# Supporting Information

# Multifunctional $Fe_3O_4$@ZIF-8 Nanoparticles with Antibiosis and Osteogenesis for Treatment of Jaw Osteomyelitis

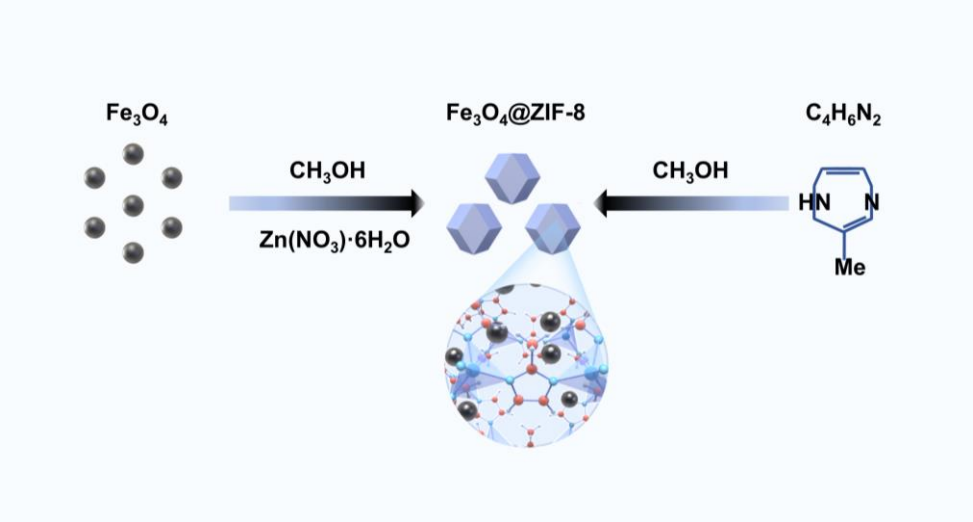



**Figure S1** Schematic illustration of the synthesis process for $Fe_3O_4$@ZIF-8 NPs.

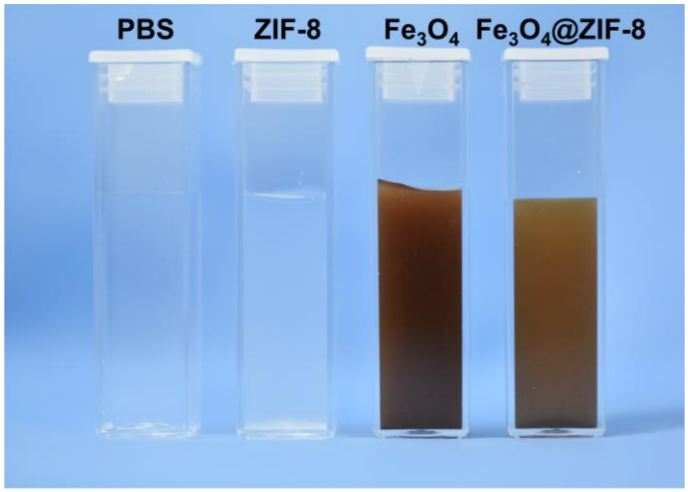



**Figure S2** Visual appearance of PBS and aqueous suspensions of ZIF-8, $Fe_3O_4$, and $Fe_3O_4$@ZIF-8 NPs.

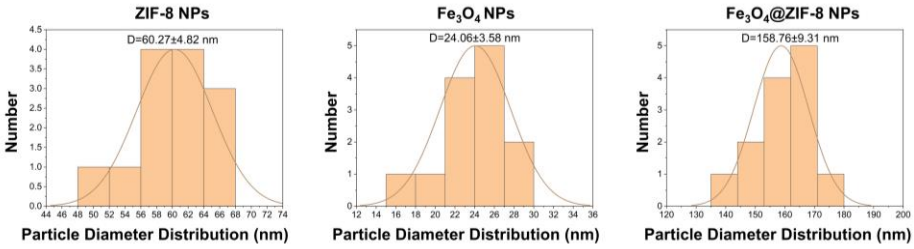



**Figure S3** Particle diameter distribution of ZIF-8, $Fe_3O_4$, and $Fe_3O_4$@ZIF-8 NPs from TEM images.

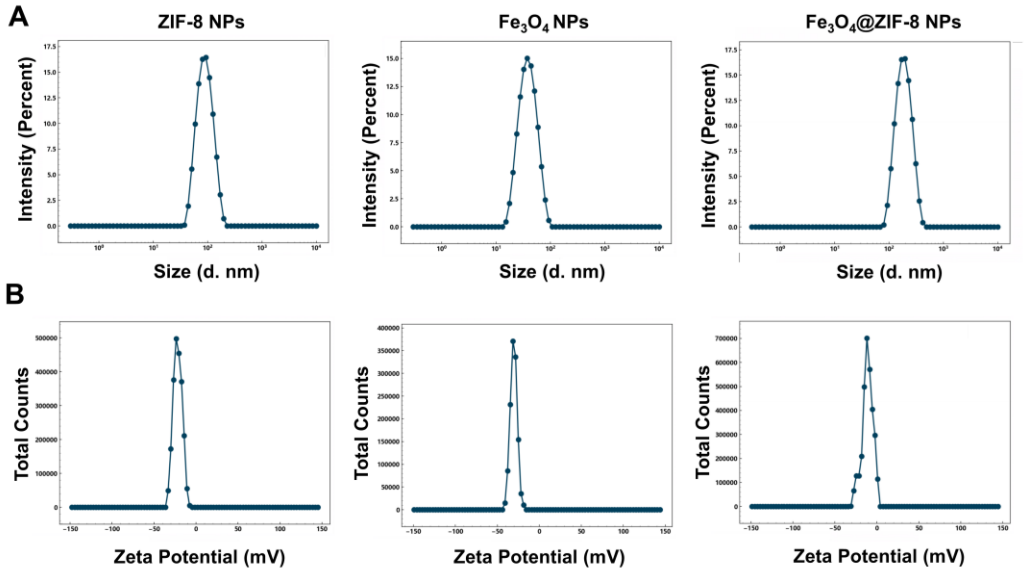



**Figure S4** (**A**): Hydrodynamic size of $Fe_3O_4$@ZIF-8 NPs in PBS; (**B**): Zeta potentials of $Fe_3O_4$@ZIF-8 NPs in PBS.

