

## **Effect of Metal Ions on Endogenous Melanin Nanoparticles for Magnetic Resonance Imaging Contrast Agents**

Anqi Chen<sup>a,b</sup>, Jinghua Sun<sup>a,b</sup>, Shijie Liu<sup>b</sup>, Liping Li<sup>b</sup>, Xiaoyang Peng<sup>b</sup>, Lixin Ma<sup>c\*</sup> and Ruiping Zhang<sup>a\*</sup>

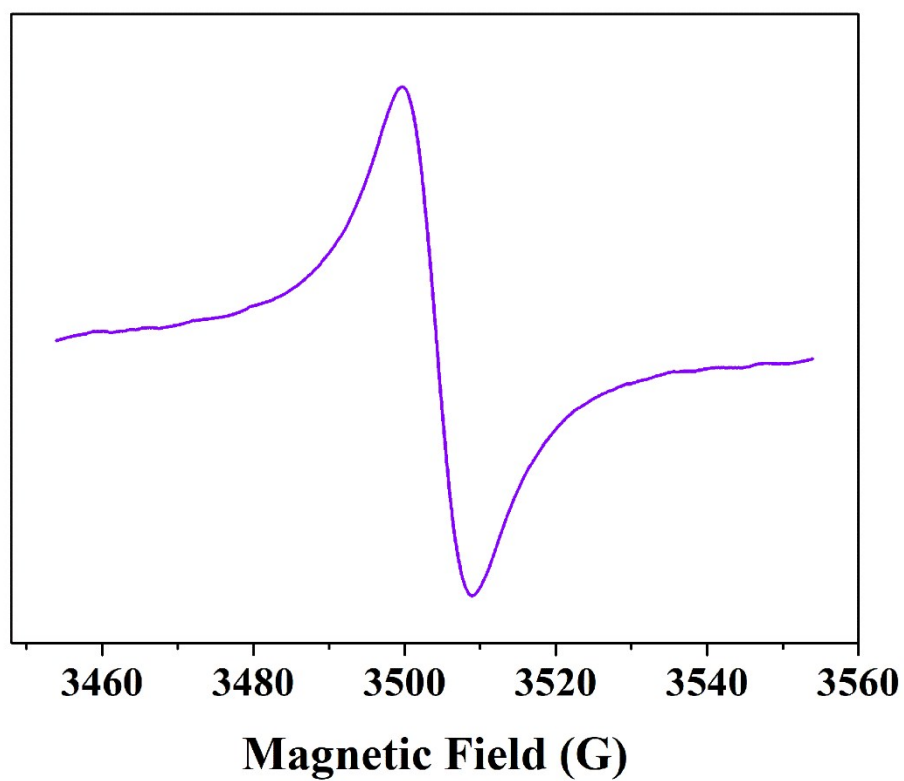
<sup>a</sup> Imaging Department, The Affiliated Da Yi Hospital of Shanxi Medical University, Taiyuan 030000, China

<sup>d</sup> Shanxi Medical University, Taiyuan 030001, China

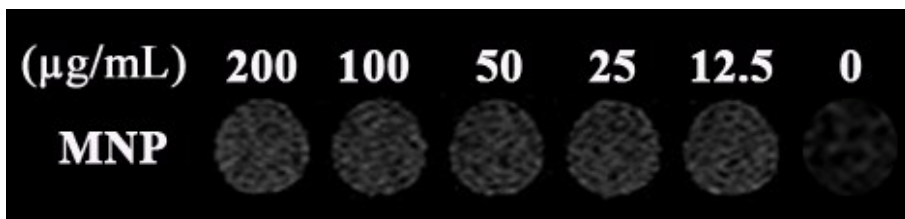
<sup>c</sup> Department of Radiology, University of Missouri, Columbia, MO, 65212, USA and Harry S. Truman Memorial Veterans' Hospital, Columbia, MO 65201, USA.

\* E-mail: zrp\_7142@sxmu.edu.cn; mal@health.missouri.edu.

