Supporting Information

A Multifunctional Nanobooster to Restore Ceftazidime Susceptibility in Mucoid *Pseudomonas aeruginosa*

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This PDF file includes:

Figs. S1 to S23

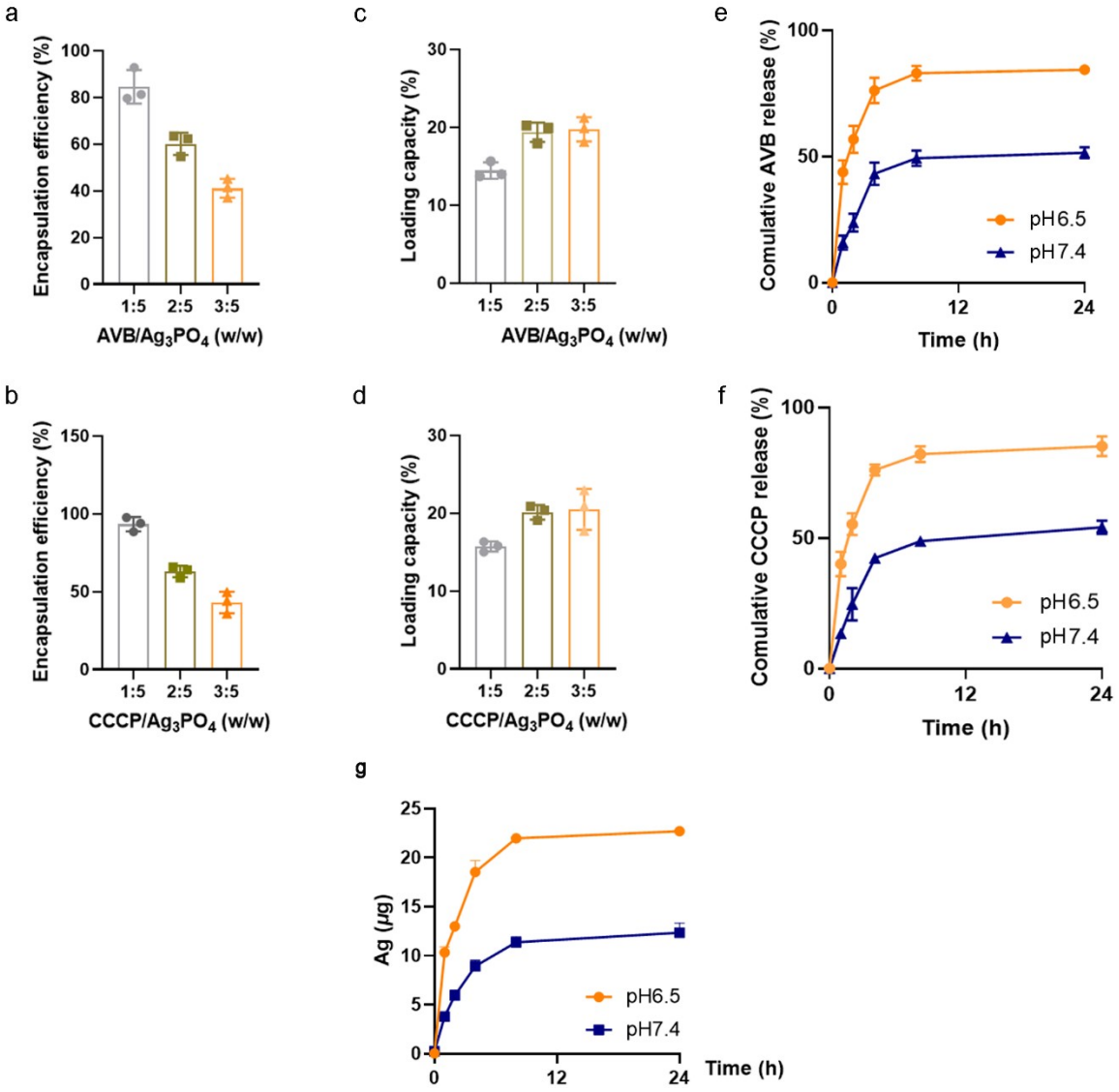

Figure S1. Loading and *in vitro* release behaviors of AVB, CCCP, and Ag^+ from A/C-pAg_3PO_4. (a, b) Encapsulation efficiency of AVB (a) and CCCP (b) onto pAg_3PO_4 as a function of weight ratio (w/w). (c, d) Loading capacity of AVB (c) and CCCP (d) onto the pAg_3PO_4 at different weight ratios (w/w). (e, f) Cumulative release profiles of AVB (e) and CCCP (f) from A/C-pAg_3PO_4 at pH 6.5 and pH 7.4 over 24 h. (g) Cumulative release profiles of Ag^+ from A/C-pAg_3PO_4 at pH 6.5 and pH 7.4 over 24 h. Data are represented as mean ± SD (n = 3).

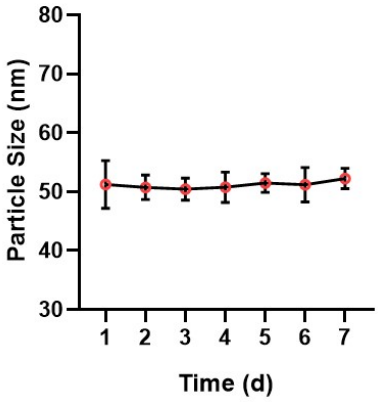

Figure S2. Stability of A/C-pAg_3PO_4 in 7 days. Data are represented as mean ± SD (n = 3).

