Supporting Information

Gadolinium Doping Enhances the Photoacoustic Signal of Synthetic Melanin Nanoparticles: A Dual Modality Contrast Agent for Stem Cell Imaging.

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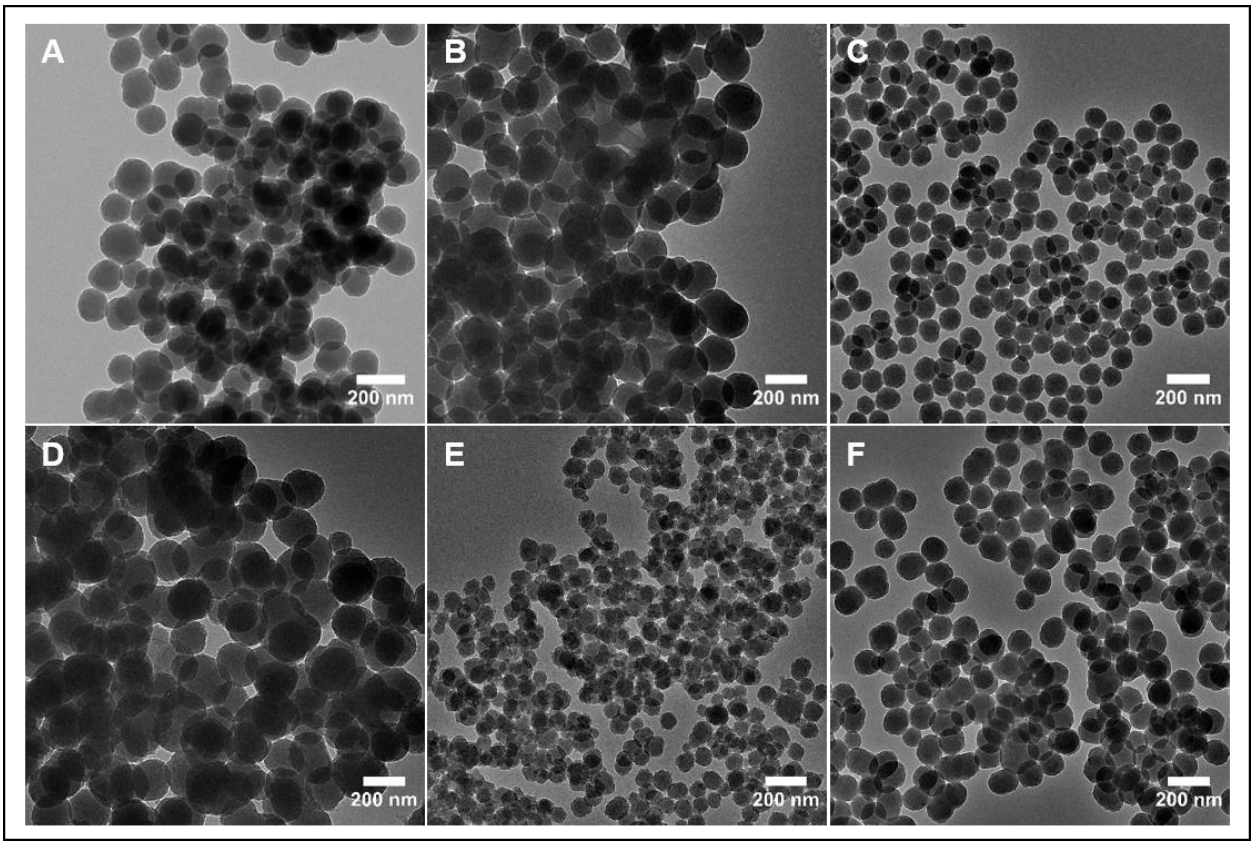


Figure S1. Representative TEM images show spherical shape and uniform size distribution of synthetic melanin nanoparticles. A) SMNP made by polymerization of L-3,4-dihydroxyphenylalanine. **Figures B-F** show metal-doped SMNPs. **B)** Mn-doped SMNP, **C)** Fe-doped SMNP, **D)** Ni-doped SMNP, **E)** Cu-doped SMNP, and **F)** Zn-doped SMNP.

