Supporting information

Drug-Internalized Bacteria Swimmers for Magnetically Manipulable Tumor-Targeted Drug Delivery

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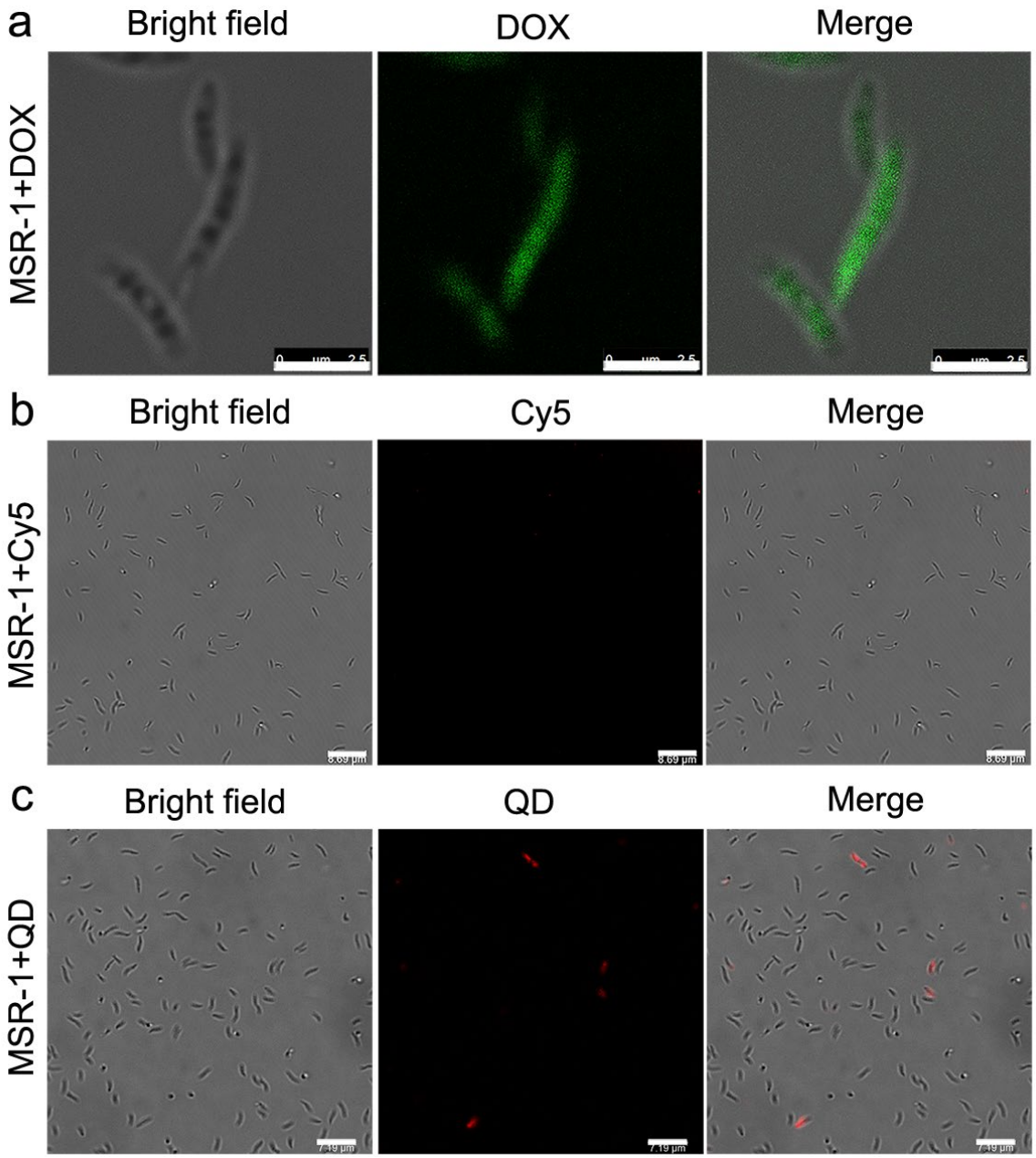

Figure S1. Confocal fluorescence images of MSR-1 incubated with (a) DOX (green), (b) Cy5 (red), and (c) QD (red) for 2 h. Compared with DOX, both Cy5 and QD did not internalize into MSR-1 bacteria efficiently. Scale bars: 2.5 μm (a), 8.69 μm (b), 7.19 μm (c).