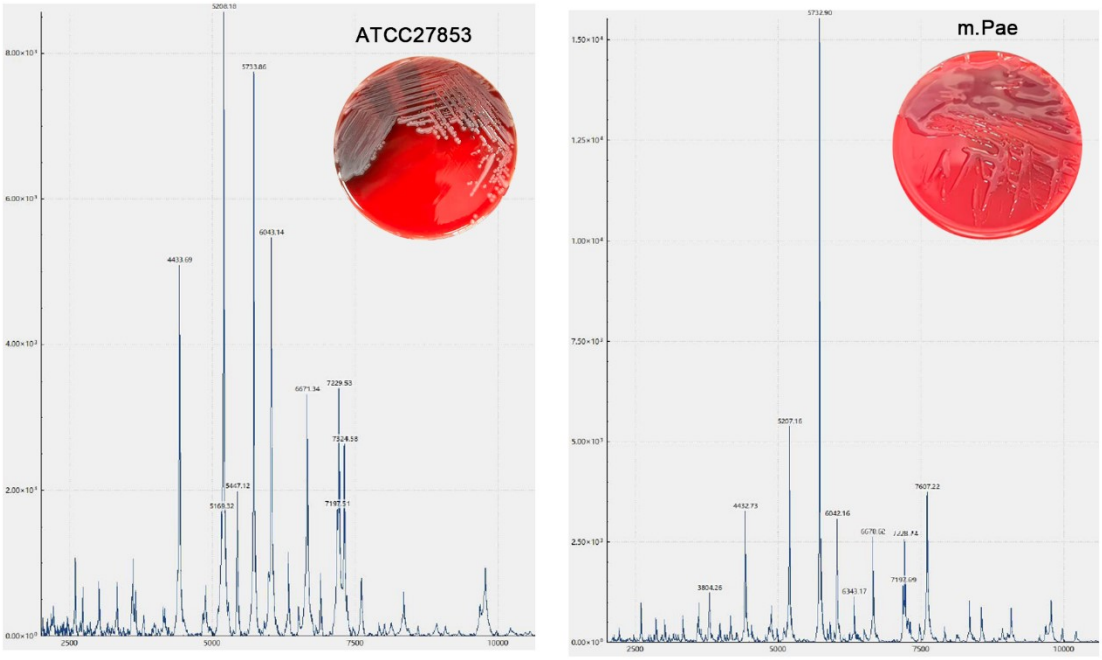

Figure S3. Mass spectrometry identification and photographs of the *PAE* ATCC 27853 (left) and the m.*PAE* (right).

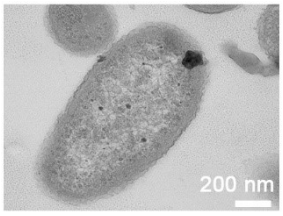

Figure S4. Representative TEM images of m.*PAE* treated with A/C-pAg_3PO_4 for 6 h. Scale bar represents 200 nm.

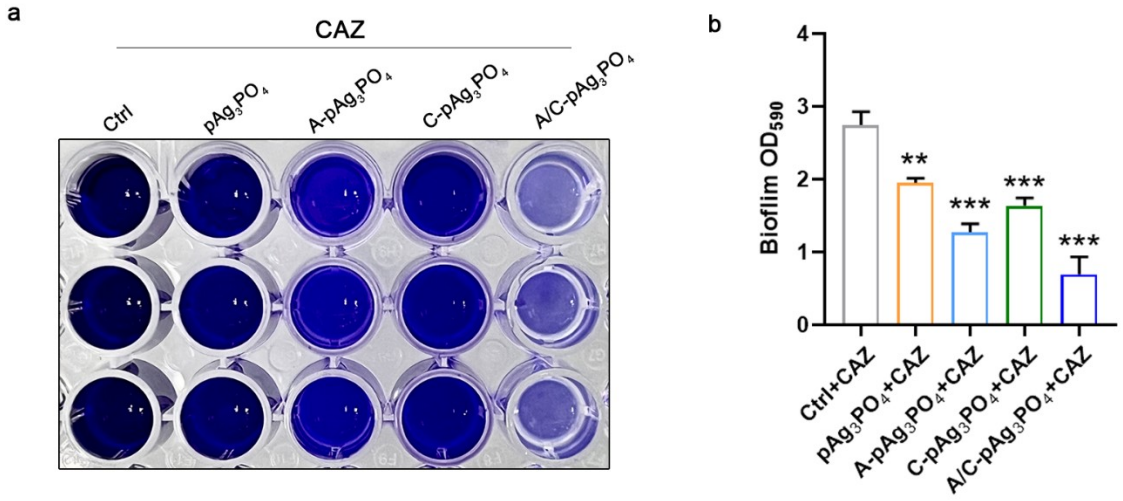

Figure S5. Biofilm elimination effects of nanobooster. (a) Photographs of crystal-violet-stained biofilms after treatment with CAZ and nanobooster. (b) Residual biofilm quantitation by crystal violet absorbance at 590 nm. Data are represented as mean ± SD (n = 3). Student's *t*-test, ** $P < 0.01$, *** $P < 0.001$.