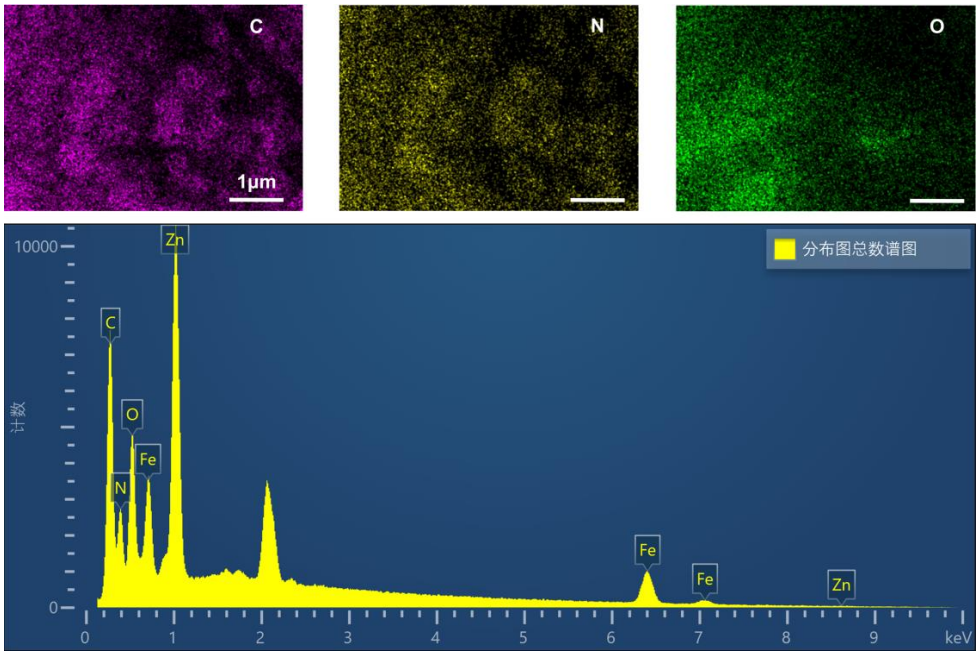



**Figure S5** EDS mapping image, EDS spectrum of $Fe_3O_4$@ZIF-8 NPs.

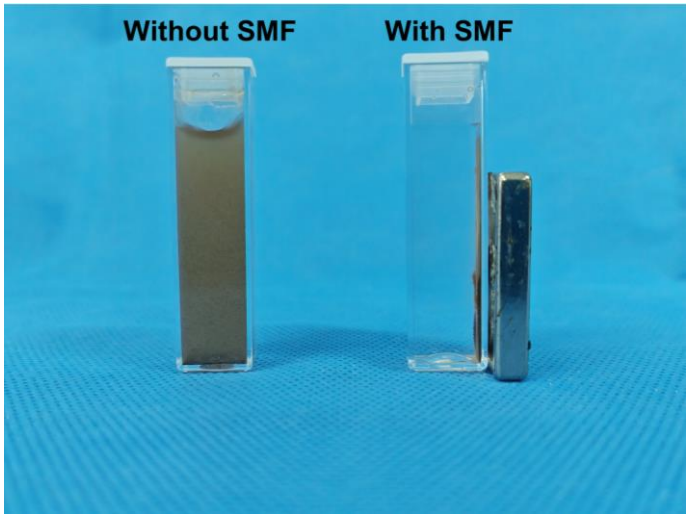



**Figure S6** Photograph of aqueous suspensions of $Fe_3O_4$@ZIF-8 NPs without/with SMF.

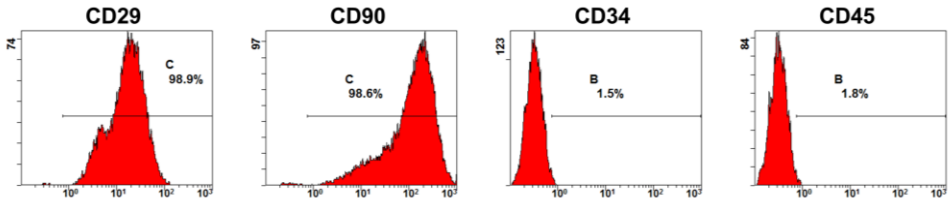



**Figure S7** Flow cytometry identification of BMSCs specific surface markers (CD29, CD90, CD34, and CD45).

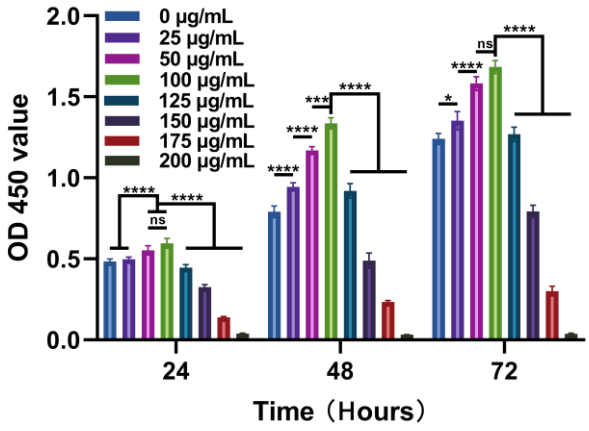



**Figure S8** CCK-8 assay of BMSCs co-cultured with $Fe_3O_4$@ZIF-8 NPs at various concentrations (including 125, 150, and 175 μg/mL) for 24, 48, and 72 h. $n$ = 3, ns: no significance, *$p$ < 0.05, ***$p$ < 0.001, and ****$p$ < 0.0001.

