Supporting Information

Ciprofloxacined peptided-based nanoparticles confer antimicrobial efficacy against multidrug-resistant bacteria

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Characterization

Proton Nuclear Magnetic Resonance (^{1}H NMR)

The NMR spectra were recorded on a Bruker AV 400 MHz spectrometer, using tetramethylsilane as an internal standard and DMSO-d_6 as solvent.

DLS and Zeta potential study

Particle size and Zeta potential of (PAC-NPs) were measured on a Malvern Zetasizer Nano-ZS at a fixed scattering angle of 90° at room temperature. The polymer PAC solution (1mg/mL) was centrifuged to remove the insoluble particles

Scanning Electron Microscopy (SEM)

The morphologies of nanoparticles and bacteria were observed by SEM. To obtain SEM images of the nanoparticles (PAC-NPs), a drop of nanoparticle was spread on the silicon wafer and freeze-dried. In addition, the bacterial cells were incubated at 37℃ to the mid log growth phase (OD_{600}=0.4~0.6), and then treated with PAC. The treated bacteria was collected, washed with PBS and fixed with 2.5% (v/v) glutaraldehyde for 2-4 h, then washed again with PBS and distilled water, respectively. After dehydrating by 30, 50, 70, 90 and 100% ethanol and then replacing with tertiary butyl alcohol, which was dripped on the silicon wafer and freeze-dried. Samples were treated with gold before observation.