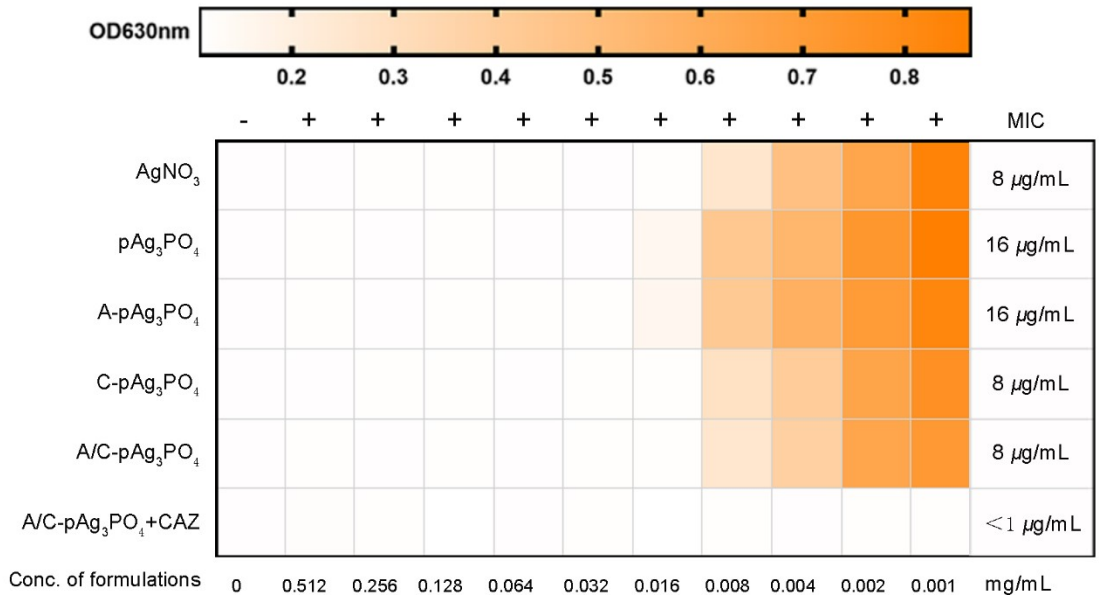

Figure S6. The MIC of different treatments ($AgNO_3$, pAg_3PO_4, A-pAg_3PO_4, C-pAg_3PO_4, A/C-pAg_3PO_4, and A/C-pAg_3PO_4+CAZ) against the m.*PAE*.

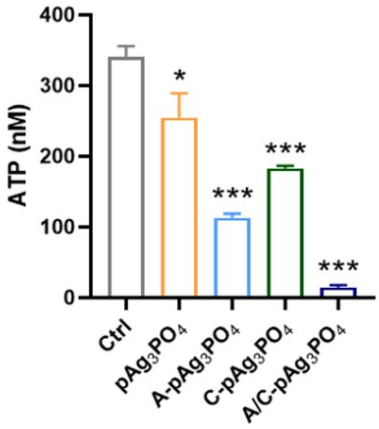

Figure S7. ATP levels of bacterial supernatant. Data are represented as mean ± SD (n = 3). Student's *t*-test, * $P < 0.05$, *** $P < 0.001$.

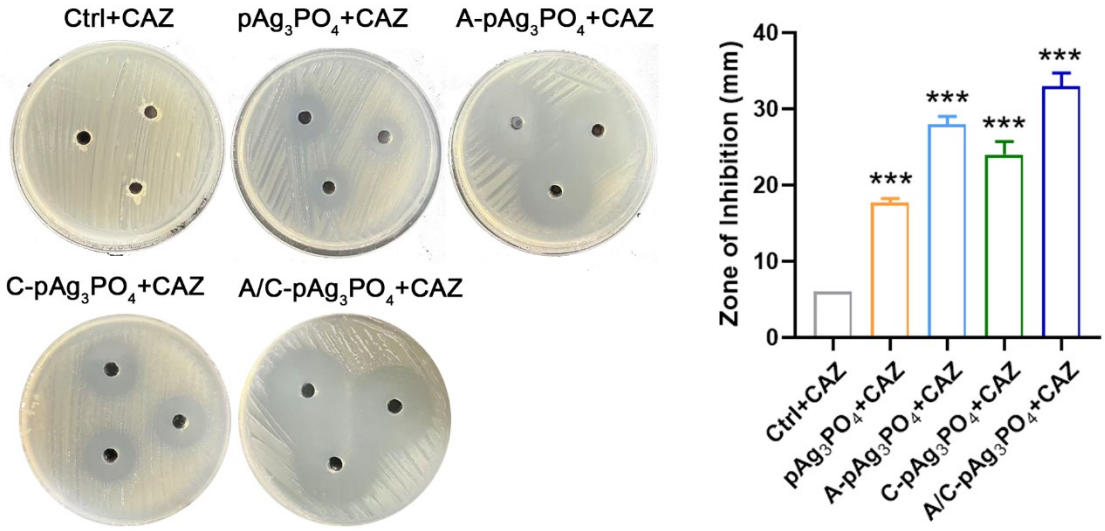

Figure S8. Antibacterial activity of nanobooster against m.*PAE*. Data are represented as mean ± SD (n = 3). Student's *t*-test, *** $P < 0.001$.