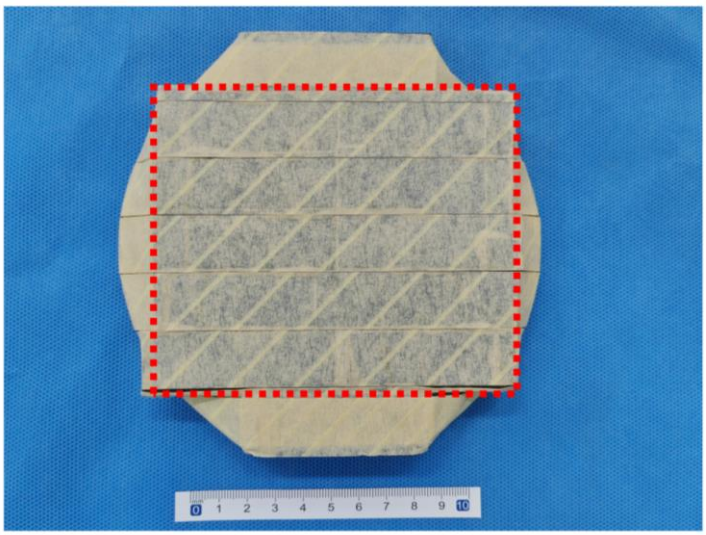



**Figure S9** Photograph of the magnetic device for in vitro experiments.

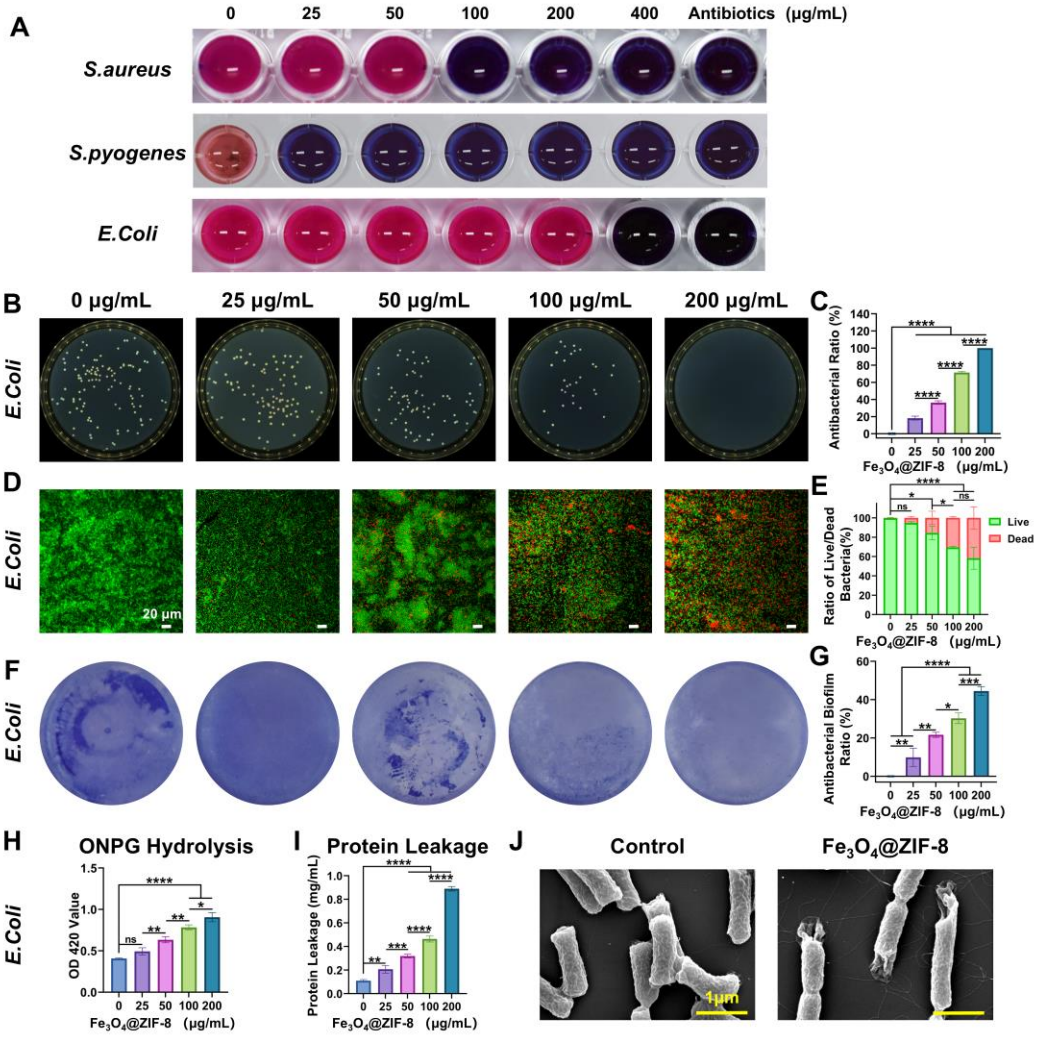



**Figure S10** In vitro antibacterial effect of $Fe_3O_4$@ZIF-8 NPs. (**A**): Photograph of the MIC of $Fe_3O_4$@ZIF-8 NPs against *S. aureus*, *S. pyogenes* and *E. coli*; (**B**)： Plate colony counting of *E. coli*; (**C**)： Quantitative analysis of bacterial colonies; (**D**): Live/dead staining fluorescence images of *E. coli*; (**E**): Quantitative analysis of live/dead bacteria ratio; (**F**): Crystal violet staining image of bacterial biofilms of *E. coli*; (**G**): Quantitative