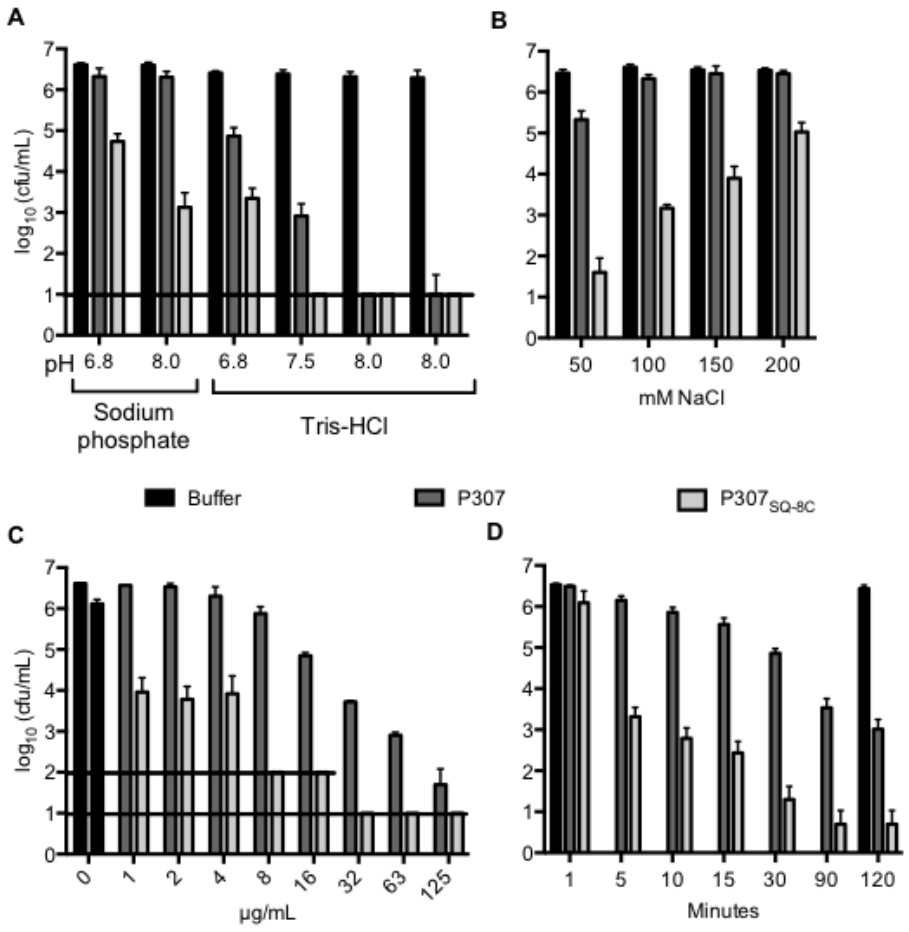
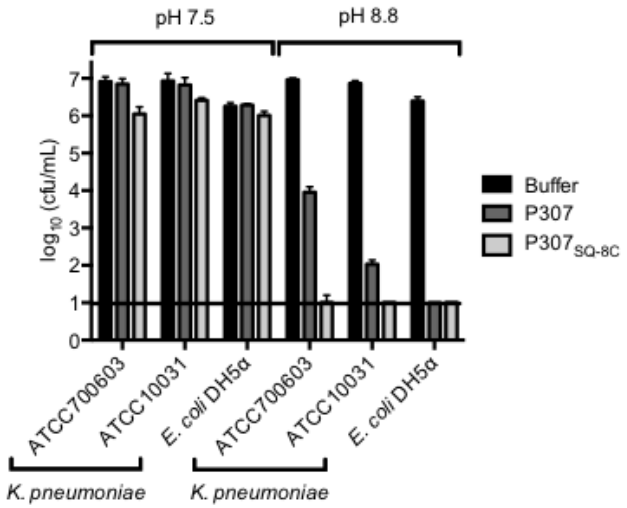
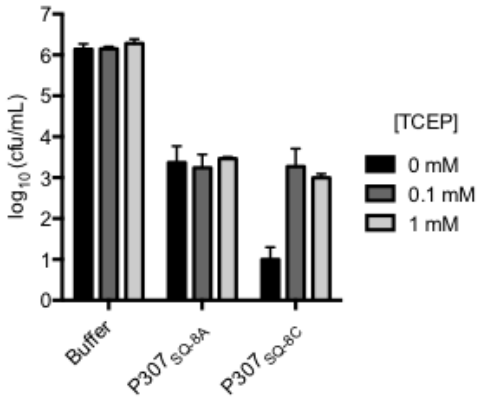