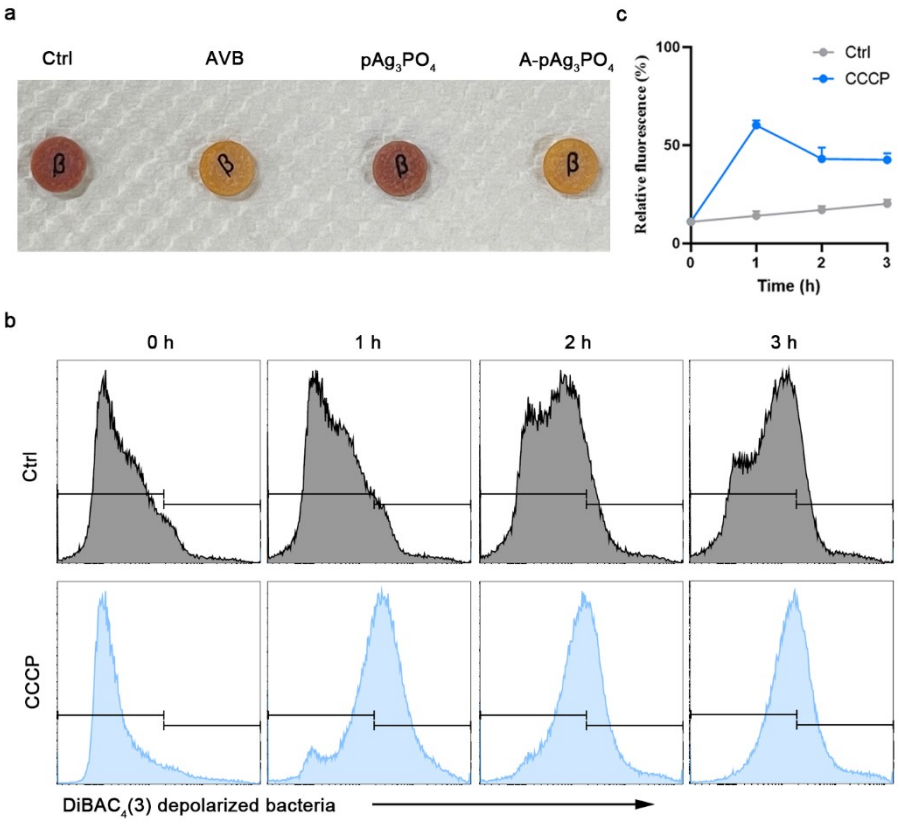

Figure S9. Mechanistic studies of AVB and CCCP. (a) Nitrocefin disc assay for m.*PAE* with different treatments. (b, c) Fluorescence (b) and the quantification (c) for m.*PAE* with the membrane depolarization dye $DiBAC_4(3)$. Data are represented as mean ± SD (n = 3).

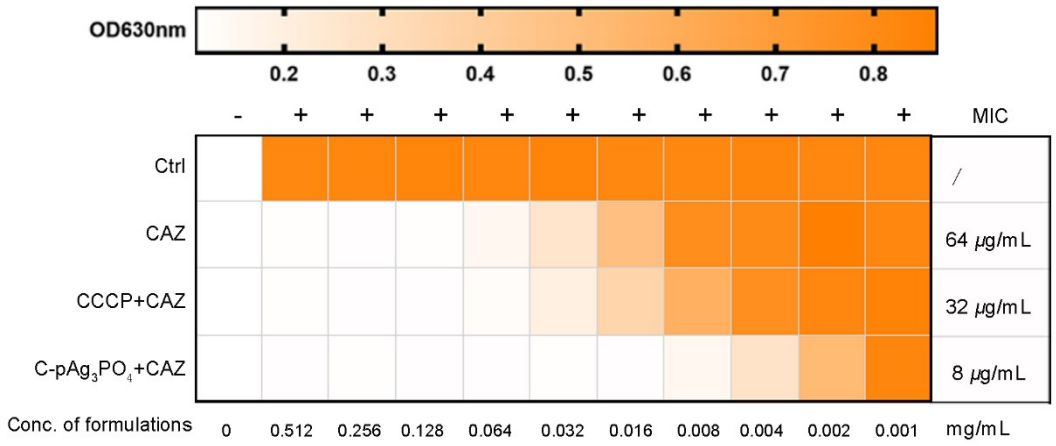

Figure S10. The MIC of different treatments (CAZ, CCCP+CAZ, C-pAg_3PO_4+CAZ) against the m.*PAE*.