analysis of antibacterial biofilm ratio; (**H**): Permeability of bacterial membrane of *E. coli*; (**I**): Protein leakage of *E. coli*; (**J**): SEM images of *E. coli* following treatment without or with $Fe_3O_4$@ZIF-8 NPs. $n = 3$, ns: no significance, $^*p < 0.05$, $^{**}p < 0.01$, $^{***}p <$

0.001, and ****$p < 0.0001$.

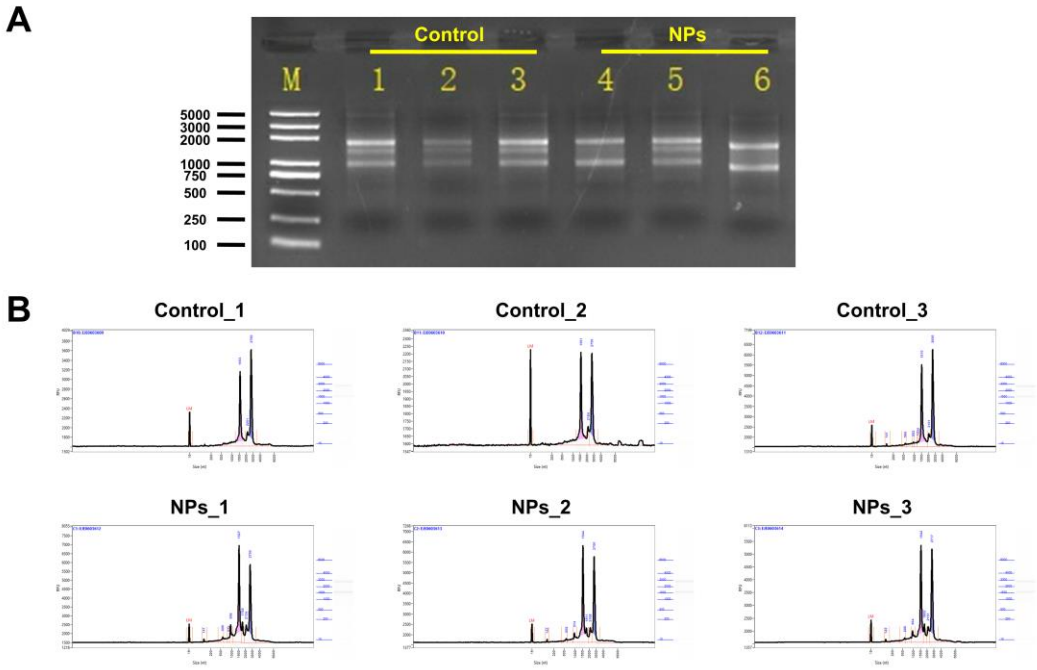



**Figure S11** (**A**): RNA quality control of *S. aureus* in the control and NPs groups, confirmed by Aligent electropherograms. M: RNA lader; 1-3: the control group; 4-6: the NPs group; (**B**): rRNA ratio (23S/16S) and RNA quality number (RQN).