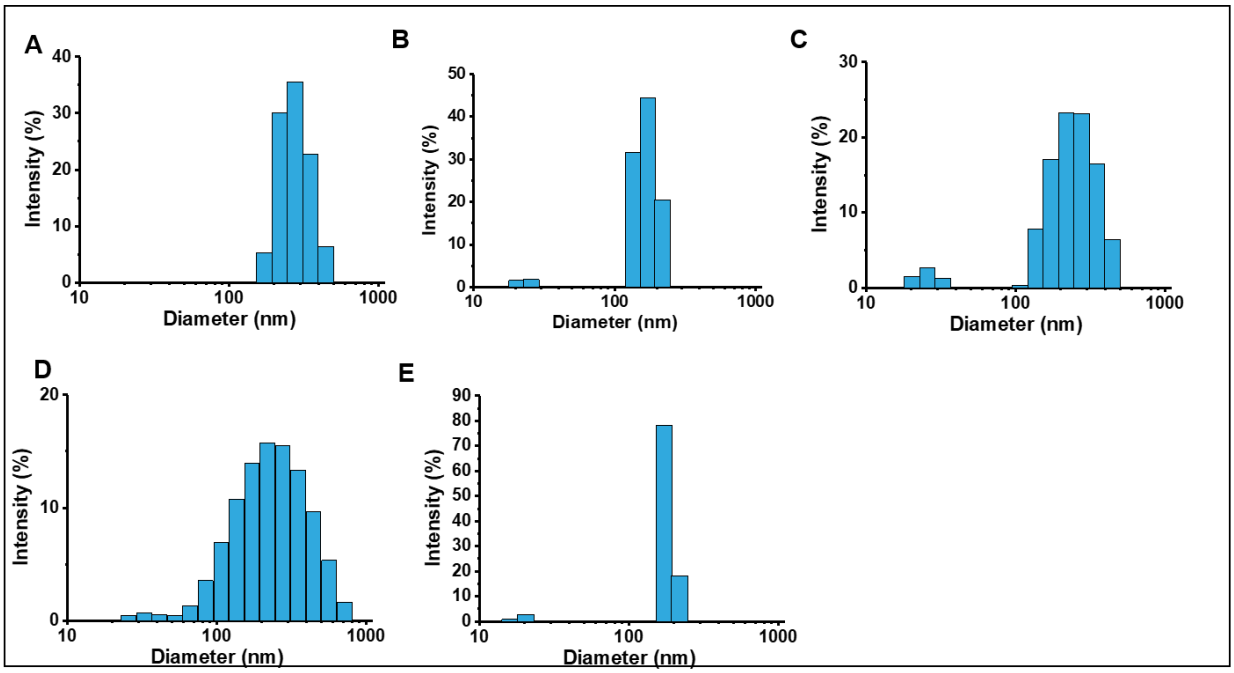
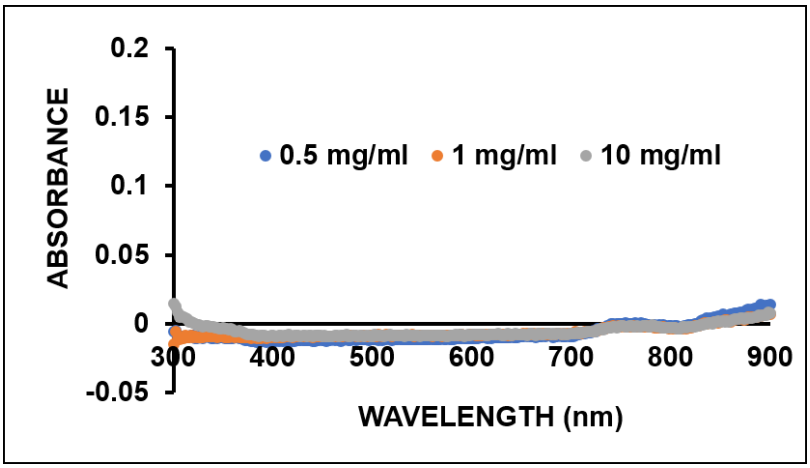
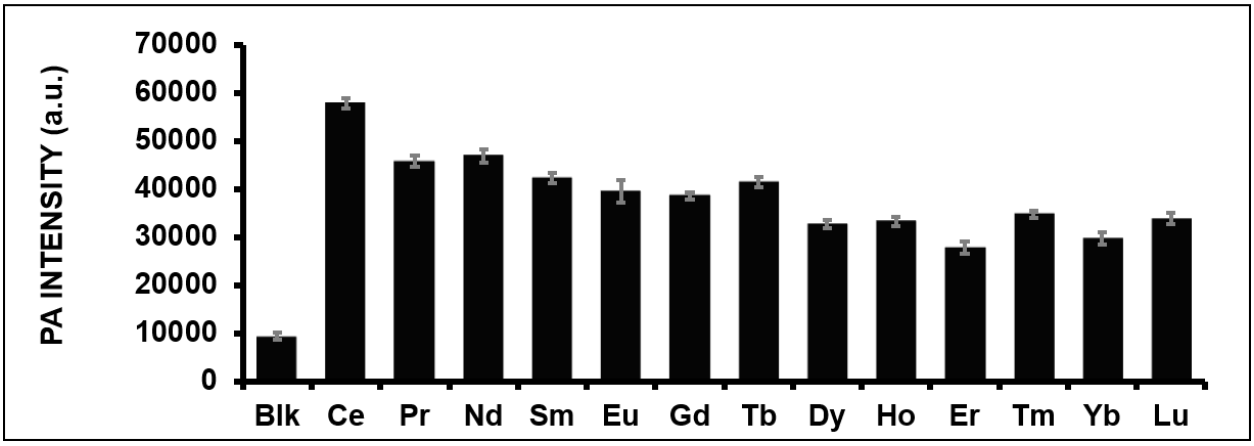


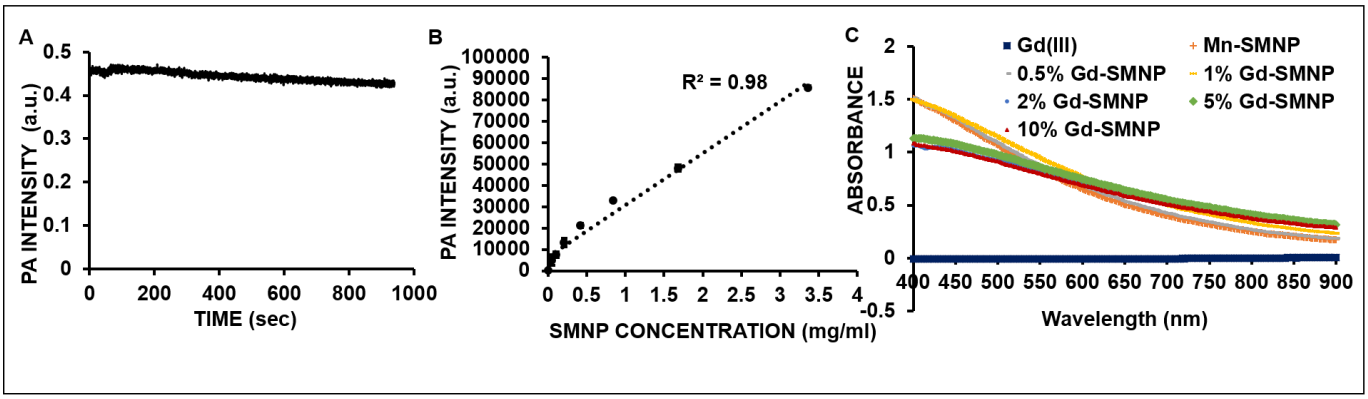
Figure S2. Representative DLS data show size distribution of synthetic melanin nanoparticles. Figures A-F show metal-doped SMNPs. **A)** Mn-doped SMNP, **B)** Fe-doped SMNP, **C)** Ni-doped SMNP, **D)** Cu-doped SMNP, and **E)** Zn-doped SMNP.