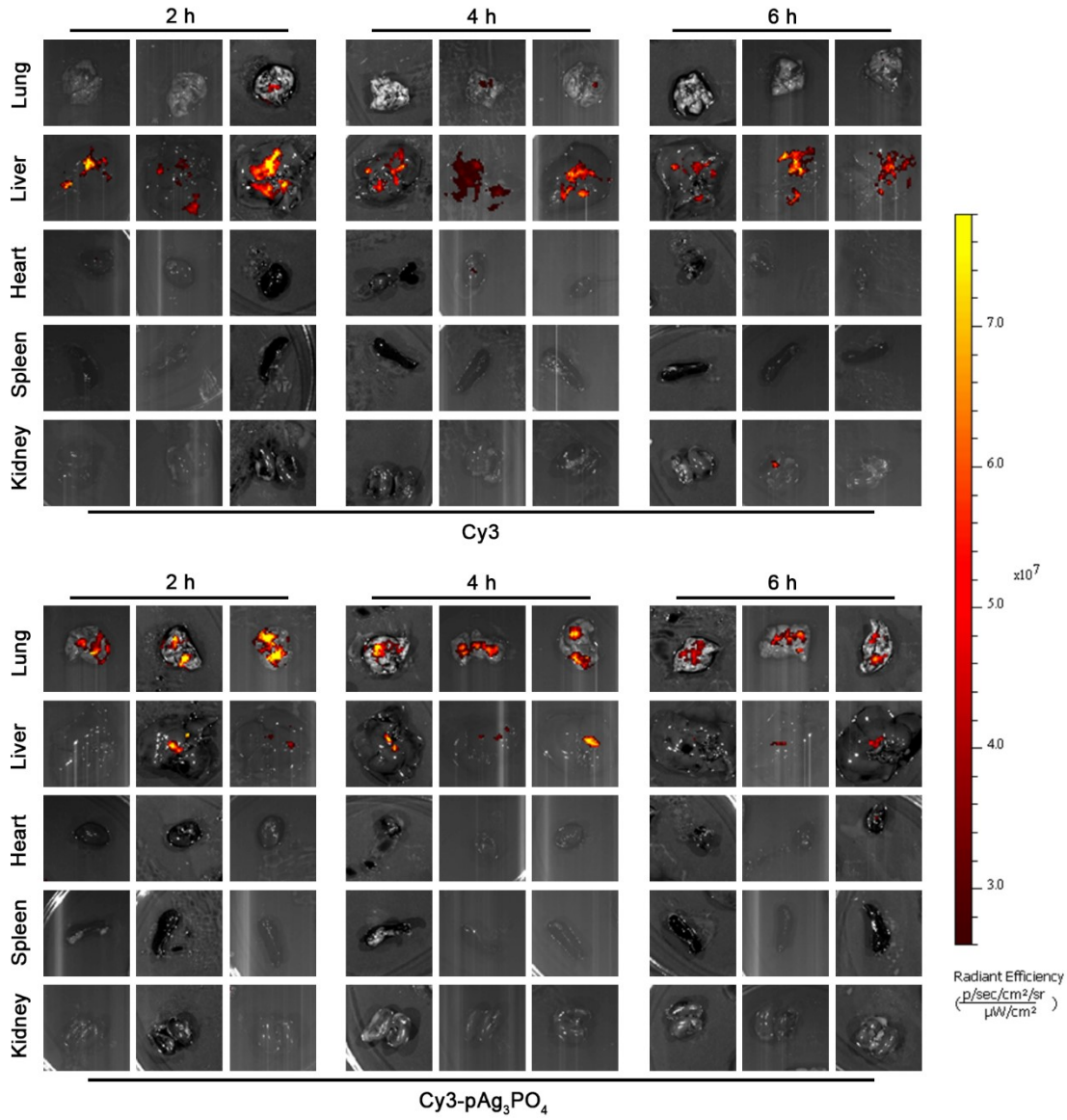

Figure S11. Representative *ex vivo* fluorescence images of main organs at various timepoints after intranasal administration of Cy3 or Cy3-pAg$_3$PO$_4$.

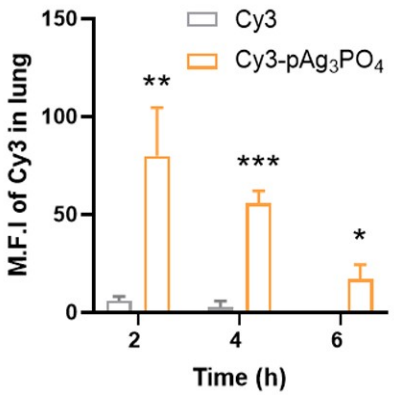

Figure S12. Quantification of Cy3 or Cy3-pAg_3PO_4 (red) distribution in lung sections. Data are represented as mean ± SD (n = 3). Student's *t*-test, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

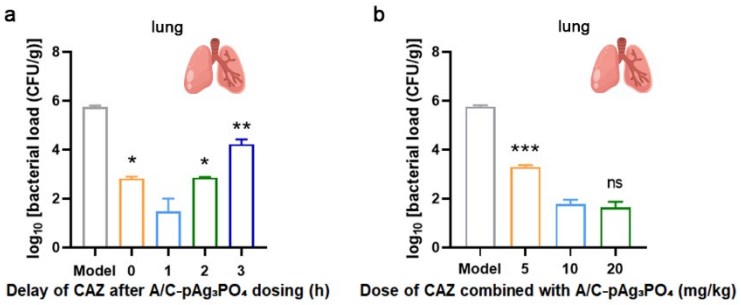

Figure S13. Quantitative analysis of CFUs from lung homogenates after treatment with CAZ at different time points (a) or at different doses (b) in a bacterial pneumonia model infected with m.*PAE*. Data are represented as mean ± SD (n = 3). Student's *t*-test, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns means not significant.

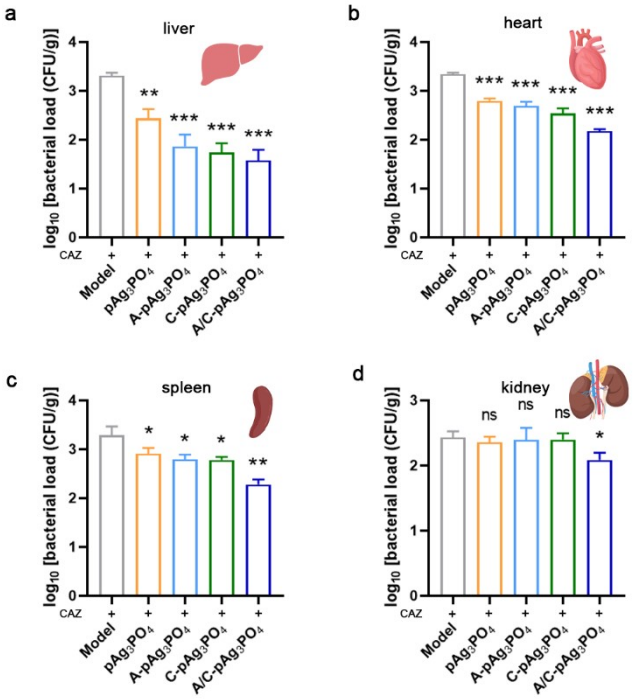

Figure S14. Quantitative analysis of CFUs from liver (a), heart (b), spleen (c) and kidney (d) homogenates in a bacterial pneumonia model infected with m.*PAE*. Data are represented as mean ± SD (n = 3). Student's *t*-test, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, ns means not significant.