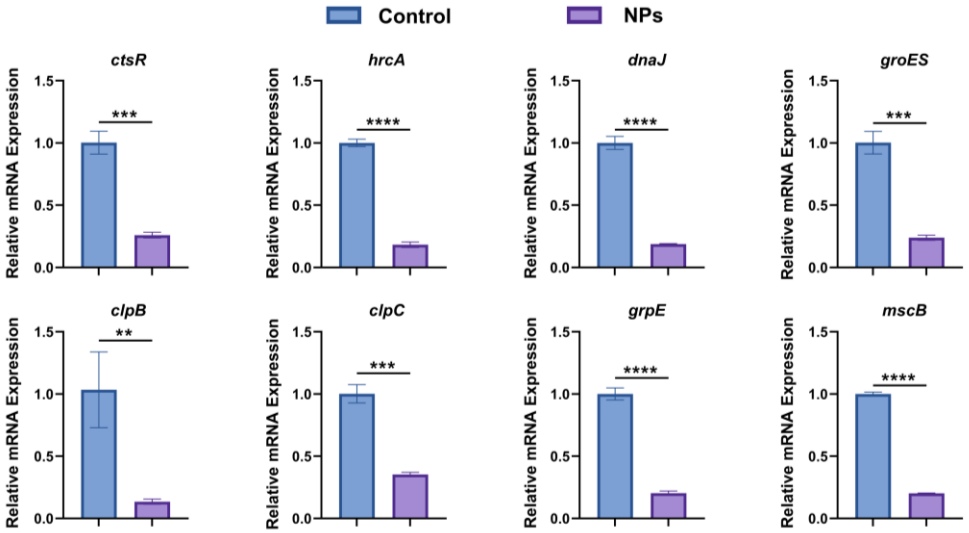



**Figure S12** Gene expression of heat shock response-related genes in *S. aureus* with different treatments. $n = 3$, $^{**}p < 0.01$, $^{***}p < 0.001$, and $^{****}p < 0.0001$.

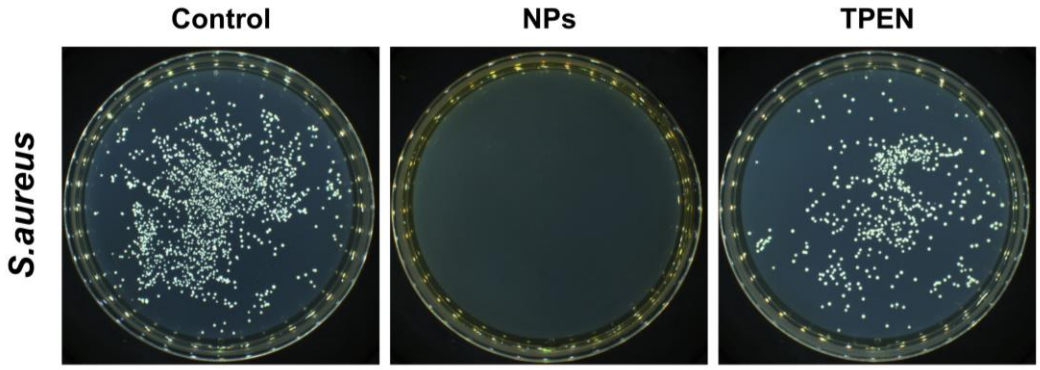



**Figure S13** Photograph of plate colony counting for *S. aureus* with different treatments.

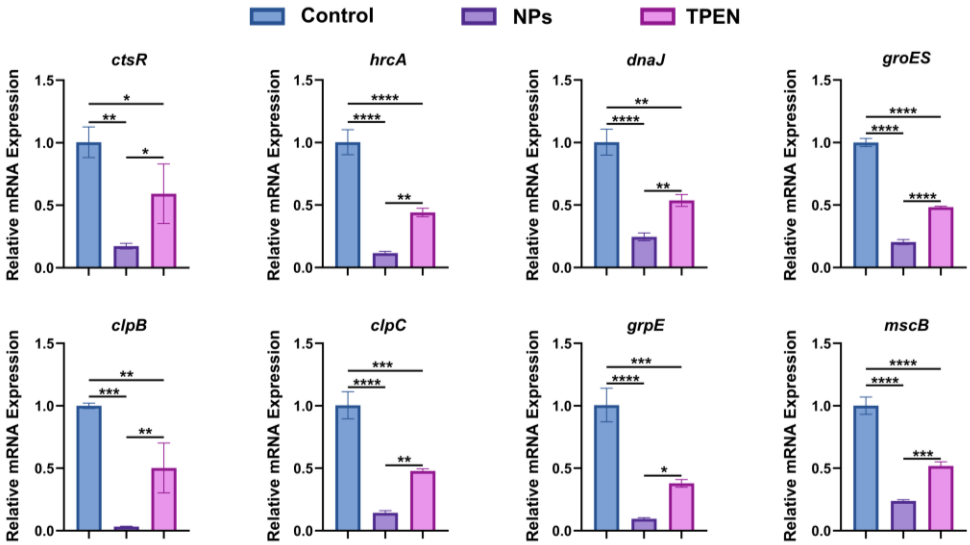



**Figure S14** Relative expressions of heat shock response-related genes in *S. aureus* with different treatments. $n = 3$, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, and ****$p < 0.0001$.

