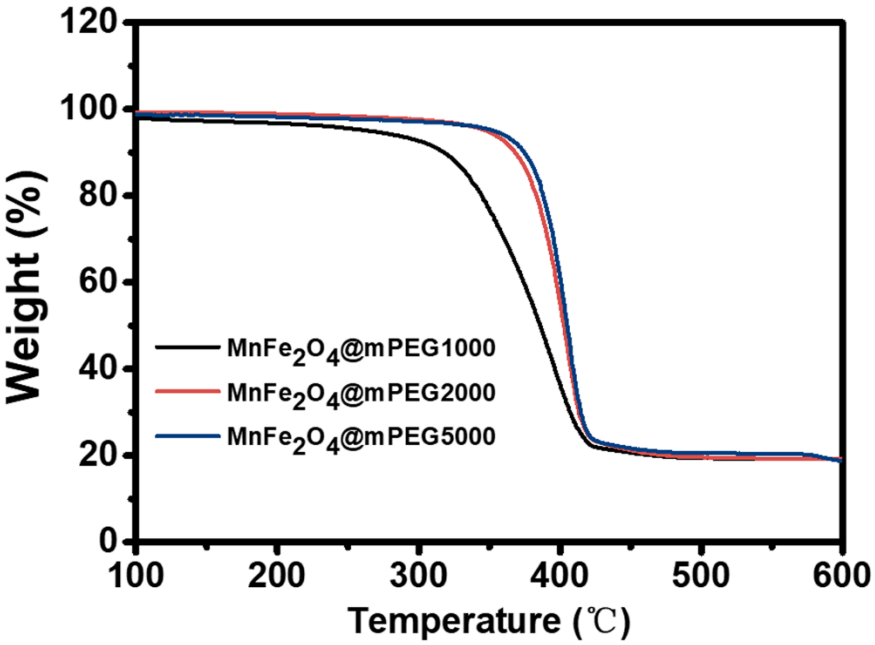

Figure S3. Thermogravimetric analysis (TGA) of the UMFNPs modified with mPEG1000, mPEG2000 and mPEG5000, respectively.

Table S3. Surface content of $MnFe_2O_4$ nanoparticles with different PEG chain lengths

Molecular weight	Surface content of $MnFe_2O_4$ nanoparticles
mPEG1000	8×10^{-7} mol/mg
mPEG1000	4×10^{-7} mol/mg
mPEG1000	1.6×10^{-7} mol/mg