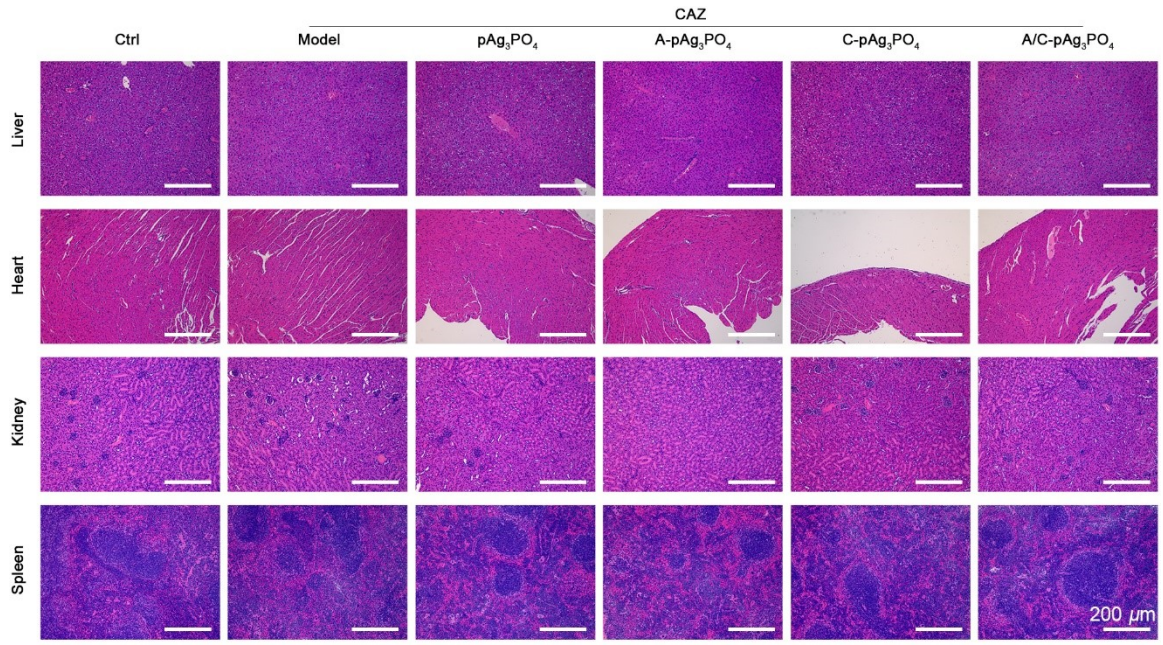

Figure S15. Representative H&E-stained major organ sections in a bacterial pneumonia model infected with m.*PAE*. Scale bars = 200 μm.

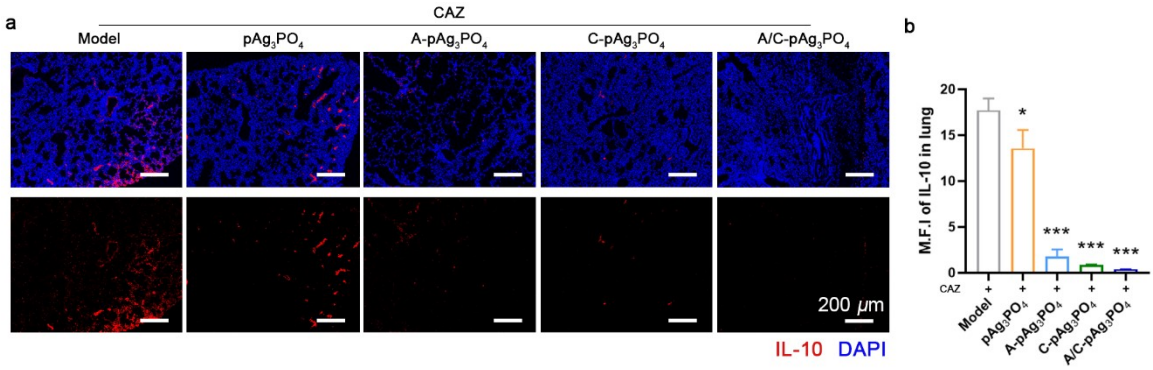

Figure S16. Fluorescent imaging(a) and quantifications(b) of IL-10 in lung tissues. Red: IL-10; Blue: DAPI (nuclei). Scale bars = 200 μm. Data are represented as mean ± SD (n = 3). Student's *t*-test, * $P < 0.05$, *** $P < 0.001$.

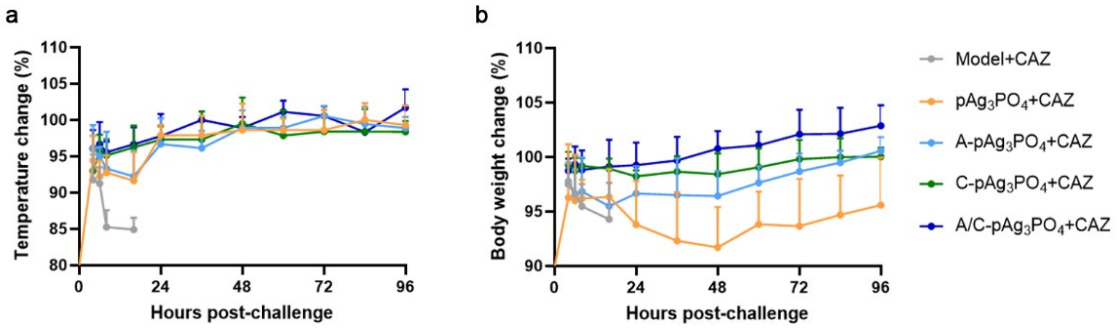

Figure S17. The average percent temperature change (a) and the average percent body weight change (b) of each group in a sepsis model infected with m.*PAE*. Data are represented as mean ± SD (n = 5).