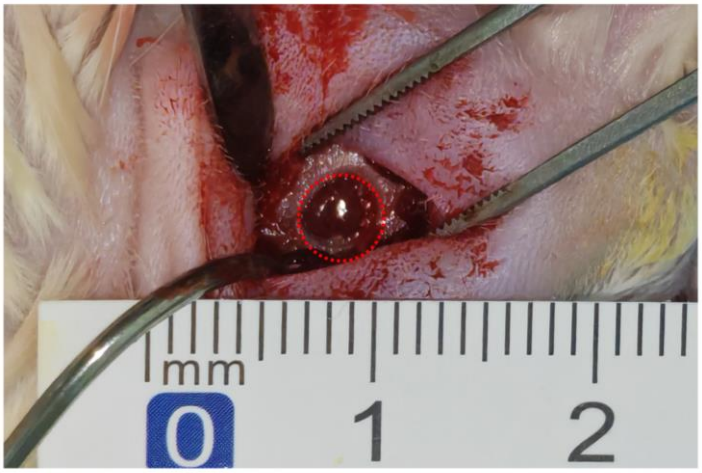



**Figure S15** A 4-mm diameter defect on the left mandible of rat (red circle: initial size of bone defect).

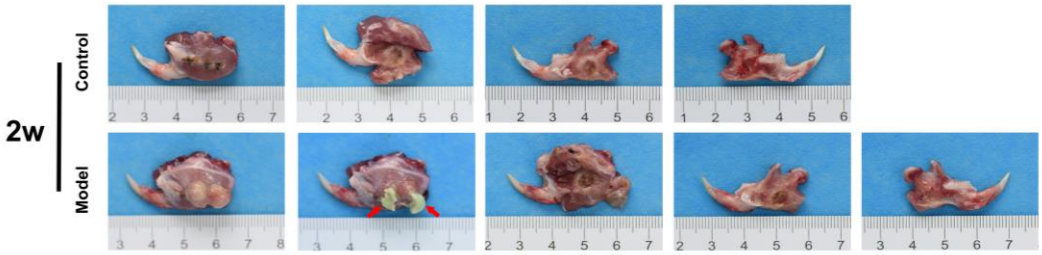



**Figure S16** Gross morphology of left mandible and peripheral soft tissues of rats in control and model groups at 2 weeks post-treatment (red arrow: yellowish-white pus).