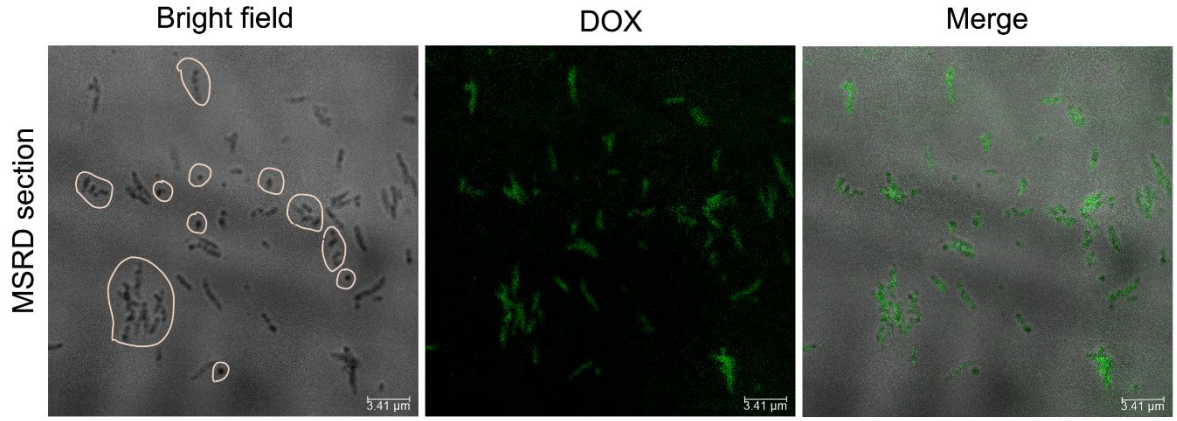

Figure S2. The confocal fluorescence images of sections of MSRDs. In the bright field, the white circles indicate the cross sections of MSRD bacteria.

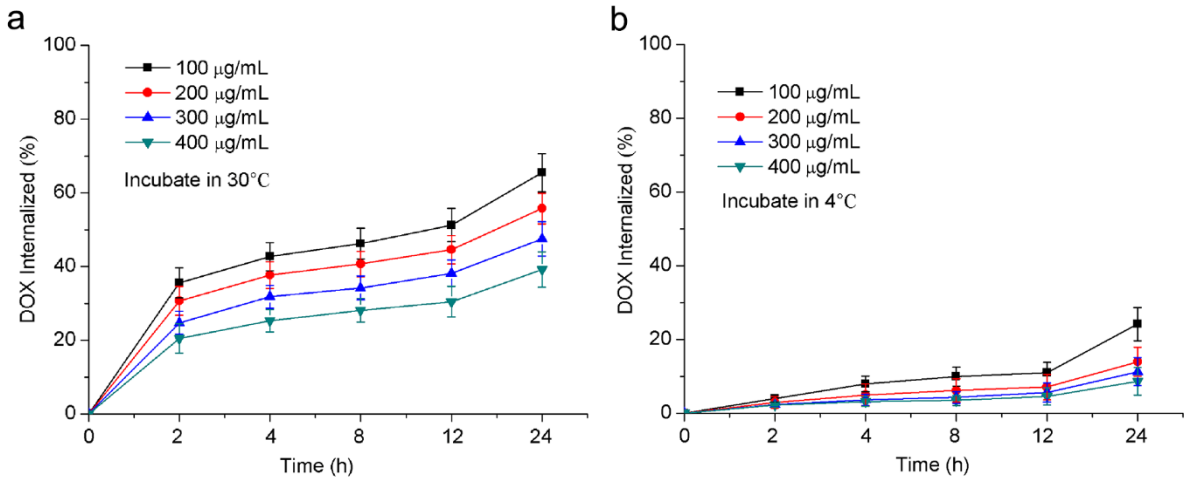

Figure S3. The DOX internalization profiles of MSR-1 bacteria with different amounts of DOX added. The bacteria were incubated with DOX at (a) 30 ℃ and (b) 4 ℃, respectively. Data are represented as means ± SD (n=3).