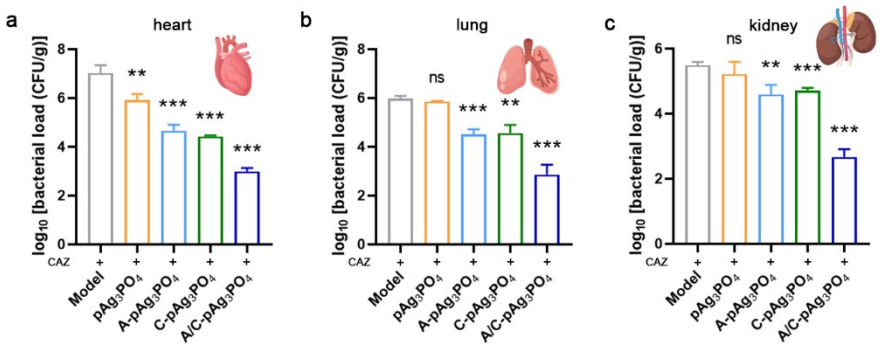

Figure S18. Quantitative analysis of CFUs from heart (a), lung (b) and kidney (c) homogenates in a sepsis model infected with m.*PAE*. Data are represented as mean ± SD (n = 3). Student's *t*-test, ** $P < 0.01$, *** $P < 0.001$, ns means not significant.

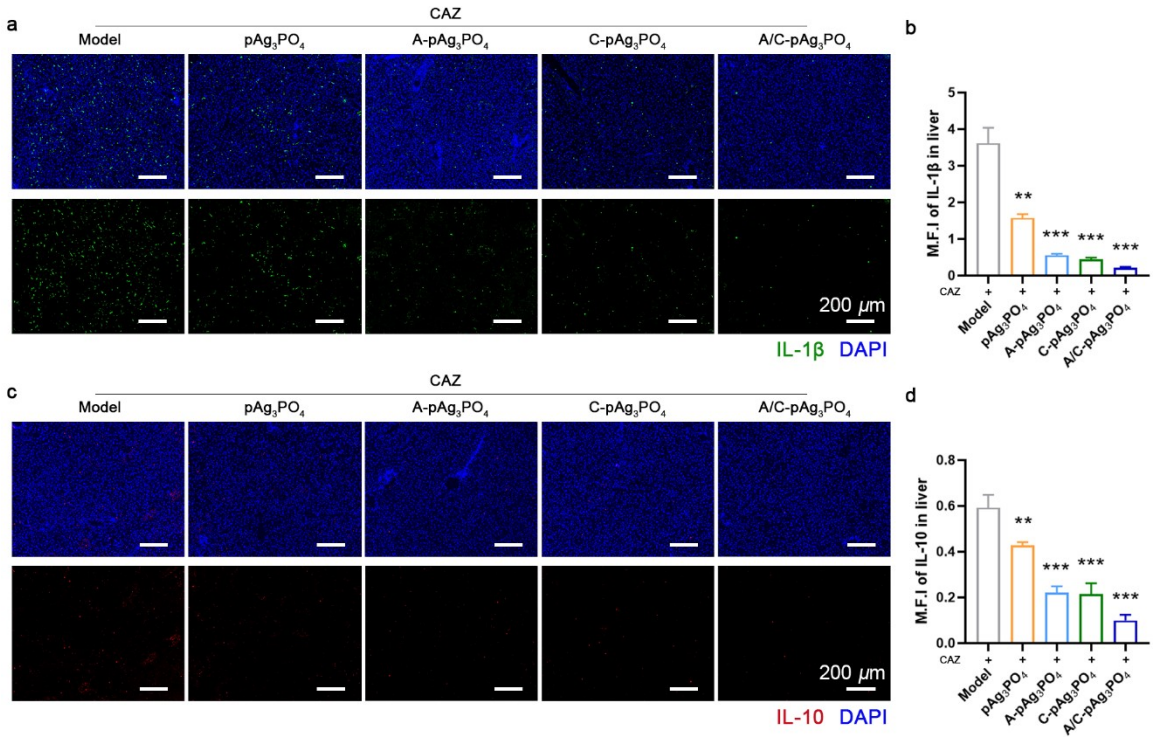

Figure S19. Immunofluorescence staining and quantification of IL-1β (a, b) and IL-10 (c, d) in liver tissues in a sepsis model infected with m.*PAE*. Green: IL-1β; Red: IL-10; Blue: DAPI (nuclei). Scale bars = 200 μm. Data are represented as mean ± SD (n = 3). Student's *t*-test, ** $P < 0.01$, *** $P < 0.001$.