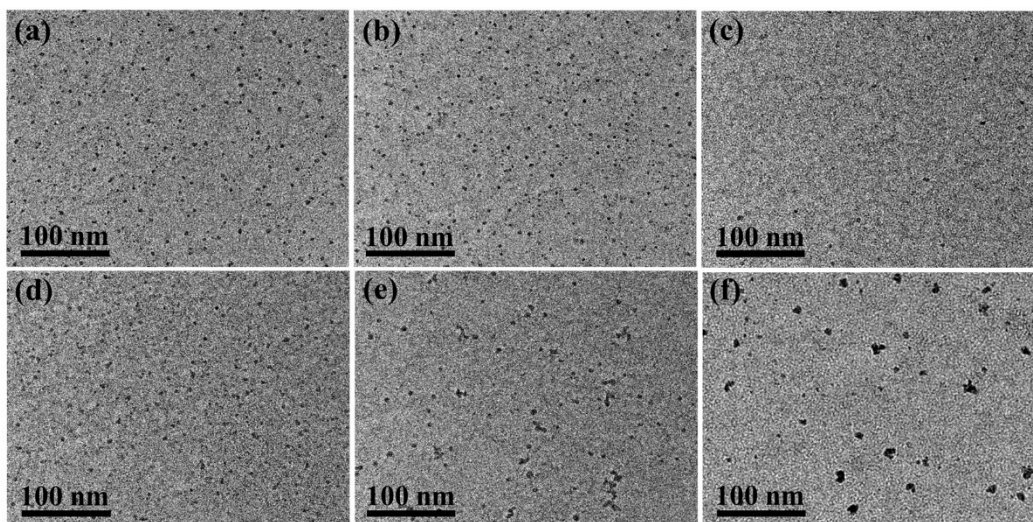
Anqi Chen and Jinghua Sun were contributed equally to this work.



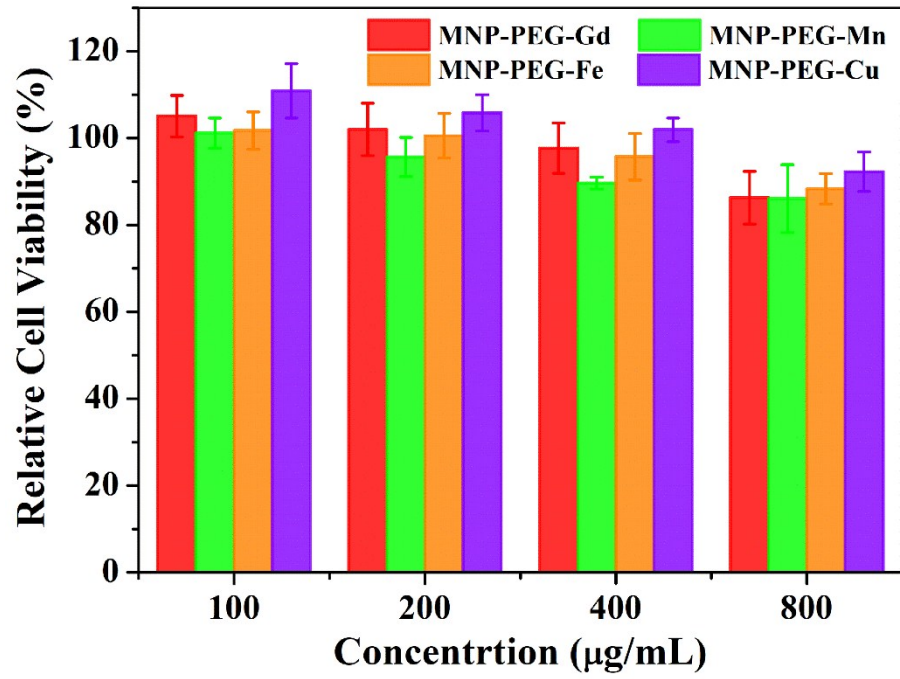
**Figure S1.** EPR spectrum of prepared melanin nanoparticles.