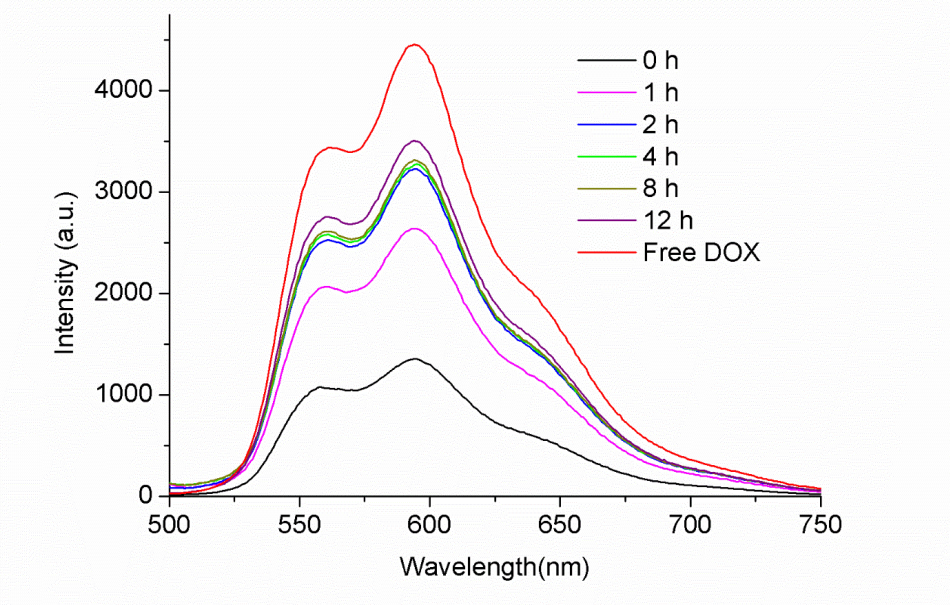

Figure S4. Fluorescence spectra of MSRDs and released DOX after being incubated in PBS (10% FBS) for different time spans. The excitation wavelength was 480 nm and the emission was collected between 500 and 750 nm. Free DOX (86 μM) is served as a positive control.

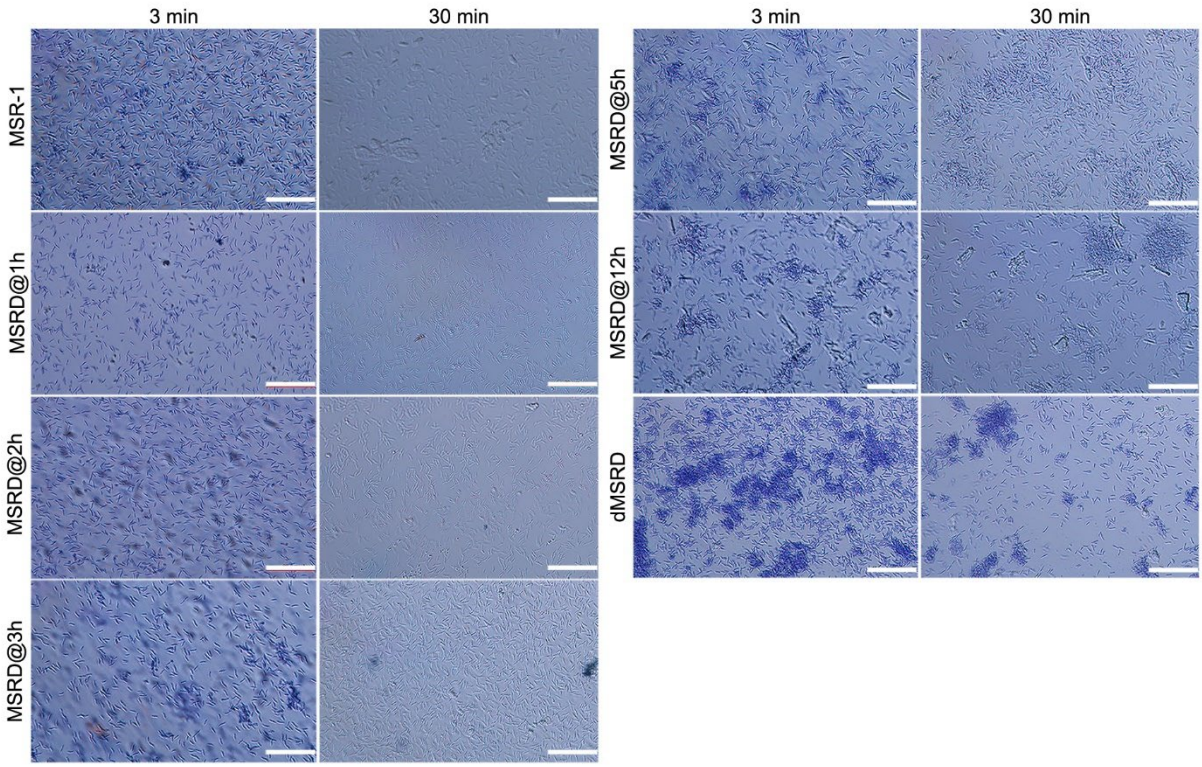

Figure S5. Methylene blue removal analysis of MSRDs incubated with DOX (0.1 mg/mL) over spans of 1 h, 2 h, 3 h, 5 h and 12 h. Corresponding images of methylene blue-treated cells at 3 min and 30 min after the treatments were collected. Free MSR-1 and dMSRD bacteria were used as controls. Scale bars: 20 μm.

