Supporting Information for

Magneto Mitochondrial Dysfunction Mediated Cancer Cell Death Using Intracellular Magnetic Nano-Transducers

Wooram Park, ^{1,2†} Seok-Jo Kim, ^{3,4,5†} Paul Cheresh, ^{3,4} Jeanho Yun, ⁶ Byeongdu Lee, ⁷ David W. Kamp, ^{3,4} and Dong-Hyun Kim^{1,8,9*}

¹Department of Radiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois 60611, United States

²Department of Biomedical-Chemical Engineering, The Catholic University of Korea, 43 Jibong-ro, Wonmi-gu, Bucheon-Si, Gyeonggi 14662, Republic of Korea

³Department of Medicine, Division of Pulmonary & Critical Care Medicine, Jesse Brown VA Medical Center, Chicago, Illinois 60612, United States

⁴Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois 60611, United States

⁵Division of Rheumatology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI 48109, United States

⁶Department of Biochemistry, College of Medicine, Dong-A University, Busan 49201, Republic of Korea

⁷X-Ray Science Division, Argonne National Laboratory, Argonne, IL, 60439 United States ⁸Department of Biomedical Engineering, McCormick School of Engineering, Evanston, IL 60208, United States

⁹Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, Illinois 60611, United States

[†]These authors contributed equally to this work.

*Corresponding authors

E-mail: dhkim@northwestern.edu (Prof. D.-H. Kim)

Sample	β-FeOOH1	β-FeOOH2
Feed iron (Fe) concentration (mg/mL)	10	20
Length (nm)	48 ± 12	128 ± 26
Width (nm)	15 ±3	32 ±7
Aspect ratio	3 ±1	4 ±1

Table S1. Characterization of β-FeOOH nanorods.



Figure S1. Transmission electron microscopy (TEM) image of β -FeOOH nanorods synthesized under different conditions of iron (Fe) concentration. (a-b) TEM image of β -FeOOH nanorods synthesized at feed iron concentration of (a) 4 and (b) 20 mg/mL, respectively. Detailed particle size analysis of the β -FeOOH nanorods was described in Table S1. The particle size was increased proportionally with increasing feed iron concentration. In this study, we selected the rod-shaped nanoparticle (synthesized at 10 mg/mL of iron) smaller than 100 nm, known to have high accumulation efficiency in tumors.^[1]

(a) Reduction for 4 h

(b) Reduction for 12 h



Figure S2. Transmission electron microscopy (TEM) image of iron oxide nanospindles (IONSs) under different reduction conditions. (a-b) TEM images of IONSs reduced for (a) 4 and (b) 12 h, respectively. The nanoparticles reduced at olyelamine at 200 °C for 4 h remained in the rod shape, but when reduced for 12 h the nanoparticles lost their shape and aggregated. This result was similar to the previous outcome of the Hyeon group.^[2] Based on this result, the nanoparticles that underwent a 6 h reduction process were selected in this study.



Figure S3. ¹**H-NMR analysis of TPP-PEG-DOPAC in DMSO-d6.** The proton signals of the benzene group of TPP (a, b, and c), the ethylene group of PEG (f), and the catechol group of DOPAC (e and d) were clearly shown in the ¹H-NMR spectrum, respectively.



Figure S4. FT-IR analysis of bare iron oxide nanospindles (Bare IONSs) and TPP-IONSs (*i.e.*, mitochondria-targeting magnetic nano-transducers). In TPP-IONSs surface-modified with TPP-PEG-DOPAC, methylene stretches (-CH₂) of DOPAC and PEG were at 2920 and 2850 cm⁻¹, and C=O bond stretches of DOPAC were at 1750 cm⁻¹.^[3]



Figure S5. Western blot for *in vitro* expression of TOM 20 and TIM 23 in the cancer cells treated with nano-transducers under conditions with or without magnetic fields.

References for Supporting Information

- [1] A. K. Parchur, G. Sharma, J. M. Jagtap, V. R. Gogineni, P. S. LaViolette, M. J. Flister, S. B. White, A. Joshi, *ACS nano* **2018**, 12, 6597.
- [2] Y. Piao, J. Kim, H. B. Na, D. Kim, J. S. Baek, M. K. Ko, J. H. Lee, M. Shokouhimehr, T. Hyeon, *Nat Mater* **2008**, 7, 242.
- [3] K. Zeng, J. Li, Z. Zhang, M. Yan, Y. Liao, X. Zhang, C. Zhao, *Journal of Materials Chemistry B* 2015, 3, 5249.