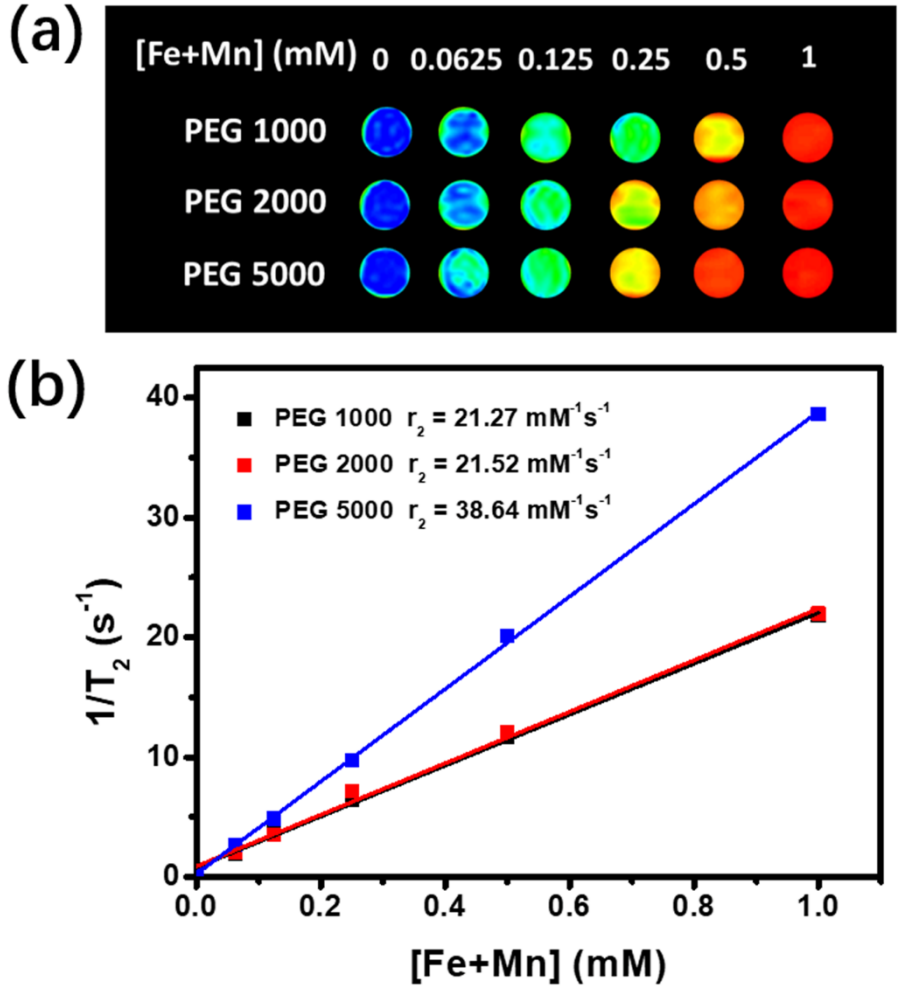

Figure S4. (a) T_2-weighted phantom imaging of ultrasmall $MnFe_2O_4$ nanoparticles with different PEG chain lengths. (b) Plot of $1/T_2$ over [Fe+Mn] concentration of the ultrasmall $MnFe_2O_4$ nanoparticles different PEG chain lengths.

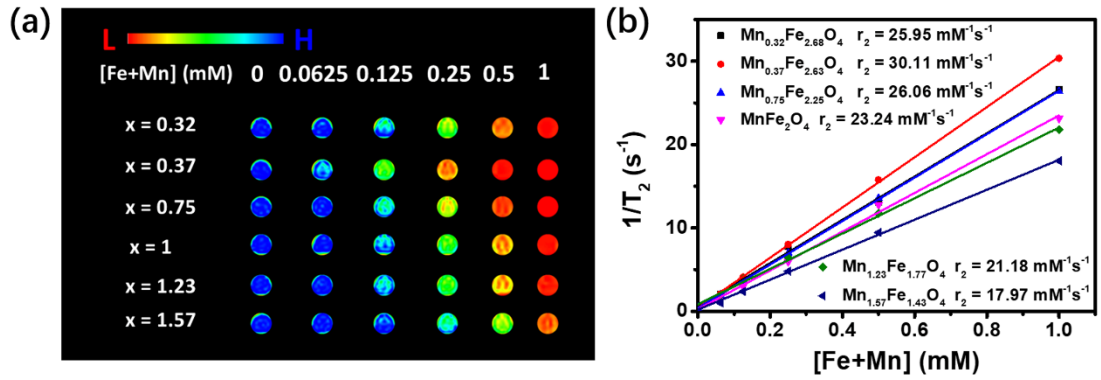

Figure S5. (a) T_2-weighted phantom imaging of ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles with different Mn doping level. (b) Plot of $1/T_2$ over [Fe+Mn] concentration of the ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles with different Mn doping level.

Table S4. The magnetization at 3T, T_1 relaxivities, T_2 relaxivities and r_2/r_1 ratios of the ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles with various Mn doping ratios measured at 300 K

Mn doping level (x)	Average size (nm)	Ms (emu/g)	r_1 ($mM^{-1}s^{-1}$)	r_2 ($mM^{-1}s^{-1}$)	r_2/r_1
0.32	3.11	21.78	7.02	25.95	3.70
0.37	2.95	31.07	7.08	30.11	4.25
0.75	3.28	26.92	10.35	26.06	2.52
1	3.05	25.59	9.91	23.24	2.34
1.23	3.07	10.69	9.23	21.18	2.29
1.57	3.14	8.2	7.64	17.97	2.36

Table S5. Pharmacokinetic parameters for the ultrasmall $Mn_xFe_{3-x}O_4$ nanoparticles

Parameter (unit)	$t_{1/2\alpha}$ (h)	$t_{1/2\beta}$ (h)	CL (mL/h)
$Mn_{0.32}Fe_{2.68}O_4$	0.64	8.01	1.00
$Mn_{0.37}Fe_{2.63}O_4$	0.62	9.59	0.67
$Mn_{0.75}Fe_{2.25}O_4$	0.53	10.03	0.42
$MnFe_2O_4$	0.50	10.56	0.48
$Mn_{1.23}Fe_{1.77}O_4$	0.34	12.70	0.41
$Mn_{1.57}Fe_{1.43}O_4$	0.17	17.29	0.26