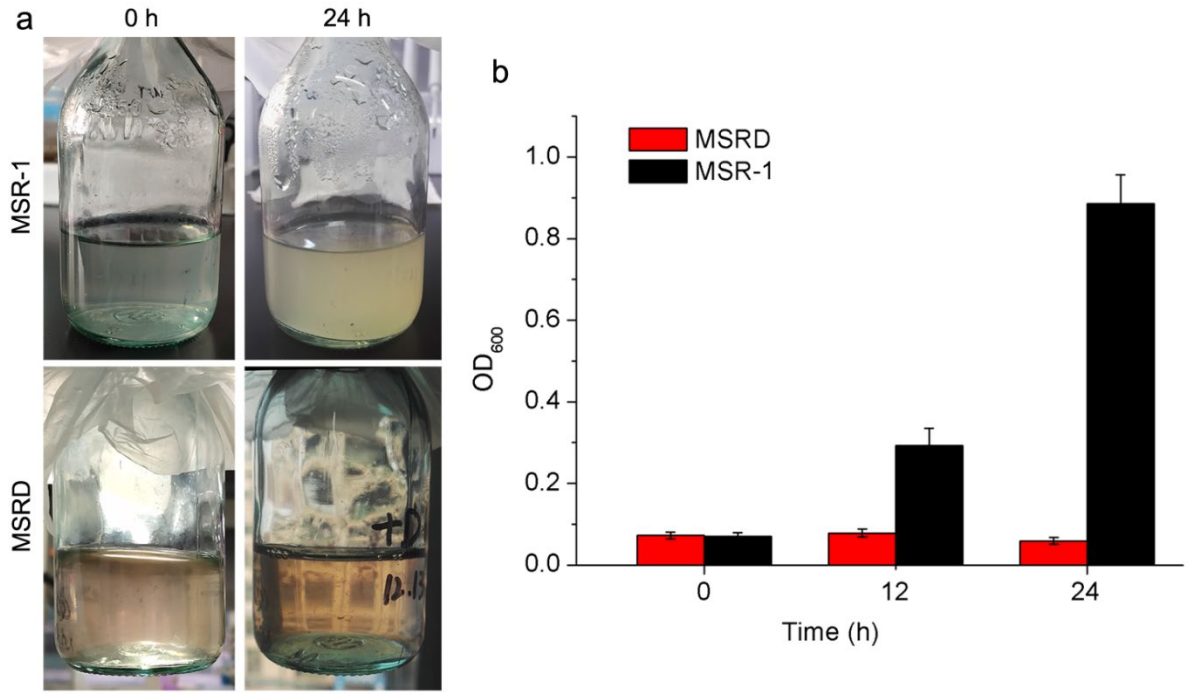

Figure S6. The proliferation of MSR-1 and MSRD bacteria cultured in LAY medium (100 rpm, 30 ℃). (a) Representative images of MSR-1 and MSRD before and after cultivation for 24 h (left). (b) OD_{600} values of MSR-1 and MSRD cells cultured over spans of 0 h, 12 h, 24 h. Data are represented as means ± SD (n=3).

