Supporting Information

Conjugated Polymers Act Synergistically with Antibiotics to Combat Bacterial Drug Resistance

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1. Concentration optimization of PBF to combine with PLB for antibacterial effect.

The kana^r *E. coli* BL21 was cultured to optical density 0.5 at 600 nm (OD_{600}=0.5). After that, the proper amount of bacteria solution was transferred and centrifuged at 8000 rpm for 2 min, and discarded the supernatant. Then, the *E. coli* solution was washed with PBS buffer (1×) for two times and suspended with PBS buffer. Aliquot of 980 μL the above *E. coli* solution and 4 μL PLB (1 mg/mL) were transferred into 24-well plate, in which each well contained PBF with the final concentration of 0, 5, 10, and 15 μM in 1 mL, respectively. Then, the 24-well plate was cultured 2 h at 37℃, 180 rpm in the dark. Subsequently, aliquot of 50 μL cultured solution from each well was transferred into a 48-well plate, and following addition of 450 μL LB medium, respectively. Each sample was performed in triplicate. The 48-well plate was incubated at 37℃, 180 rpm for 3 h. Finally, the absorbance at 600 nm was measured with microplate reader and used to calculate the bacteria killing efficiency according to the following equation:

$$\text{killing efficiency}\ (\%) = \{[(A - B) - (C - B)]/(A - B)\} \times 100\%$$

where *A* was the absorbance of the bacteria control without adding antibiotics and the other operations were identical to the experiment group, *B* was the absorbance of the LB culture medium itself as the background value, and *C* was the absorbance of the every experiment group.

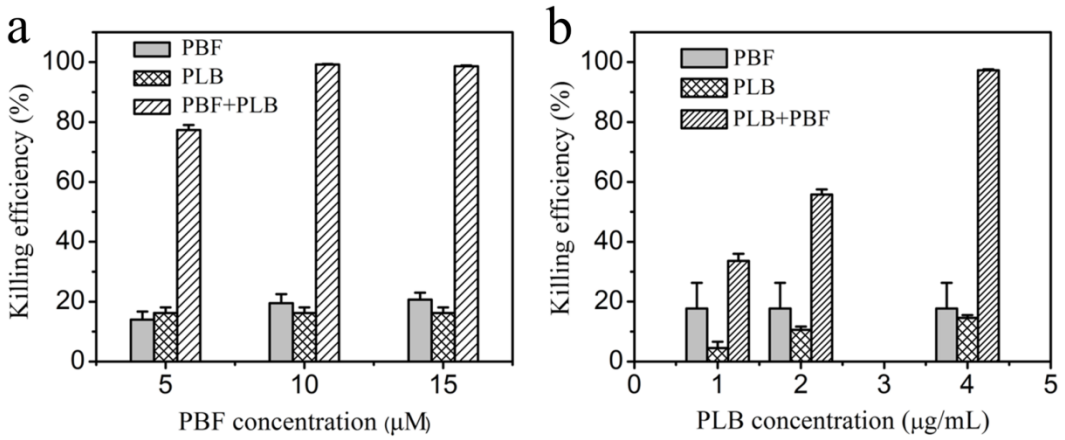

Figure S1. (a) Antibacterial effect by different concentration of PBF with 4 μg/mL PLB. (b) Antibacterial effect by different concentration of PLB with 10 μM PBF.

As shown in Figure S1a, the killing efficiency of PBF itself for *E. coli* was low, which was 14%, 19.5%, and 20.7% with the corresponding concentration of 5 μM, 10 μM, and 15 μM, respectively. For PLB alone with 4 μg/mL, its killing efficiency for *E. coli* was about 18%. However, when the PLB with PBF were added together to *E. coli* solution, the bacteria killing efficiency was significantly enhanced to 79%, 99%, and 99%, respectively, showing high efficient synergistic antibacteria activity.

2. Concentration optimization of PLB to combine with PBF for antibacterial effect.

Aliquot of 980 μL the PBS buffer suspended kana^r *E. coli* solution and 10 μL PBF (1 mM) were transferred into 24-well plate to the final volume as 1 mL, which contained the different amount of PLB with 0, 1, 2, and 4 μg/mL, respectively. The following processes were the same as described above. As shown in Figure S1b, the bacteria killing efficiencies of PLB itself were 4.5%, 10.5%, and 14.6% with the concentration of 1, 2, 4 μg/mL, respectively. However, the bacteria killing efficiencies

of PLB with 10 μM PBF were clearly enhanced to 33.6%, 55.8%, and 97.3%, respectively. Obviously, the bacteria killing efficiencies of combination of PBF and PLB were much larger than the sum of those of PLB and PBF alone. These results suggested that the bacteria killing by combination of PLB and PBF was based on synergistic enhanced antibacterial mechanism action.