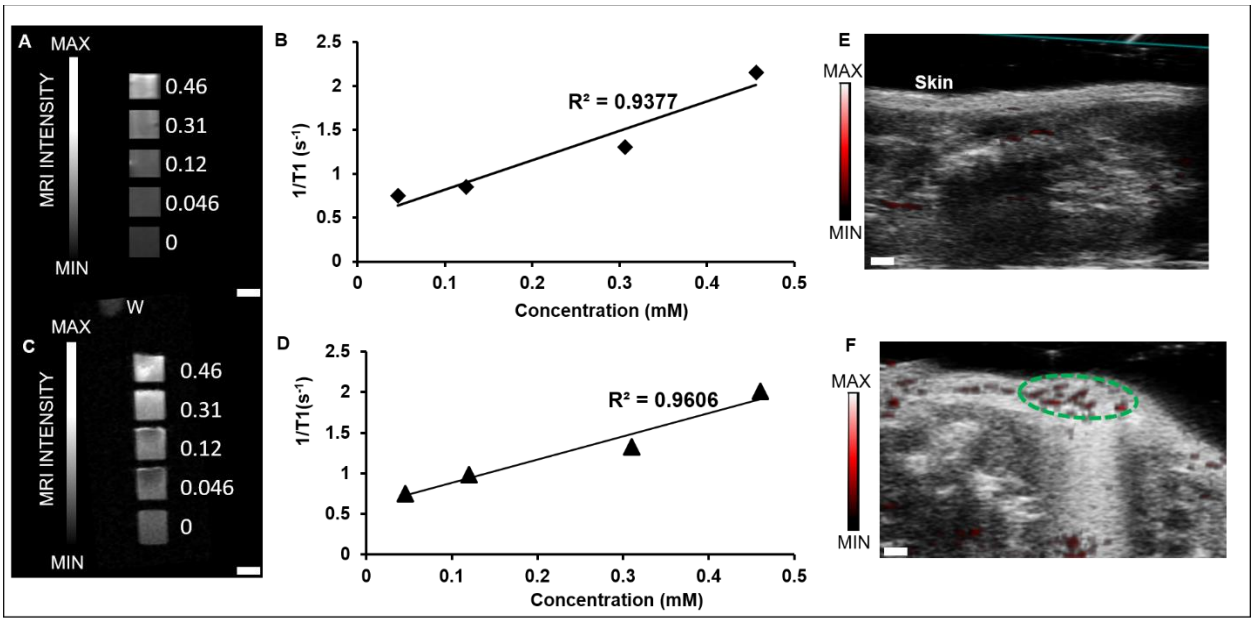
Supplementary Figure S3. Absorbance of Gd(III) solution. Gd(III) was dissolved in water at 0.5 mg/ml, 1 mg/ml, and 10 mg/ml and showed low absorbance from 300-900 nm.