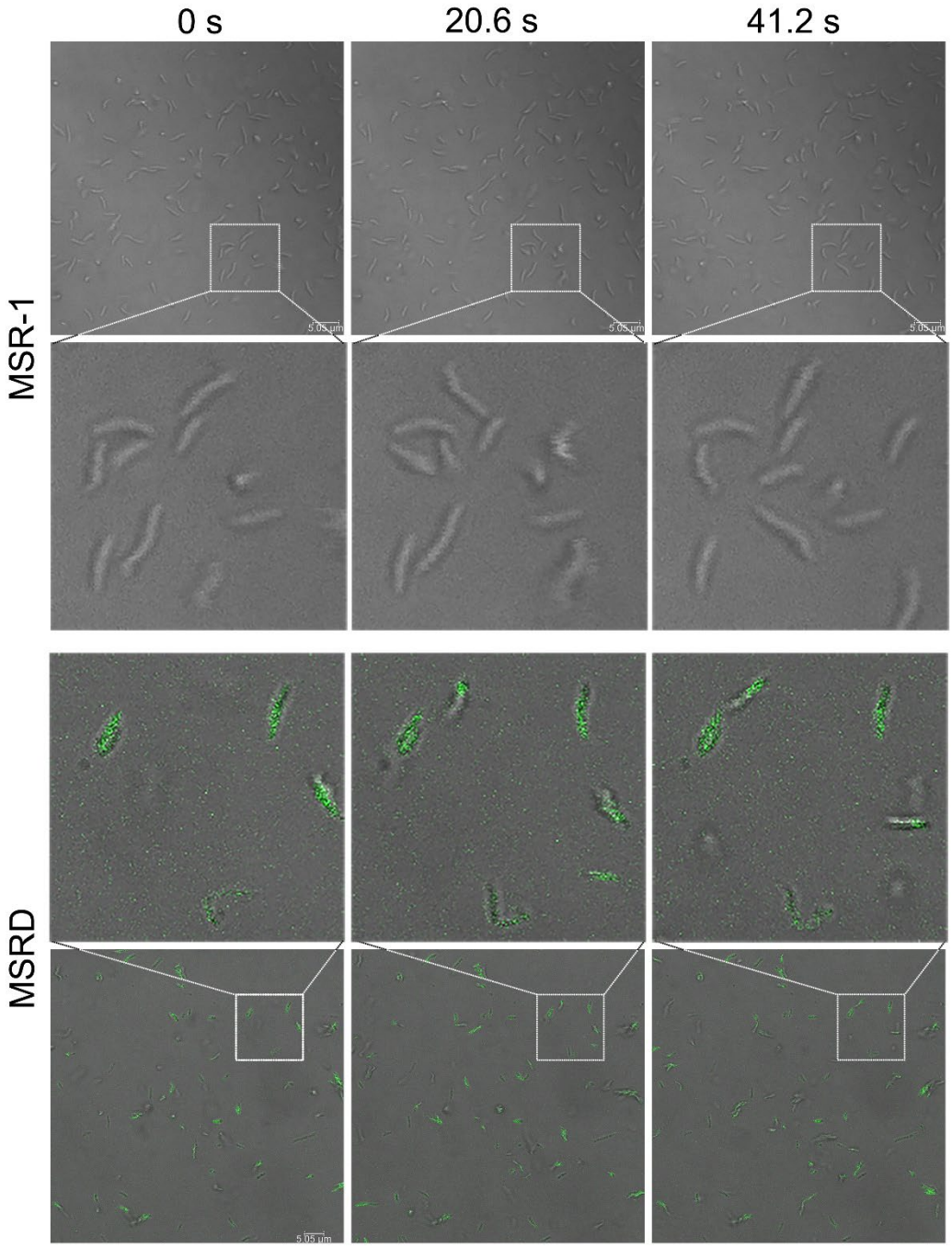

Figure S7. The enlarged MSR-1 and MSRD bacteria to show the motility of MSRD bacteria swimmers.

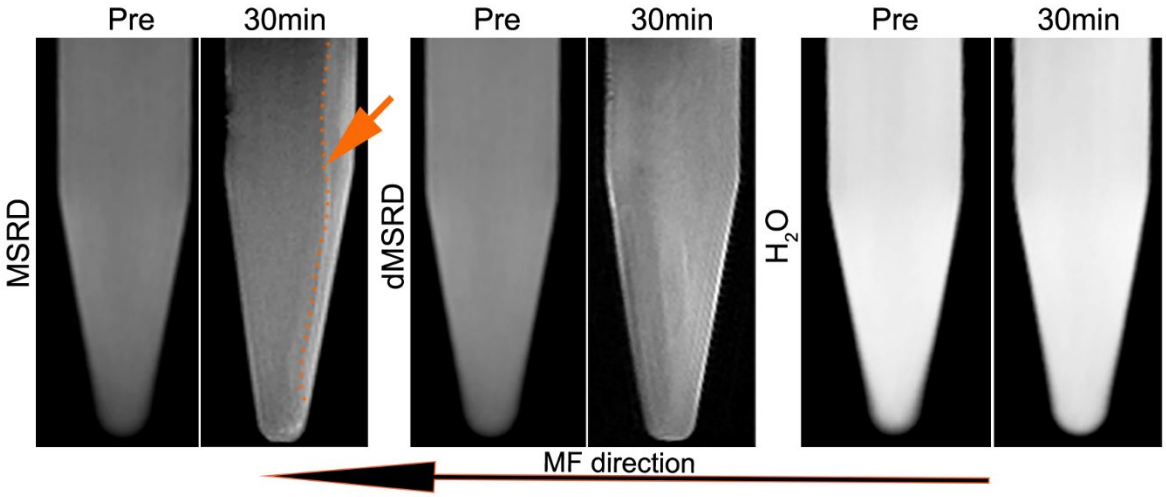

Figure S8. MRI images of MSRD and dMSRD swimmers after exposed to directional MF for 30 min. The orange arrow in MSRD group indicates the boundary of bacteria and solution due to the directional movement of bacteria swimmers under external MF.