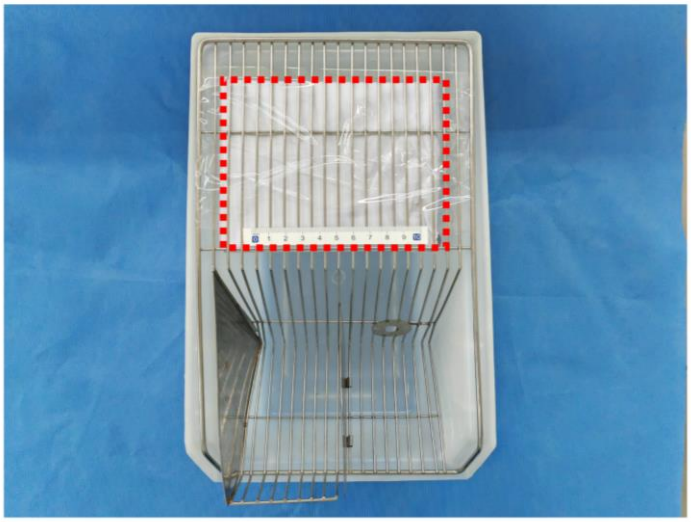


**Figure S17** Photograph of the magnetic device for in vivo experiments.

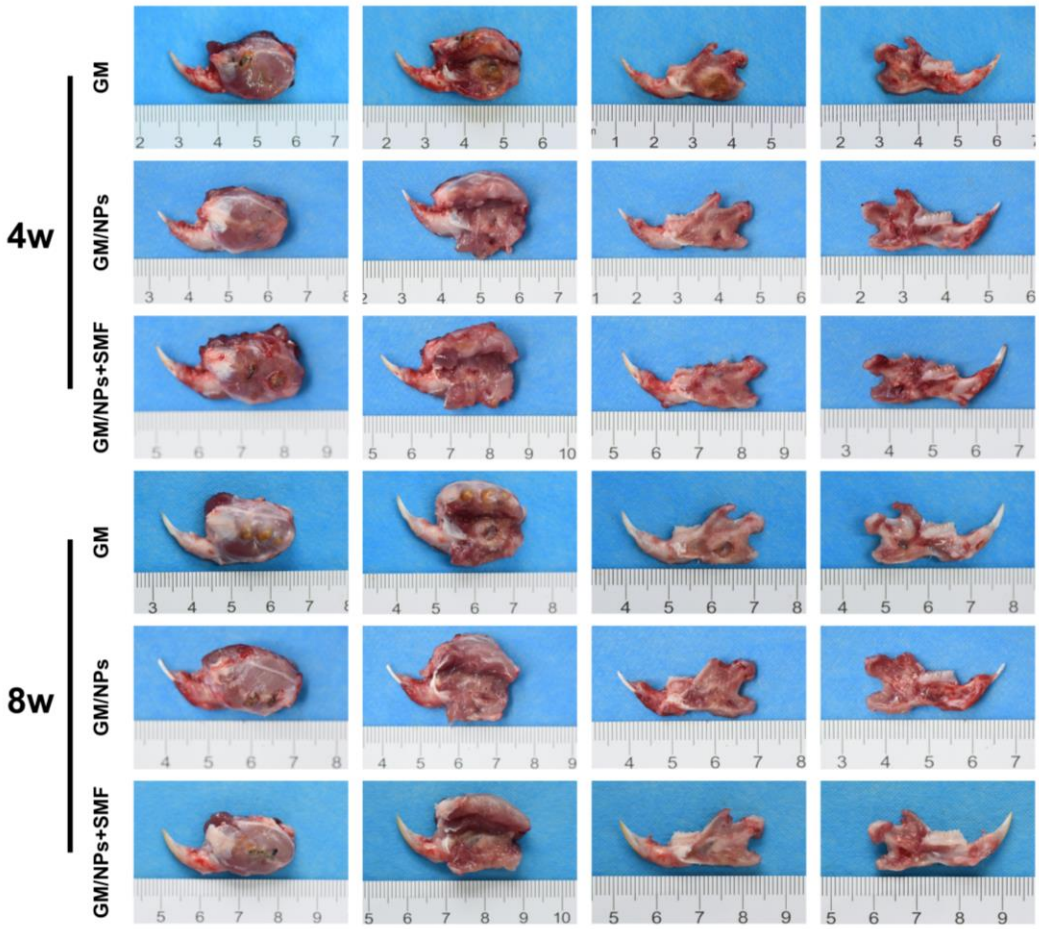



**Figure S18** Gross morphology of left mandible and peripheral soft tissues of rats in each group after 4 and 8 weeks of treatment.

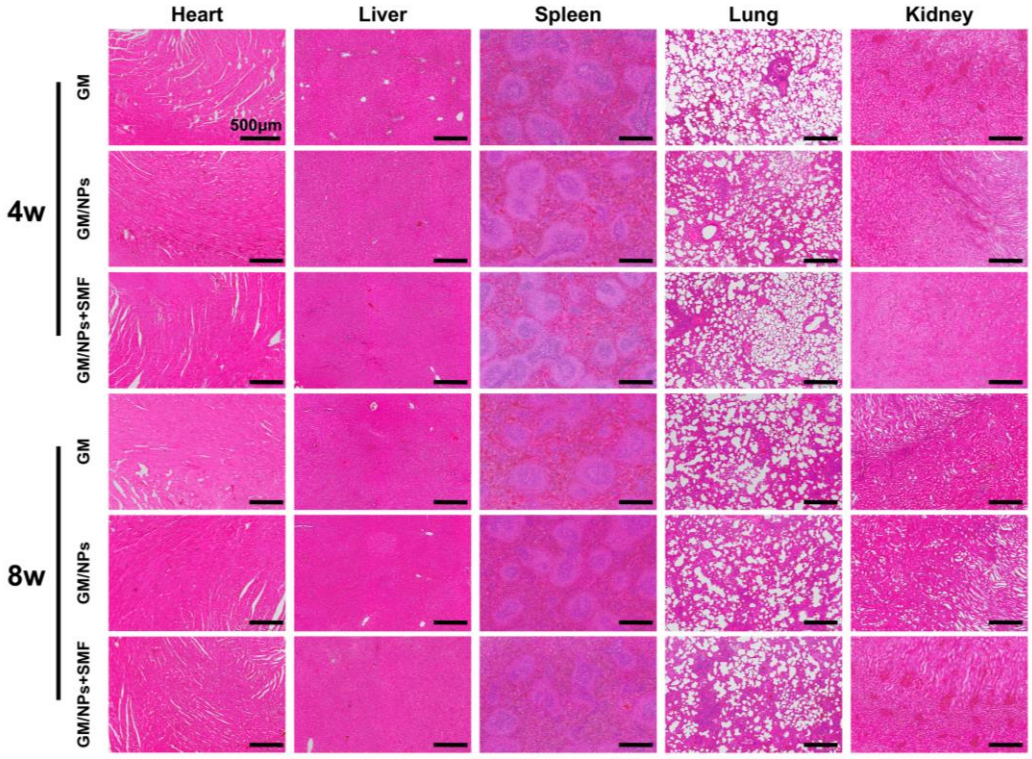



**Figure S19** H&E staining of heart, liver, spleen, lung, and kidney tissues of rats in each group after 4 and 8 weeks of treatment.