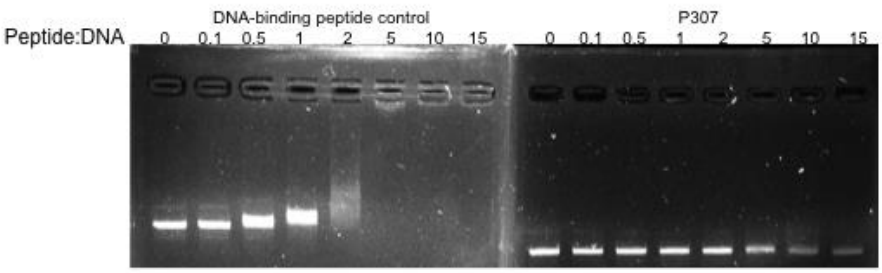
Supplementary Figure 1. *In vitro* bactericidal activities of P307 and $P307_{SQ-8C}$. *A. baumannii* strain #1791 was treated with 50 µg/mL of P307 or $P307_{SQ-8C}$ for 2 h at 22-25°C to investigate the optimal (A) pH and (B) NaCl concentration for killing. The same conditions, except for the variables, were used with 50 mM Tris-HCl, pH 7.5 to determine the (C) optimal killing concentration, and (D) killing kinetics. The error bars show standard deviation and the black horizontal line marks the limit of detection.



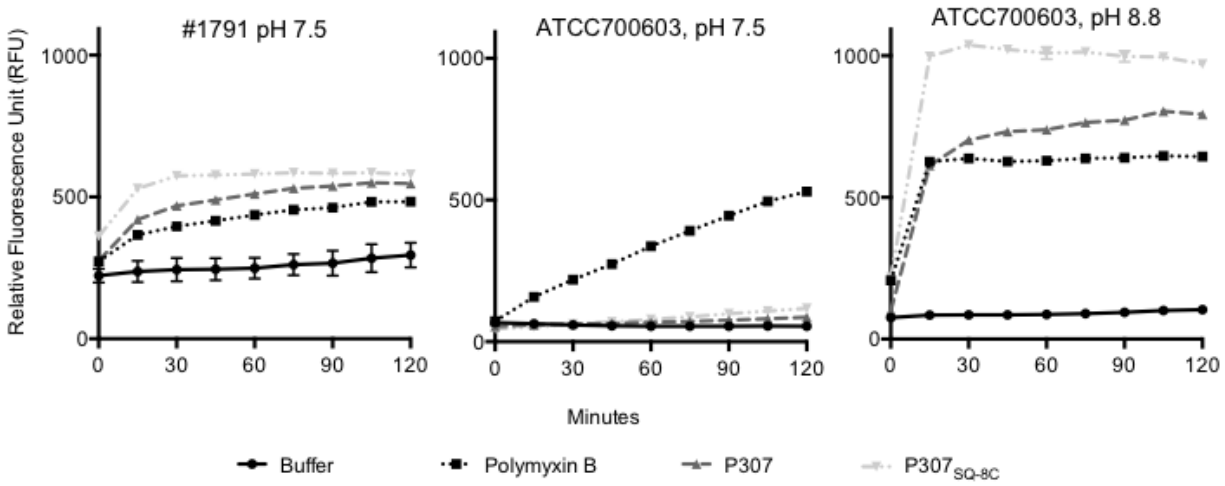
Supplementary Figure 2. Bactericidal activities of P307 against *K. pneumoniae* and *E. coli* at pH 7.5 and 8.8. The bacteria were treated with 50 μg/mL peptides in 50 mM Tris-HCl for 2 h at 22-25°C. Serial dilutions were plated for cfu counting. The error bars show standard deviation and the black horizontal line marks the limit of detection.