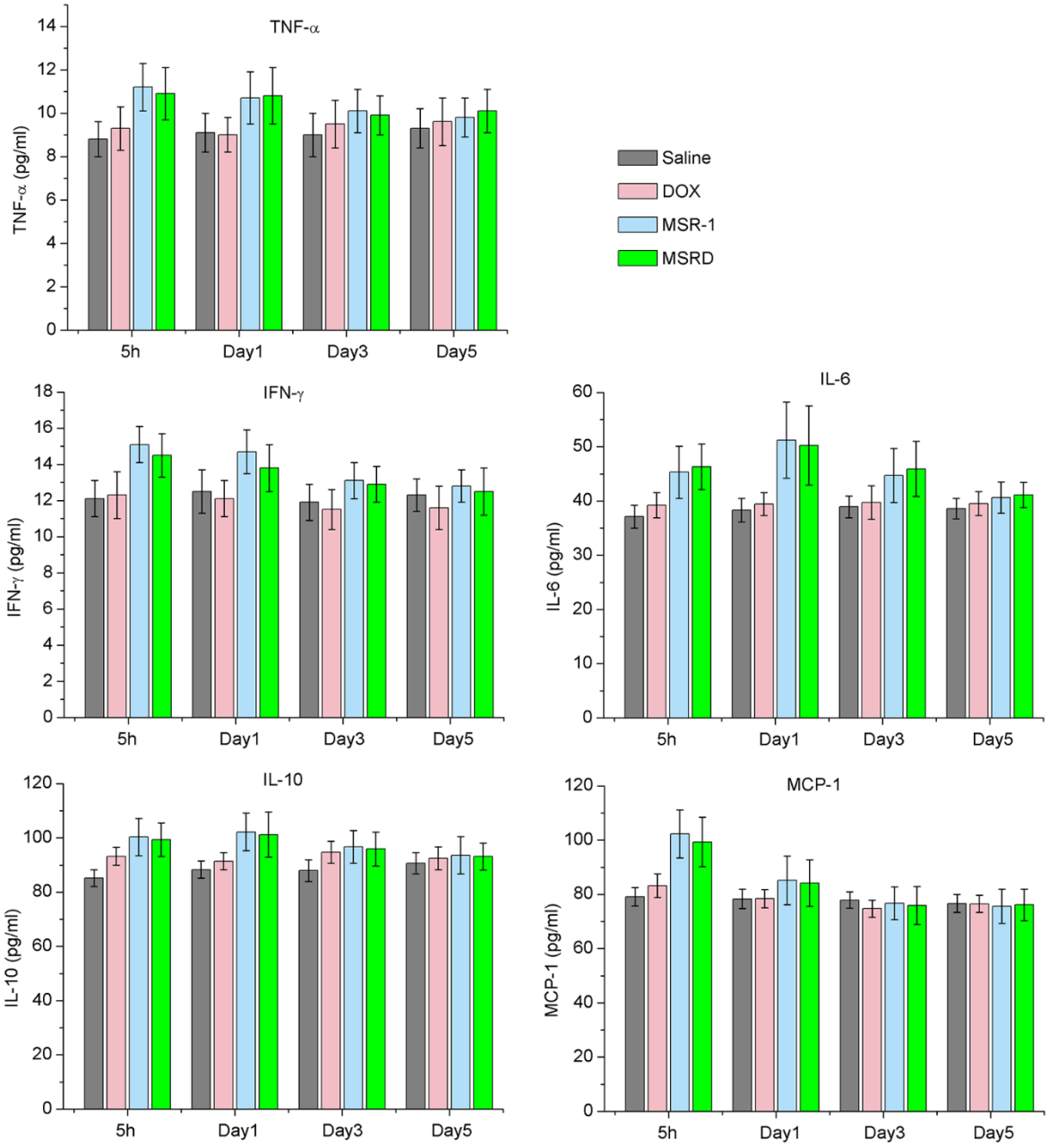

Figure S9. Inflammatory cytokine secretion analysis of mice in different groups. Mice were randomly divided and administered with saline, DOX, MSR-1, and MSRD, respectively. The blood was sampled at 5 h, day 1, day 3, day 5 post injections, and the cytokine levels were analyzed using a BD Mouse Inflammation Kit. Data are represented as means ± SD (n=3).