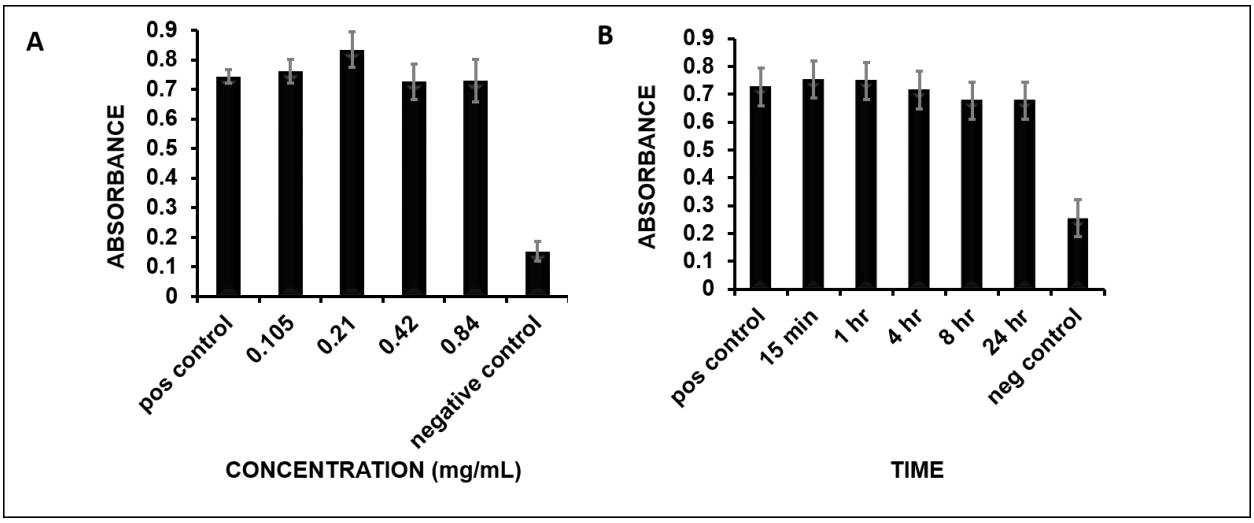
Supplementary Figure S4. PA intensity data of lanthanide-doped SMNPs. Ce-doped SMNP had the highest PA signal of 57,766.6 +/- 1,073.5 while Er-doped had the lowest PA signal of 9,375.6 +/- 838.2 of the lanthanide-doped samples. Error bars represent the standard deviation (n=8).



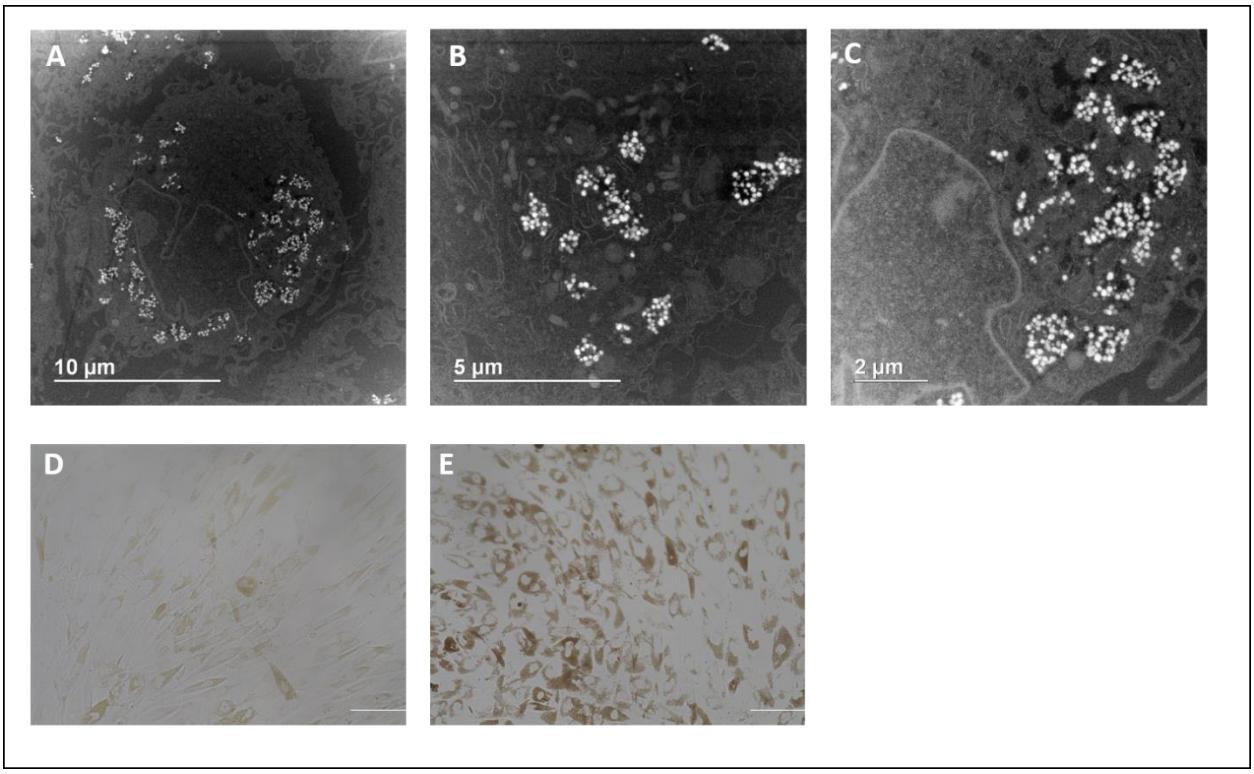
Supplementary Figure S5. **A**) The PA signal difference between the first 100 frames and the last 100 frames is 6.6% indicating that the SMNPs are stable under photoacoustic irradiation. **B**) There is a linear relationship of PA signal based on SMNP concentration