3.

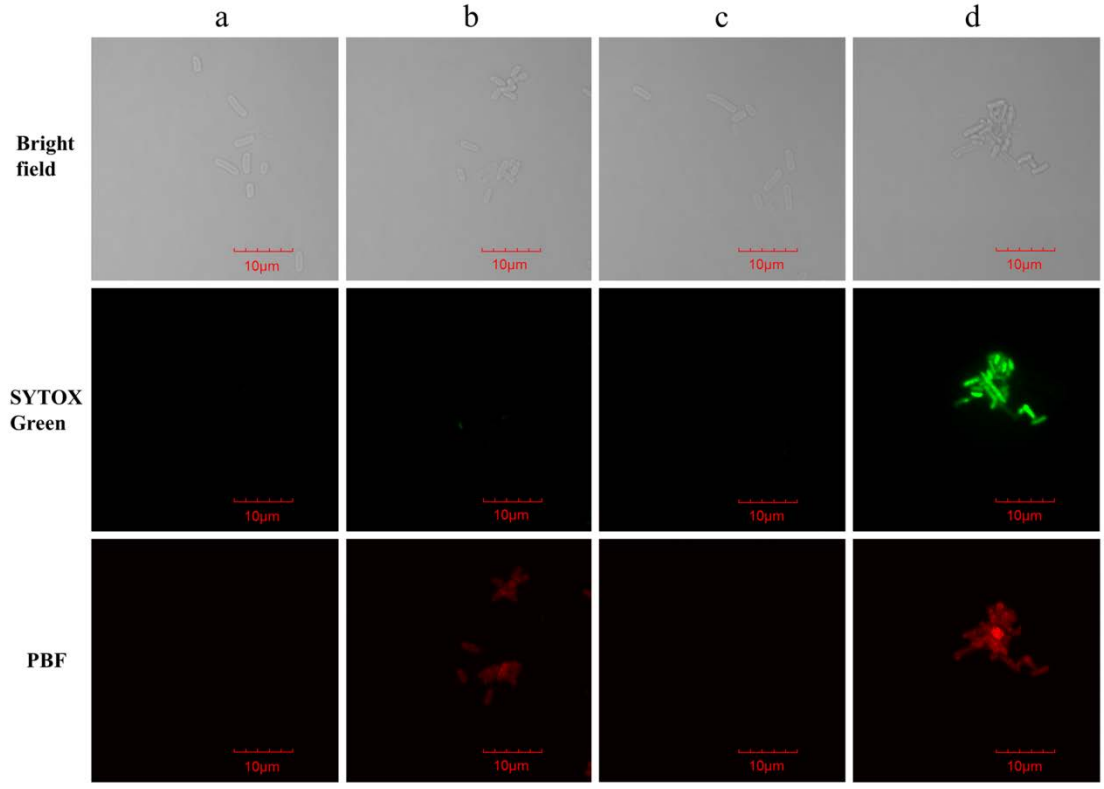

Figure S2. Confocal laser scanning microscope imaging (CLSM) of kana^{r} *E. coli* stained by SYTOX Green dye. (a) *E. coli*. (b) *E. coli* + PBF. (c) *E. coli* + PLB. (d) *E. coli* + PBF-PLB combination. [PBF] = 10 μM. [PLB] = 4 μg/mL.

4.