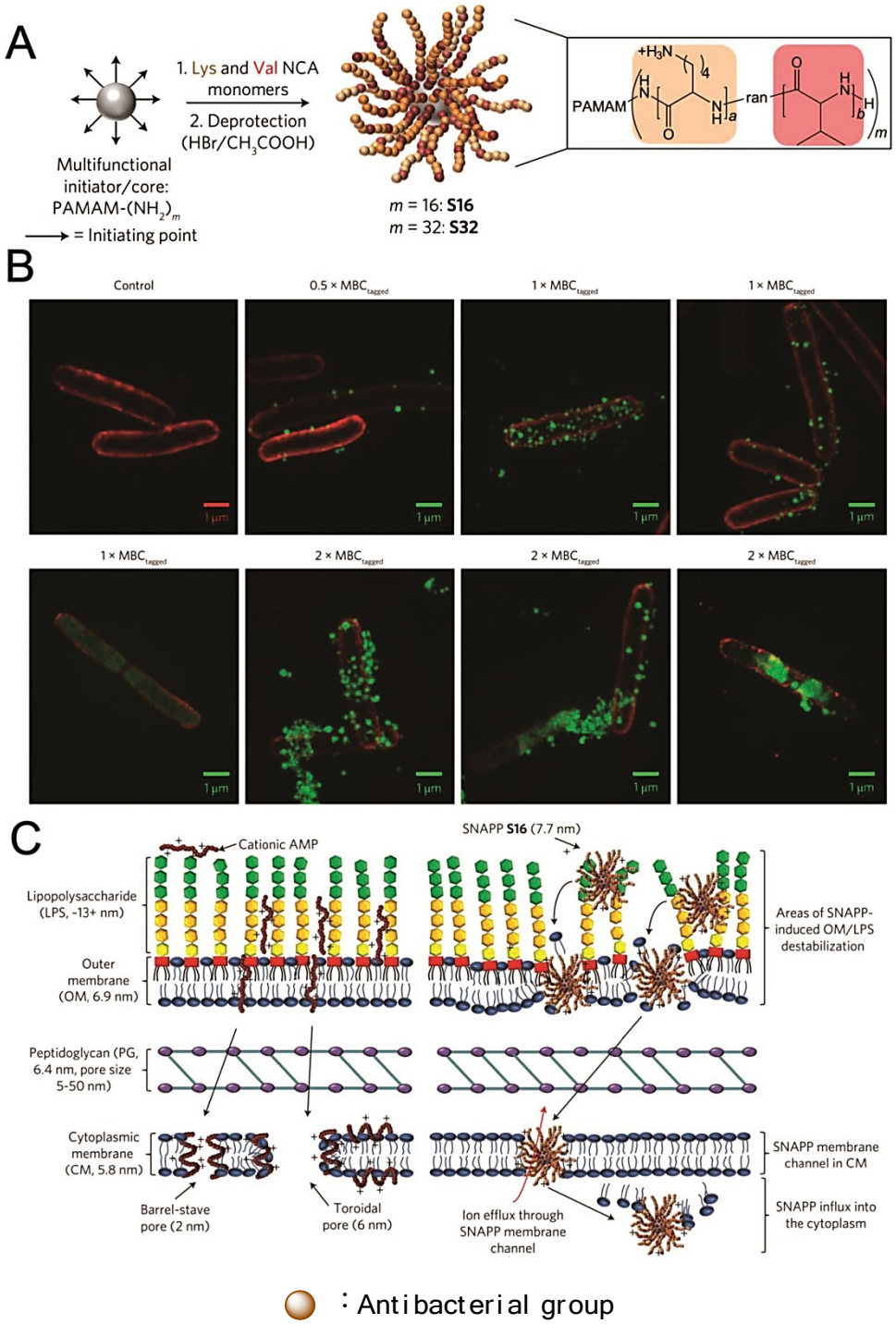

Figure S1. A) Synthesis of SNAPPs via ring-opening polymerization of lysine and valine N-carboxyanhydrides (NCAs). Second- and third-generation poly(amido amine) (PAMAM) dendrimers with 16 and 32 peripheral primary amines were used as the initiators to prepare 16- and 32-arm SNAPPs, respectively. The number of repeat units for lysine and valine are a and b, respectively, which served as antibacterial groups. B) Optical microscope experimental 3D-SIM images of *E. coli* before and after treatment with AF488-tagged SNAPP S16 in Mueller-Hinton Broth (MHB). The *E. coli* cell membrane was stained with FM4-64FX (red) and S16 with AF488 (green) in all images. Note that the MBC used refers to the MBC of the fluorescently tagged SNAPP. C) Antimicrobial mechanisms of typical

membrane-disrupting cationic AMPs and the possible mechanism of SNAPPs against Gram-negative bacteria.[1]

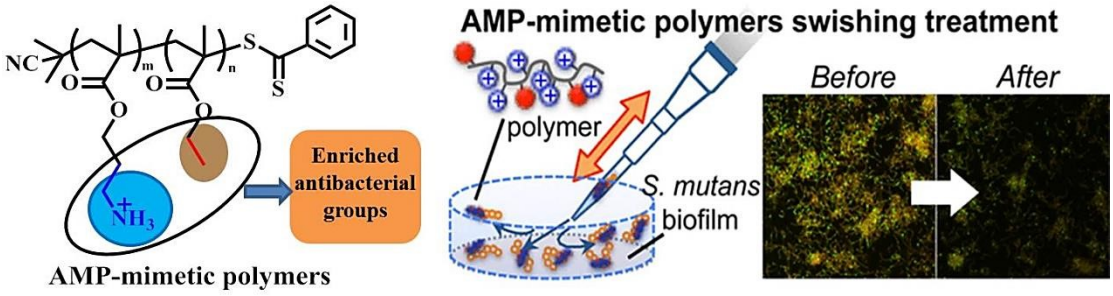

Figure S2. The structure of Cationic amphiphilic methacrylate polymers (AMP-mimetic polymers) and the antibiofilm activity of AMP-mimetic polymers.[2] AMP-mimetic polymers with enriched antibacterial groups could inhibited the growth of planktonic *S. mutans* as well as prenented the formation of *S. mutans* biofilm.