measured from 0-3.5 mg/mL. **C**) The absorbance of 5% and 10% Gd-SMNP was higher from 600-900 nm than Mn-SMNP and 0.5 – 2% Gd-SMNP.



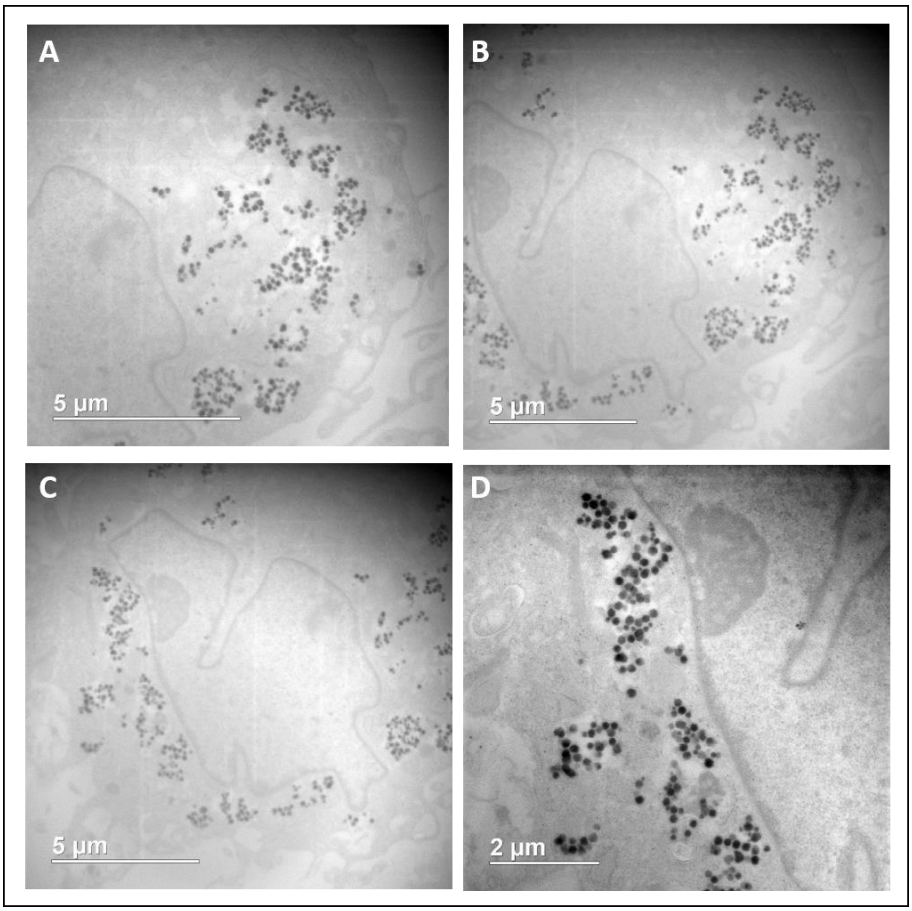
Supplementary Figure S6. MRI and PA data of Gd(III)-SMNP. A) MRI of Gd(III)-SMNP particles in 4.7 T. **B**) 1/T1 (s^{-1}) vs Concentration (mM) for 4.7T field. **C**) MRI of Gd(III)-SMNP particles in 7 T. **D**) 1/T1 (s^{-1}) vs Concentration (mM) for 7 T field. Scale bar = 2 mm. **E**) PA imaging of mouse prior to injection of Gd-SMNP nanoparticles. **F**) PA imaging of mouse after injection of Gd-SMNP shows increased PA signal (area circled in green).