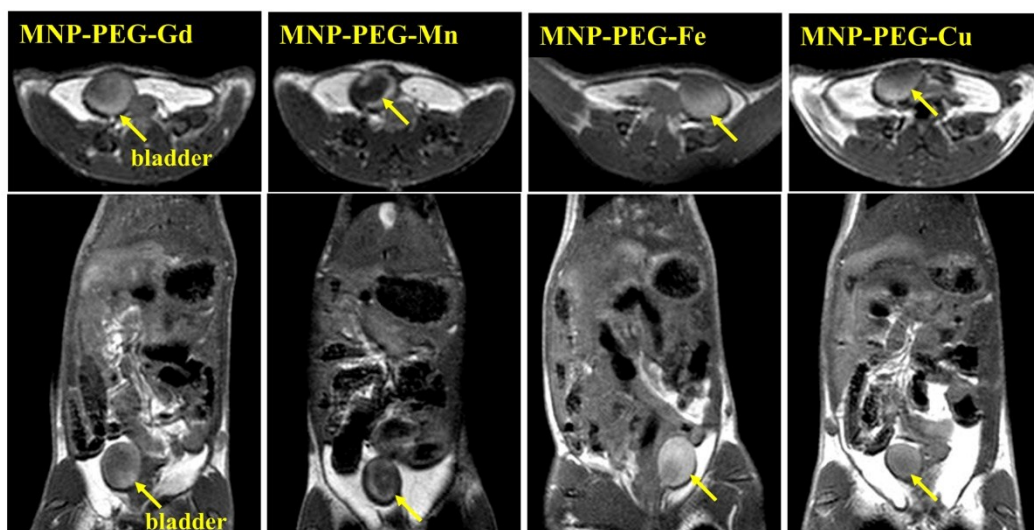
**Figure S2.** T<sub>1</sub>-weighted images of melanin nanoparticles with different concentration.



**Figure S3.** TEM images of MNP-PEG-Gd with different Gd<sup>3+</sup>:MNP mass ratio: (a) Gd<sup>3+</sup>:MNP=0.05:1, (b) Gd<sup>3+</sup>:MNP=0.1:1, (c) Gd<sup>3+</sup>:MNP=0.5:1, (d) Gd<sup>3+</sup>:MNP=1:1, (e) Gd<sup>3+</sup>:MNP=3:1 and (f) Gd<sup>3+</sup>:MNP=5:1.



**Figure S4.** Relative viabilities of Rat H9C2 cardiomyocytes incubated with MNP-PEG-M nanoparticles at various concentrations for 24 h by CCK-8 assay.



**Figure S5.** T<sub>1</sub>-weighted MRI axial and coronal images of BALB/c mice at 4 h after intravenously injected MNP-PEG-M at 1 mg / per mouse performed on a 3.0 T clinical MRI scanning. The bladders were indicated by yellow arrows.

**Table S1.** The hematological data after intravenous injection with either MNP-PEG-M or with saline (control). Error bars represent standard deviation from 3 to 4 independent replicates. Reference ranges of hematology data of healthy Balb/c mice.

Mean±SE		WBC( $10^9/L$ )	RBC( $10^{12}/L$ )	HGB(g/L)	HCT(%)
Reference range		5.67~14.84	8.16~11.69	124.00~189.00	43.00~67.00
Control		7.10±0.72	8.88±0.22	151.67±4.04	48.27±0.86
MNP-PEG-Gd	1d	7.27±0.71	9.18±0.16	156.67±10.69	50.83±1.96
	7d	7.61±0.28	9.15±0.07	162.67±10.60	51.67±0.91
MNP-PEG-Mn	1d	7.27±1.00	8.32±0.13	147.00±6.25	46.73±1.34
	7d	7.54±0.32	8.75±0.28	150.67±4.04	48.60±1.08
MNP-PEG-Fe	1d	7.60±1.45	8.77±0.15	147.33±4.51	47.87±1.76
	7d	7.45±0.28	8.85±0.06	142.67±11.93	44.47±1.11
MNP-PEG-Cu	1d	6.93±0.27	8.42±0.11	141.33±5.51	47.63±1.99
	7d	6.79±0.15	8.84±0.09	146.00±6.56	45.80±1.60
Mean±SE		MCV(fL)	MCH(pg)	MCHC(g/L)	PLT( $10^9/L$ )
Reference range		50.80~64.10	13.00~17.60	239.00~331.00	476.00~1611.00
Control		54.77±0.70	17.10±0.30	315.33±11.06	731.33±8.50
MNP-PEG-Gd	1d	55.53±0.50	17.23±0.50	315.33±8.50	658.00±24.06
	7d	52.77±0.67	17.40±0.40	315.67±4.04	643.67±29.91
MNP-PEG-Mn	1d	55.30±0.57	17.47±0.25	318.33±12.06	633.00±19.00
	7d	56.60±1.35	17.37±0.55	316.00±5.57	656.67±29.02
MNP-PEG-Fe	1d	51.77±0.50	16.63±0.31	313.67±13.20	643.00±9.85
	7d	54.40±1.21	16.70±0.46	314.33±4.73	656.33±26.76
MNP-PEG-Cu	1d	54.10±0.46	16.77±0.50	323.33±12.01	483.67±7.64
	7d	53.70±0.92	16.87±0.45	315.33±4.16	525.00±19.67