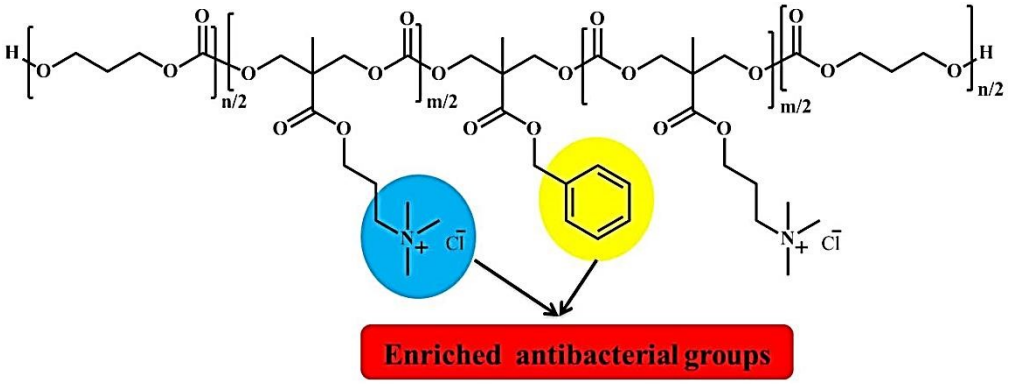

Figure S3. The structure of cationic amphiphilic polycarbonates with enriched antibacterial groups. These cationic nanoparticles formed from the polymers can efficiently kill Gram-positive bacteria, MRSA and fungi, even at low concentrations. [3]

References:

[1] S. J. Lam, N. M. O. Simpson, N. Pantarat, A. Sulistio, E. H. Wong, Y. Y. Chen, J. C. Lenzo, J. A. Holden, A. Blencowe, E. C. Reynolds, G. G. Qiao, Nat. Microbiol. 2016, 1, 16162.

[2] H. Takahashi, Enrico T. Nadres, and K. Kuroda, Biomacromolecules, 2017, 18, 257–265.

[3] Fredrik Nederberg, Ying Zhang, Jeremy P. K. Tan, Kaijin Xu, Huaying Wang, Chuan Yang, Shujun Gao, Xin Dong Guo, Kazuki Fukushima, Lanjuan Li, James L. Hedrick and Yi-Yan Yang, Biodegradable nanostructures with selective lysis of microbial membranes, Nature chem., 2011, 3, 409-

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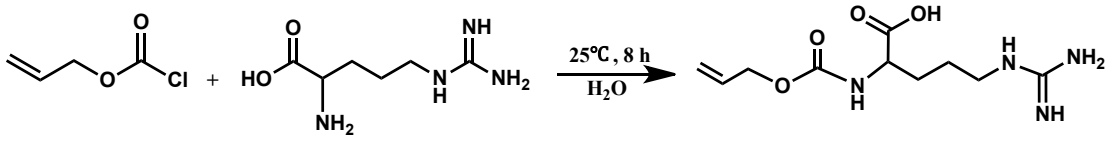
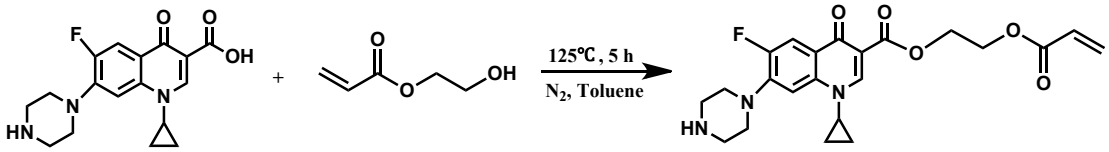
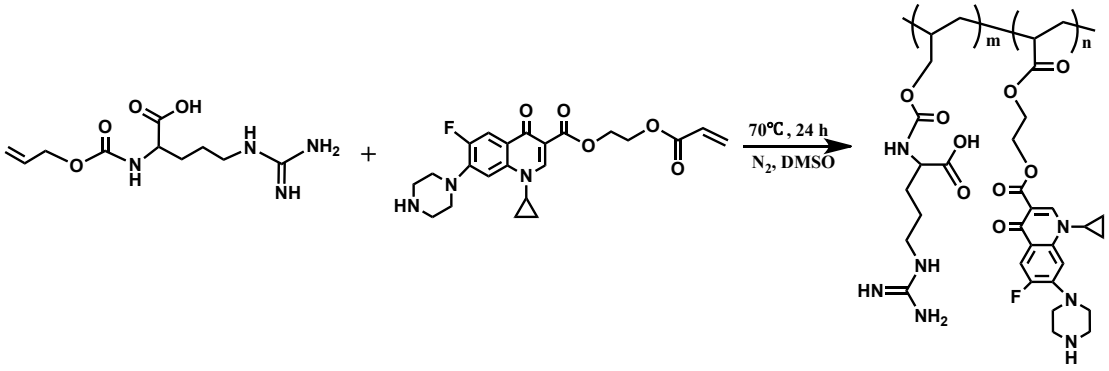


Scheme S1. Synthetic route of the AA.