**Table S1** RT-qPCR primer sequences

| Name | Primer | Sequence (5'–3') |
|---|---|---|
| *Alp* | Forward | ACTGGGGCCTGAGATACCC |
| *Alp* | Reverse | TCGTGTTGCACTGGTTAAAGC |
| *Ocn* | Forward | GGCGCTACCTGTATCAATGG |
| *Ocn* | Reverse | GTGGTCAGCCAACTCGTCA |
| *Runx2* | Forward | TGGTTACTGTCATGGCGGGTA |
| *Runx2* | Reverse | TCTCAGATCGTTGAACCTTGCTA |
| *GAPDH* | Forward | ACAACTTTGGTATCGTGGAAGG |
| *GAPDH* | Reverse | GCCATCACGCCACAGTTTC |

**Table S2** RT-qPCR primer sequences

| Name | Primer | Sequence (5'–3') |
|---|---|---|
| *ctsR* | Forward | CACAGCGTTTTGATTGCGTACC |
| *ctsR* | Reverse | GATTCGGATGTAACCACCACCAC |
| *hrcA* | Forward | GCGACATAACTTGAATGTTAGTCCTG |
| *hrcA* | Reverse | CGAACGCCCTGAAGAACTATGTG |
| *dnaK* | Forward | CCTACACGCCAAGCAATGAAAGAC |
| *dnaK* | Reverse | CGGCATTAGAGCGTCGTTTCC |
| *dnaJ* | Forward | GTGGACAAGGATTCAATGGCTCTG |
| *dnaJ* | Reverse | TCTGCCGCCACCGAAGAAAG |
| *grpE* | Forward | AAACTGAAGGTGAAGCATTTGATCC |
| *grpE* | Reverse | GTTCTTGAGTGATTTCGCCAGATTC |
| *groES* | Forward | ACTGGACGCCTATTAAATGATGGTAC |
| *groES* | Reverse | CAGCATATTGTTGGAACACGACAC |
| *groEL* | Forward | TTTAACGCTGCTACAAACGAGTGG |
| *groEL* | Reverse | TGGAATTGATGCTACAACCGCTTC |
| *clpB* | Forward | CGGCATTAGAGCGTCGTTTCC |
| *clpB* | Reverse | ATTCAGCGGCAGCAACTAAGG |
| *clpC* | Forward | GCTTTATCTTCCTTGGACCAACTGG |
| *clpC* | Reverse | GTCTACACGGATCATCGCATCATC |
| *mcsB* | Forward | CAACCAGCAGCCGCAGTATTAG |
| *mcsB* | Reverse | GCCTGTAATGTCGTGTCAGTTCC |
| 16S rRNA | Forward | GAGTACGACCGCAAGGTTGA |
| 16S rRNA | Reverse | TGCACCACCTGTCACTTTGT |

**Table S3** EDS elemental quantitative analysis of $Fe_3O_4$@ZIF-8 NPs.

| Element | Spectral Line Type | Wt% | Wt% Sigma | At% |
|---|---|---|---|---|
| C | K line type | 31.58 | 0.26 | 52.97 |
| N | K line type | 13.40 | 0.27 | 19.28 |
| O | K line type | 10.11 | 0.12 | 12.73 |
| Fe | L line type | 22.59 | 0.34 | 8.15 |
| Zn | L line type | 22.32 | 0.18 | 6.88 |
| Total Amount | | 100.00 | | 100.00 |

**Table S4** Summary for rRNA ratio (23S/16S) and RNA quality number (RQN) corresponding to Figure S11.

| Majorbio Number | Sample Number | Gel Image Number | OD260/280 | OD260/230 | RQN |
|---|---|---|---|---|---|
| EJE0603609 | Control_1 | 1 | 2.2 | 3.22 | 9.6 |
| EJE0603610 | Control_2 | 2 | 2.23 | 5.72 | 9.4 |
| EJE0603611 | Control_3 | 3 | 2.2 | 2.92 | 9.4 |
| EJE0603612 | NPs_1 | 4 | 2.2 | 2.76 | 9 |
| EJE0603613 | NPs_2 | 5 | 2.2 | 2.75 | 9.4 |
| EJE0603614 | NPs_3 | 6 | 2.18 | 2.78 | 9.2 |

**Table S5** Summary for the RNA sequencing outcomes of the Control and NPs groups.

| Sample Name | Raw reads | Clean Reads | Clean Bases (bp) | Clean Error Rate (%) | Clean Q20(%) | Clean Q30(%) |
|---|---|---|---|---|---|---|
| Control_1 | 20046708 | 19884880 | 2989086311 | 0.0118 | 99.29 | 96.15 |
| Control_2 | 23126778 | 22971940 | 3457299976 | 0.0119 | 99.26 | 95.97 |
| Control_3 | 22670140 | 22503810 | 3385429337 | 0.0118 | 99.29 | 96.27 |
| NPs_1 | 21328028 | 21155464 | 3181349591 | 0.0117 | 99.34 | 96.44 |
| NPs_2 | 19720564 | 19574918 | 2947327978 | 0.0116 | 99.36 | 96.51 |
| NPs_3 | 22501848 | 22342528 | 3362413015 | 0.0119 | 99.24 | 95.89 |