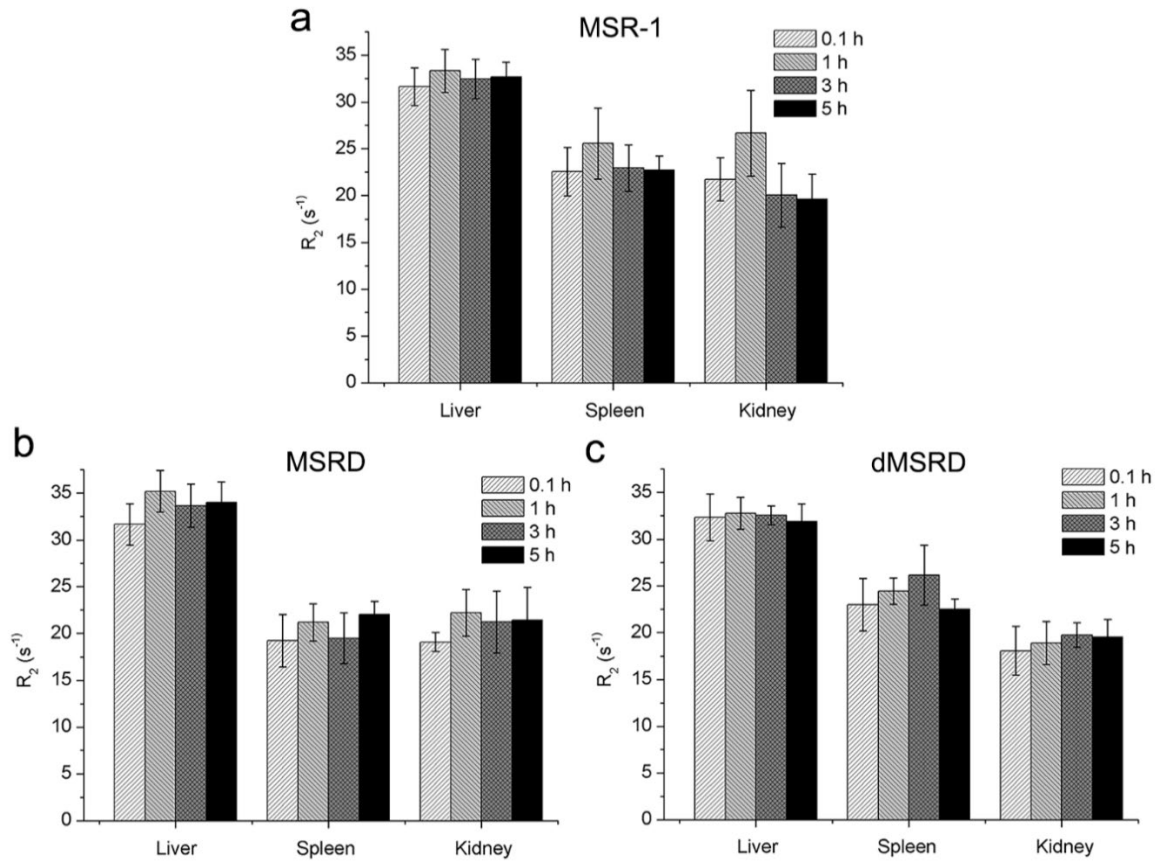

Figure S10. Transverse relaxation rate (R_2) of main organs from the mice bearing PC-3 tumors at 0.1 h, 1 h, 3 h, 5 h after exposure to directional MF. The mice in each group were treated with (a) MSR-1, (b) MSRD, and (c) dMSRD. Data are represented as means ± SD (n=3).