Scheme S2. Synthetic route of the ACE.



Scheme S3. Synthetic route of the polymer PAC.

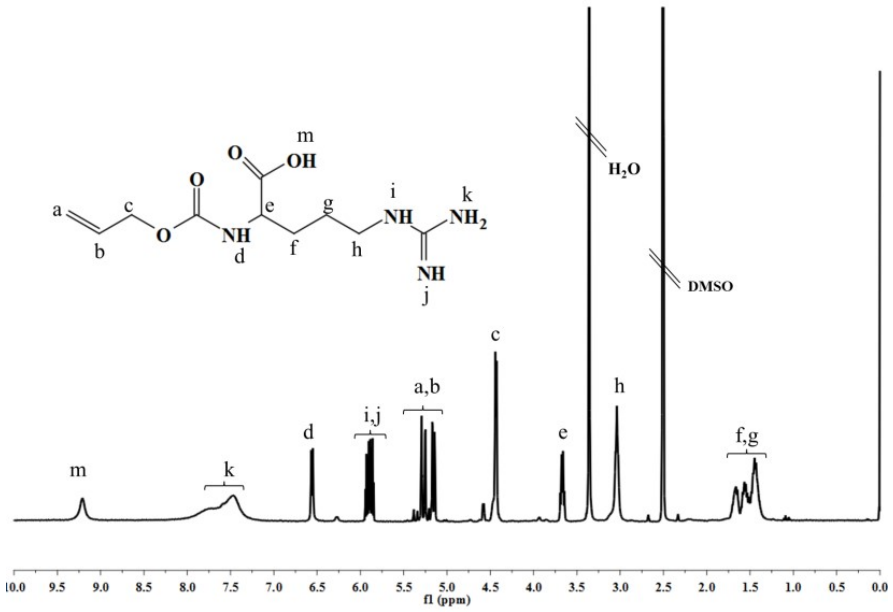


Figure S4. ^{1}H NMR spectrum of AA in DMSO-d_6

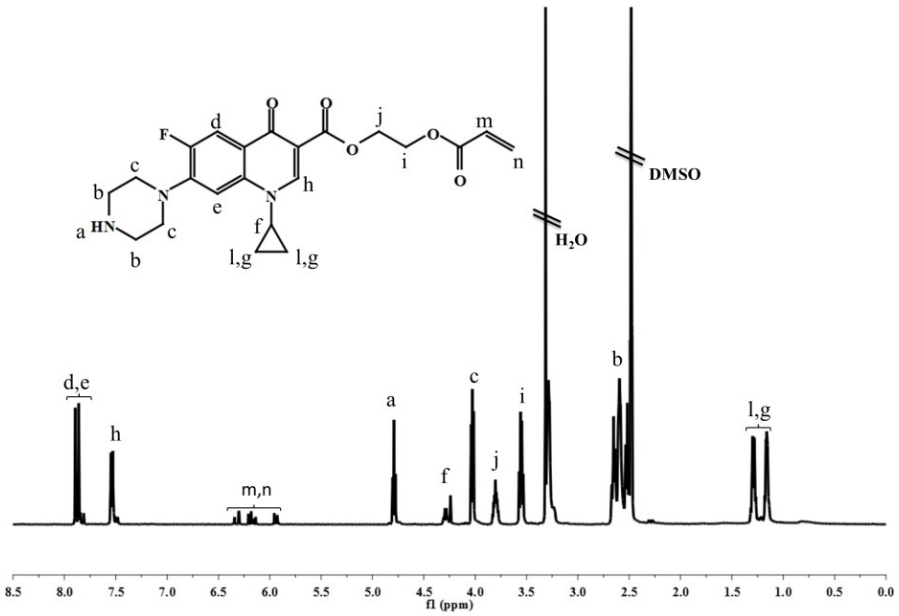


Figure S5. ^{1}H NMR spectrum of ACE in DMSO-d_6

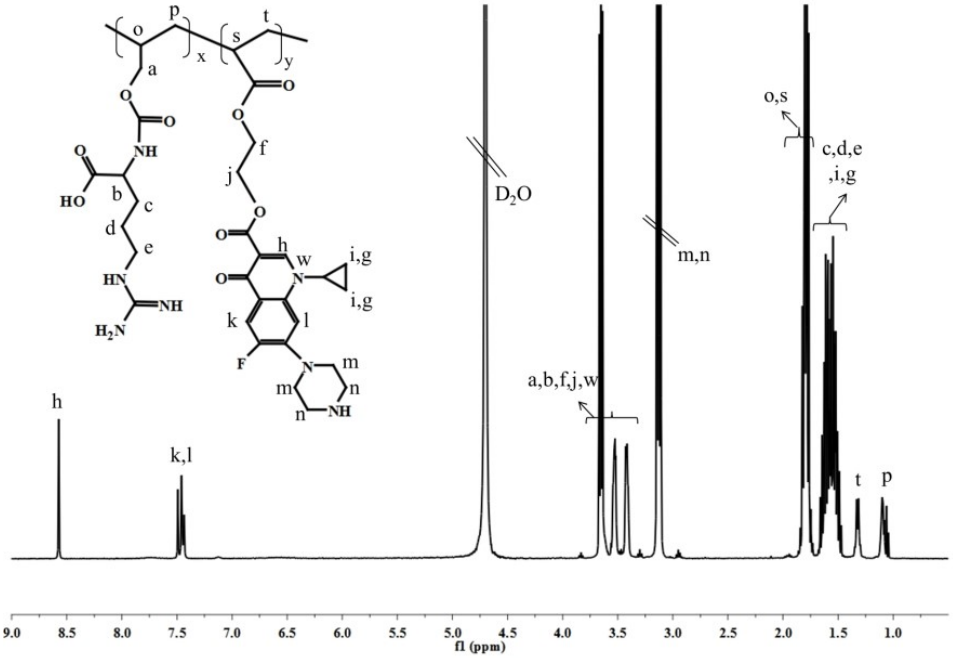