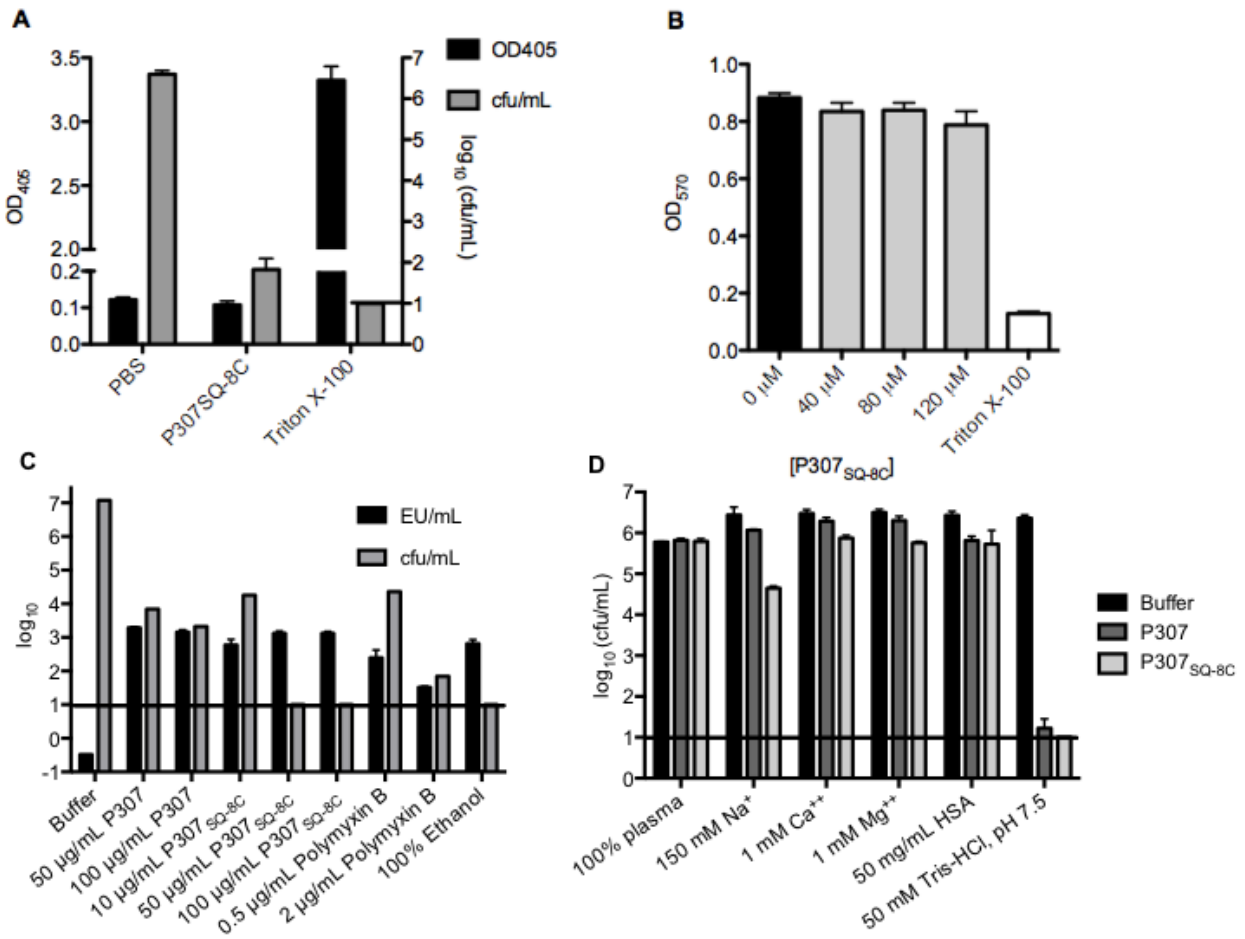
Supplementary Figure 3. The importance of terminal cysteine and its disulfide bond formation for bactericidal activity of $P307_{SQ\text{-}8C}$. *A. baumannii* strain #1791 was treated with 10 μg/mL $P307_{SQ\text{-}8A}$ (with Ala instead of Cys at the C-terminus) or $P307_{SQ\text{-}8C}$ in 50 mM Tris-HCl, pH 7.5 with or without TCEP for 2 h at 22-25°C. Serial dilutions were plated for cfu counting. The error bars show standard deviation.



Supplementary Figure 4. Affinity of P307 for DNA. The peptide P307 was mixed with DNA at different peptide:DNA ratios (0:1-15:1) and incubated for 1 h before being analyzed on an agarose gel. In comparison to positive control peptide, no electrophoretic shift was observed for P307.



Supplementary Figure 5. Membrane permeability of bacteria treated with P307 and $P307_{SQ-8C}$. *A. baumannii* strains #1791 and *K. pneumoniae* strain ATCC700603 were treated in 50 mM Tris-HCl at indicated pH with 50 μg/mL of P307 or $P307_{SQ-8C}$ in the presence of 1 μM SYTOX® Green (Invitrogen). Benzonase® nuclease (25 U/mL)(Novagen) was also added to remove extracellular DNA. The permeability of bacterial membrane was monitored for 2 h by the increase in relative fluorescence units of SYTOX® Green dye, using polymyxin B as a positive control. The error bars show standard deviation.



Supplementary Figure 6. *In vitro* safety and efficacy studies. (A) Hemolysis; red blood cells (RBCs) were incubated with 345 μg/mL $P307_{SQ-8C}$ in PBS and the release of hemoglobin into the supernatant was measured by OD_{405} to determine hemolysis, using 1% Triton X-100 as a positive control. The activity of $P307_{SQ-8C}$ was examined against *A. baumannii* strain #1791 under the same experimental conditions. (B) B cell survival; ~$5x10^5$ live B cells were incubated with 172.5, 345 and 517.5 μg/mL $P307_{SQ-8C}$ for 1 h at 37°C in a humidified 5% CO_2 atmosphere. CellTiter 96® Non-Radioactive Cell Proliferation Assay (Promega) was conducted to quantify the survival of B cells, using 1% Triton X-100 as a positive control. (C) Endotoxin release; *A. baumannii* strain #1791 (~10^7 cfu/mL) was treated with different concentrations of antibacterials for 2 h at 22-25°C. The samples were centrifuged to remove live cells. The supernatant was

analyzed with the Endpoint Chromogenic LAL Assay (Lonza) to measure endotoxin units, using 100% ethanol as a positive control. (D) Activities of peptides in plasma and its components. *A. baumannii* strain #1791 was treated with 50 µg/mL P307 or $P307_{SQ-8C}$ for 2 h at 22-25°C in 100% plasma or indicated concentrations of chloride salts of sodium, calcium and magnesium, and human serum albumin in 50 mM Tris-HCl, pH 7.5. Serial dilutions were plated for cfu counting. The error bars show standard deviation and the black horizontal lines mark the limit of detection for cfu/mL.