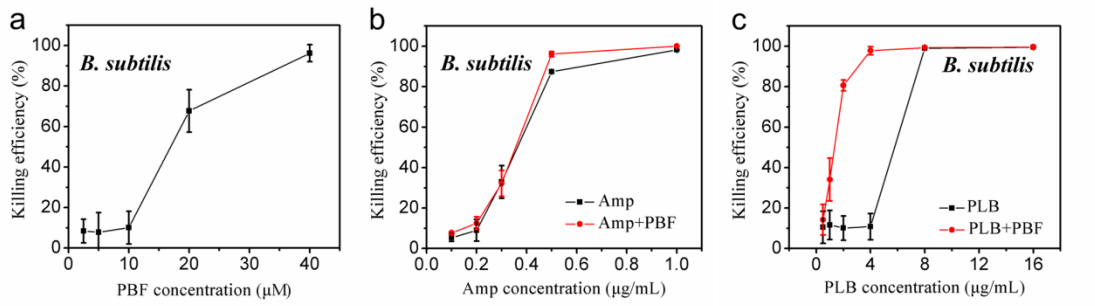

Figure S3. The antibacterial efficiency of PBF and antibiotic combinations toward gram-positive bacteria *B. Subtilis*. (a) PBF alone toward gram-positive *B. subtilis*. [PBF] = 2.5, 5, 10, 20, 40 μM. (b) PBF-Amp combination toward gram-positive *B. subtilis*. [PBF] = 10 μM. [Amp] = 0.1, 0.2, 0.3, 0.5, 1.0 μg/mL. (c) PBF-PLB combination toward gram-positive *B. subtilis*. [PBF] = 10 μM. [PLB] = 0.5, 1, 2, 4, 8, 16 μg/mL. Error bars were obtained from three replicate measurements.

5.

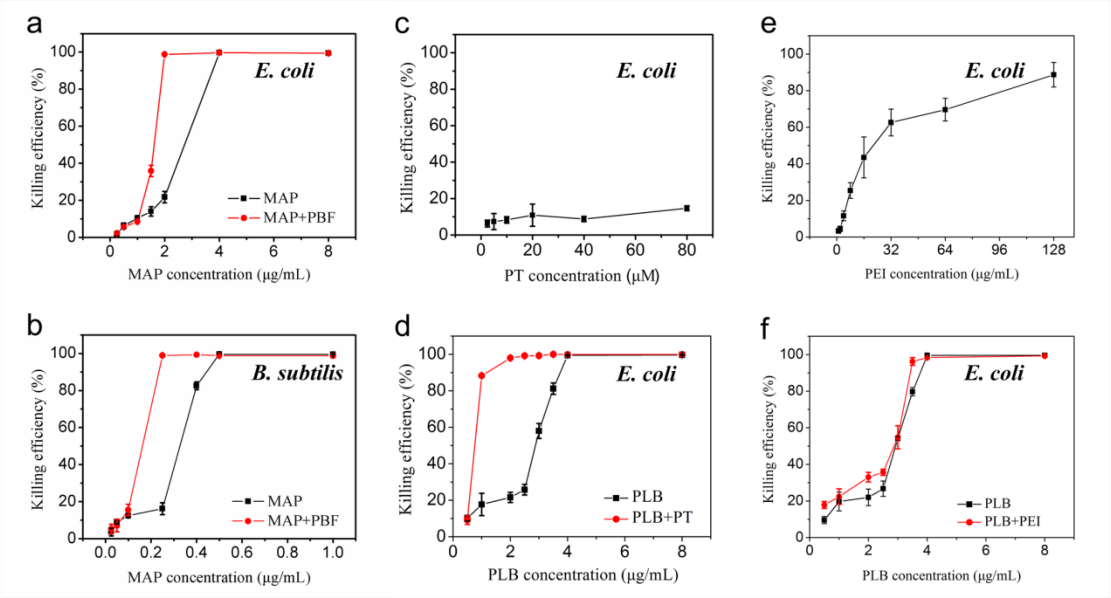

Figure S4. The antibacterial efficiency of different polymers and drug combinations toward gram-positive bacteria and gram-negative bacteria. (a) PBF-MAP combination toward *E. coli.* [PBF] = 10 μM. [MAP] = 0.25, 0.5, 1, 1.5, 2, 4, 8 μg/mL. (b) PBF-MAP combination toward *B.*

subtilis. [PBF] = 10 μM. [MAP] = 0.025, 0.05, 0.1, 0.25, 0.4, 0.5, 1.0 μg/mL. (c) PT alone toward *E. coli*. [PT] = 2.5, 5, 10, 20, 40, 80 μM. (d) PT-PLB combination toward *E. coli*. [PT] = 2.5 μM. [PLB] = 0.5, 1, 2, 2.5, 3, 3.5, 4, 8 μg/mL. (e) PEI alone toward *E. coli*. [PEI] = 1, 2, 4, 8, 16, 32, 64, 128 μg/mL. (f) PEI-PLB combination toward *E. coli*. [PEI] = 8 μg/mL. [PLB] = 0.5, 1, 2, 2.5, 3, 3.5, 4, 8 μg/mL. Error bars were obtained from three replicate measurements.