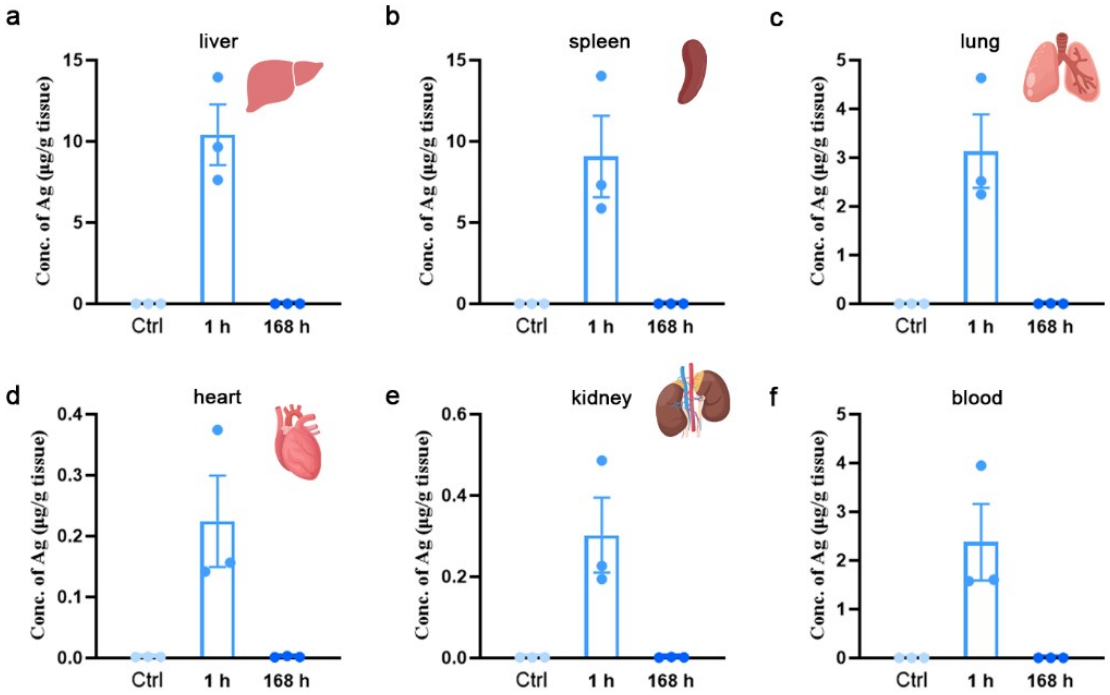

Figure S20. Silver concentrations in different organs (μg/g tissue) at different time points after A/C-pAg_3PO_4 treatment. At Ctrl group and 168 h post-treatment group, silver content in all organs did not exceed 10 ng/g tissue.

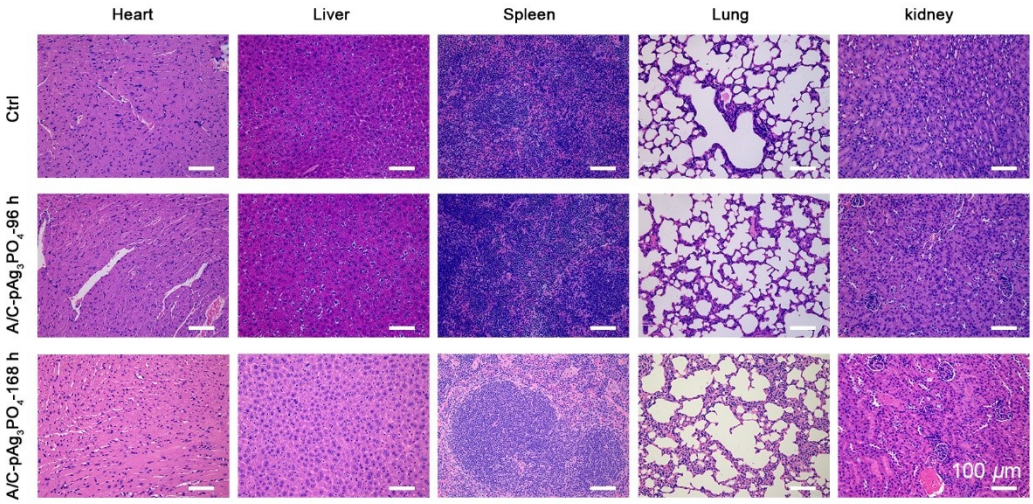

Figure S21. H&E staining of histology sections from major organs 96 h and 168 h after the intraperitoneal injection of A/C-pAg_3PO_4. Scale bars = 100 μm.

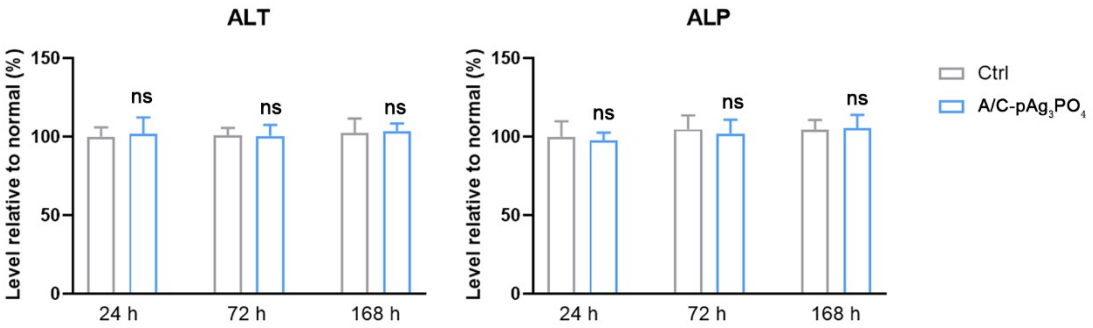

Figure S22. Comprehensive blood chemistry panel taken 24 h, 72 h and 168 h after the intraperitoneal injection of PBS or A/C-pAg_3PO_4. ALP, alkaline phosphatase; ALT, alanine transaminase. Data are represented as mean ± SD (n = 3). Student's *t*-test, ns means not significant.

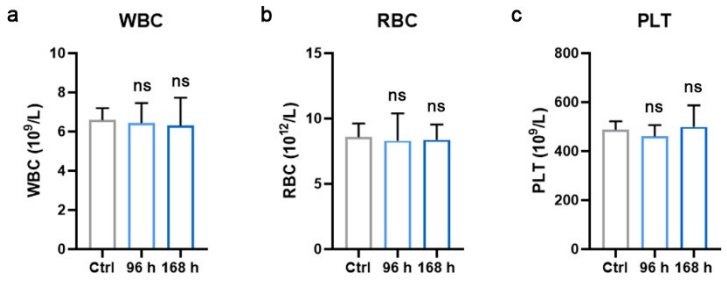

Figure S23. Counts of various blood cells 96 h and 168 h after the intraperitoneal injection of PBS or A/C-pAg_3PO_4. (a) WBC, white blood cells; (b) RBC, red blood cells; (c) PLT, platelets. Data are represented as mean ± SD (n = 3). Student's *t*-test, ns means not significant.