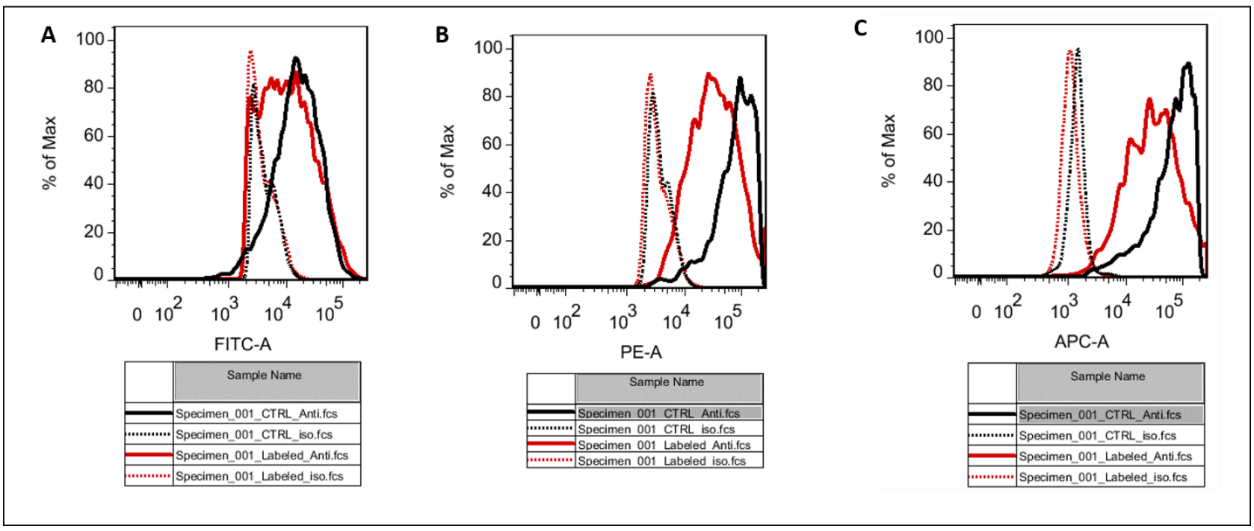
Supplementary Figure S7. MTT assays of Gd-SMNP labeled hMSCs. A) Cell viability was not affected by increasing the concentration from 0.105 – 0.84 mg/mL of Gd(III)-SMNP. **B)** Cell viability decreased approximately 7% after 24 hours of treatment with Gd(III)-SMNP (0.42 mg/mL). The positive (pos) control was unlabeled cells. The negative (neg) control was cells treated with 70% ethanol. The error bars represent the standard error. N = 6.