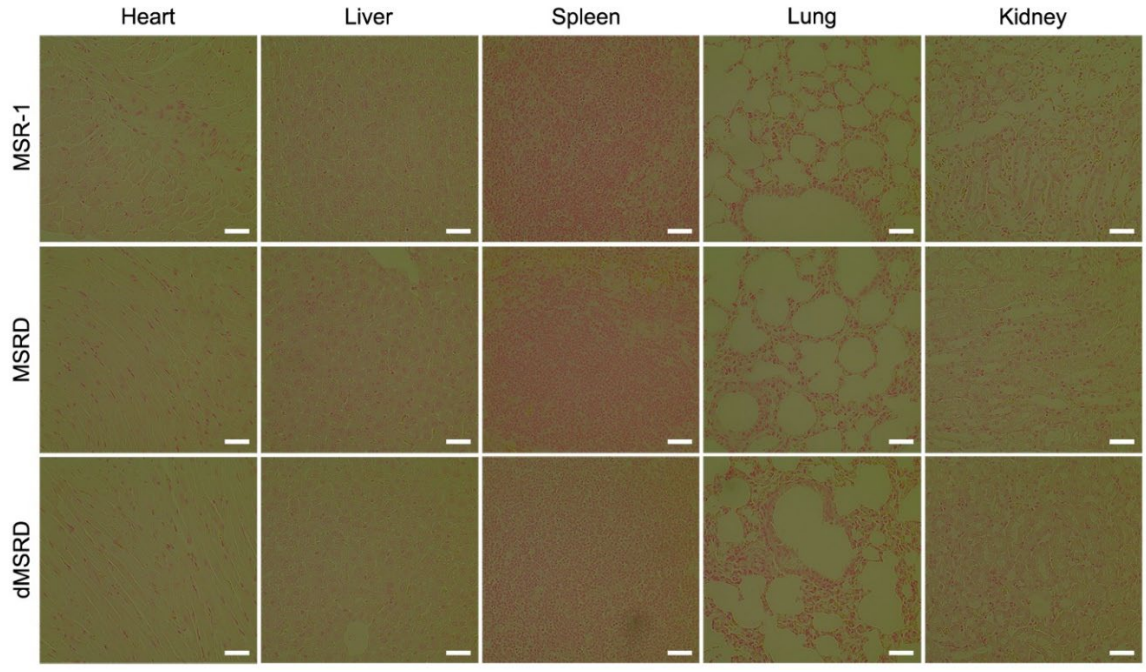

Figure S11. Representative images of Prussian blue stained organ slices from the mice 7 h after exposure to the directional MF. Scale bars: 100 μm.

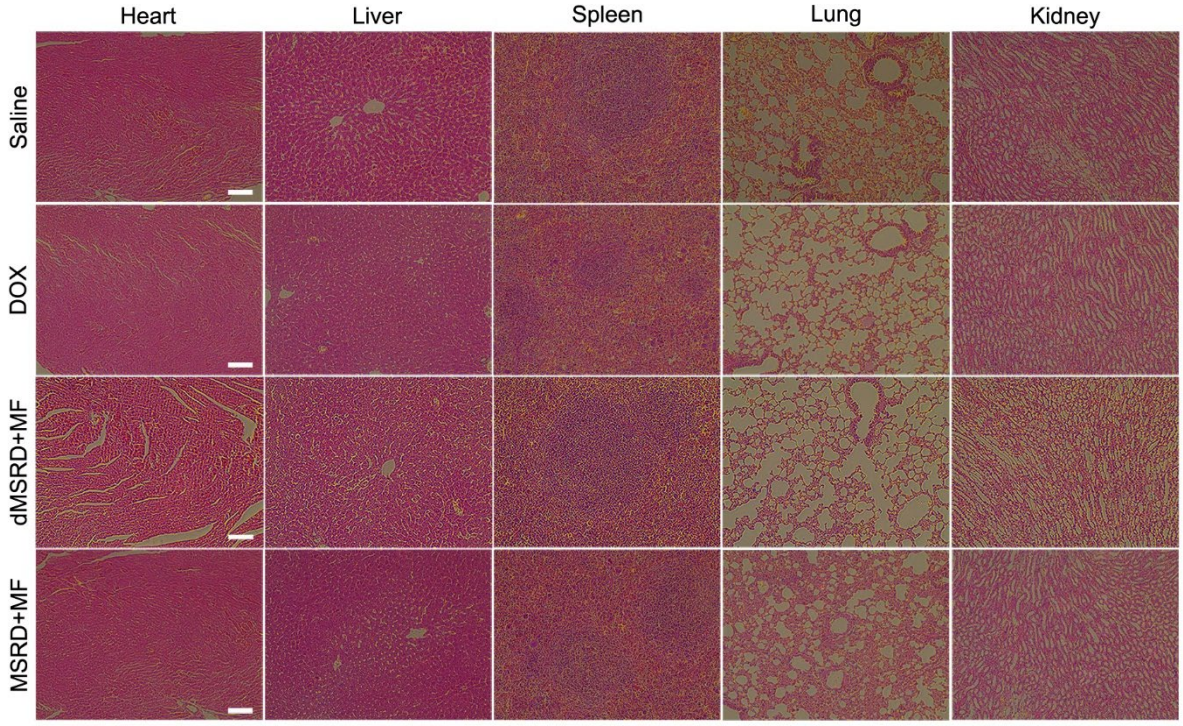

Figure S12. Representative H&E images of main organs from the mice treated with Saline, DOX dMSRD+MF, and MSRD+MF, respectively. Scale bars: 100 μm.

Abbreviations: **MF:** magnetic field, **MRI:** magnetic resonance imaging, **MTB:** Magnetotatic bacteria, **MSR-1:** *Magnetospirillum gryphiswaldense*, **MSRDs:** DOX-internalized MSR-1 bacteria swimmers, **dMSRDs:** dead MSRD cells, **FBS:** Fetal Bovine Serum, **MCTS:** multicellular tumor spheroids.