Figure S6. ^{1}H NMR spectrum of PAC in D_2O

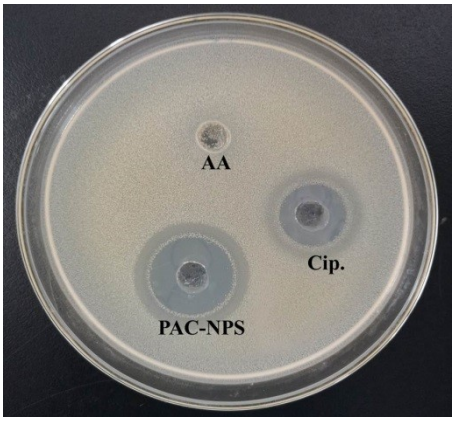


Figure S7. Inhibition zones of PAC-NPs, Ciprofloxacin and AA against *E.faecali* (ATCC29212)

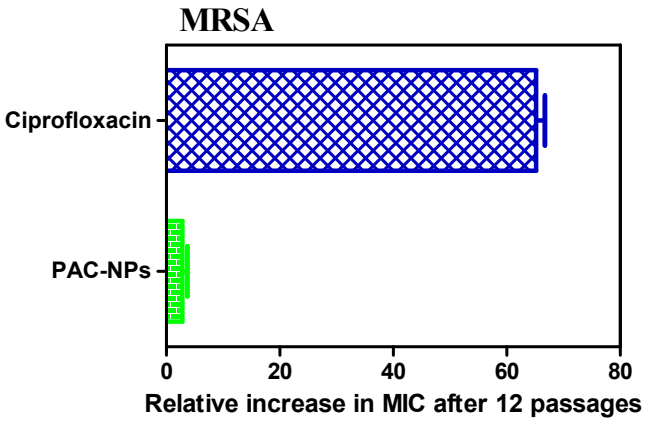


Figure S8. Resistance acquisition in the presence of sub-MIC levels of the PAC-NPs and Ciprofloxacin.