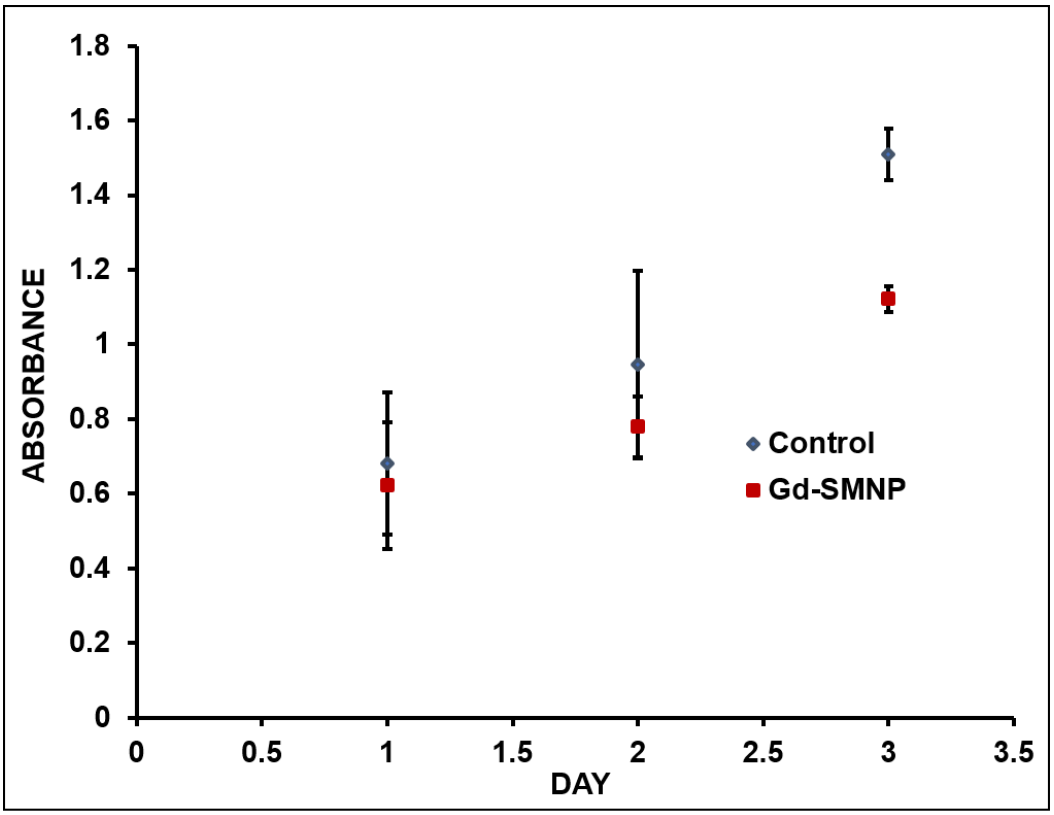
Supplementary Figure S8. Dark Field STEM microscopy and optical microscopy show internalization of nanoparticles. A-C) Dark field STEM microscopy of hMSCs labeled with Gd-SMNP (4 hrs, 0.42 mg/mL). The Gd-SMNP particles (white spheres) are located in the in the cytoplasm of cells. **D)** Brightfield microscopy of unlabeled hMSCs. **E)** Brightfield microscopy of hMSCs labeled with Gd-SMNP (4 hrs, 0.42 mg/mL). The cells continued to proliferate for 3 weeks when labeled with Gd-SMNP. Scale bar = 200 µm.



Supplementary Figure S9. Figures A-D show TEM microscopy of hMSCs treated with Gd(III)-SMNP (4 hrs, 0.42 mg/mL). The Gd(III)-SMNP particles (black spheres) are located in the cytoplasm of cells.



Supplementary Figure S10. **Flow cytometry data of hMSCs labeled with 0.42 mg/mL of-Gd(III)-SMNP. A**) CD90-FITC, **B**) CD73-PE, and **C**) CD105-APC.



Supplementary Figure S11. Viability assay of Gd(III)-SMNP treated hMSCs. Cells doubled in approximately 3 days for control (untreated hMSCs) and cells labeled with 0.42 mg/mL Gd(III)-SMNP. The error bars represent the standard error (n=8).