Supplementary table legend

Table S1 Antimicrobial activity of fatty acids

Table S2 Antibacterial activity of lipopeptides against *P. acnes* ATCC11827 in saline solution

Table S3 Antimicrobial activity of designed lipopeptides in MH media

Table S4 Thermodynamic parameters of interactions between lipopeptides with lipids

Table S5 Fluorescence spectroscopy parameters measured for blueshift of tryptophan in different lipids

Table S6 The design of *in vivo* experiment

Table S1 Antimicrobial activity of fatty acids

Fatty acids	MIC (μg/mL)*	
	***P. acnes* ATCC6919**	***P. acnes* ATCC11827**
C6:0	>125	>125
C8:0	>125	>125
C10:0	>125	>125
C12:0	62.5	62.5
C14:0	62.5	62.5
C16:0	>125	>125
C18:0	>125	>125
C20:0	>125	>125

*MIC: minimal inhibitory concentration

Table S2 Antibacterial activity of lipopeptides against *P. acnes* ATCC11827 in saline solution

Sequence	MIC (μg/mL)							
	NaCl (mM)				$MgCl_2$ (mM)		$CaCl_2$ (mM)	
	0	25	75	150	2.5	10	2.5	10
C14-KWKW	3.9	3.9	3.9	3.9	3.9	3.9	3.9	3.9
C16-KWKW	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Clindamycin	0.02	0.02	0.02	0.02	0.02	0.02	0.04	0.15

Table S3 Antimicrobial activity of designed lipopeptides in MH media

Sequence	MIC (μg/mL)			
	P. acnes ATCC 11827	*S. epidermidis* ATCC 12228	*S. aureus* ATCC 25923	*E. coli* ATC C25922
C14-KWKW	3.9	7.8	15.6	31.25
C16-KWKW	2.0	3.9	15.6	15.6
Clindamycin	0.03	0.06	0.03	31.25

Table S4 Thermodynamic parameters of interactions between lipopeptides with lipids

	K_d (μM)	K_a (μM^{-1})	△H (kJ/mol)	△G (kJ/mol)	-T△S (kJ/mol)
C16-KWKW - *P. acnes*	0.287	3.484	-11.8	-37.4	-25.6
C16-KWKW - *S. aureus*	N/A	N/A	N/A	N/A	N/A
C16-KWKW- *E. coli*	N/A	N/A	N/A	N/A	N/A
Melittin - *P. acnes*	3.58	0.279	-18.1	-38.8	-20.7
Melittin - *S. aureus*	4.68	0.213	-28.7	-30.5	-1.8
Melittin - *E. coli*	5.44	0.184	-10.9	-30.1	-19.2

N/A: Not applicable

Table S5 Fluorescence spectroscopy parameters measured for blue shit of tryptophan in different lipids

Peptide	Lipid	Wavelength (nm)	Blue shit (nm)
C16-KWKW	PBS control	359.3±0.9	-
	P. ances ATCC11827	337.7±0.5***	21.6±1.2
	S. aureus ATCC12600	358.7±0.5	0.7±0.5
	E. coli ATCC25922	357.7±1.7	1.7±1.2
C10-KWKW	PBS control	343.7±1.2	-
	P. ances ATCC11827	338.0±0.8**	5.7±0.5
	S. aureus ATCC12600	342.7±1.2	1.3±0.5
	E. coli ATCC25922	341.7±0.9	2.0±0.8
Melittin	PBS control	342.7±0.9	-
	P. ances ATCC11827	332.3±1.2***	10.3±0.5
	S. aureus ATCC12600	334.0±1.6***	8.7±0.9
	E. coli ATCC25922	330.3±0.5***	12.3±0.5

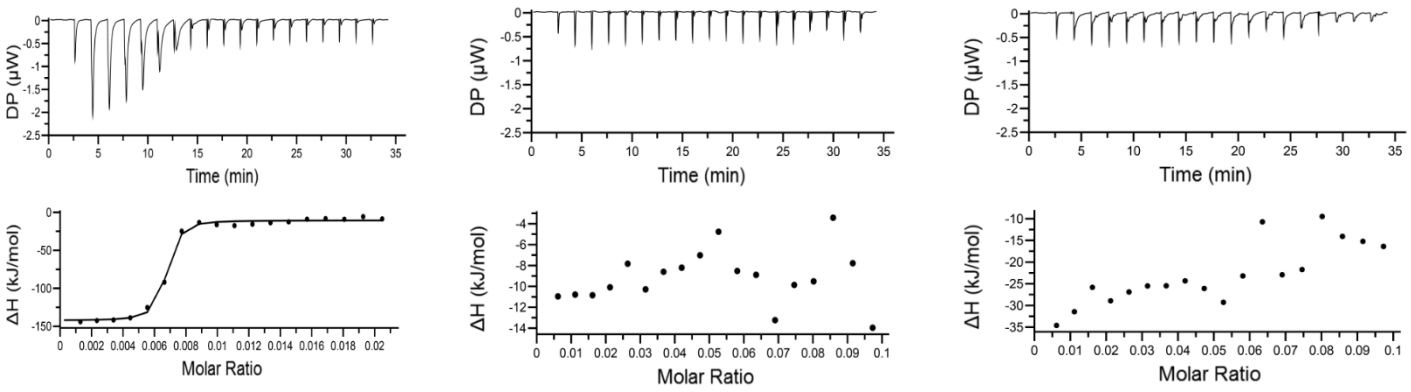
Table S6 The design of *in vivo* experiment

Group	Left ear	Right ear
Blank control	Untreated	Untreated
Clindamycin-treated	Injected with *P. acnes* and treated with 50 mg vaseline	Injected with *P. acnes* and treated with 10 μg clindamycin mixed with 50 mg vaseline
100 μg C16-KWKW-treated	Injected with *P. acnes* and treated with 50 mg vaseline	Injected with *P. acnes* and treated with 100 μg C16-KWKW mixed with 50 mg vaseline
200 μg C16-KWKW-treated	Injected with *P. acnes* and treated with 50 mg vaseline	Injected with *P. acnes* and treated with 200 μg C16-KWKW mixed with 50 mg vaseline

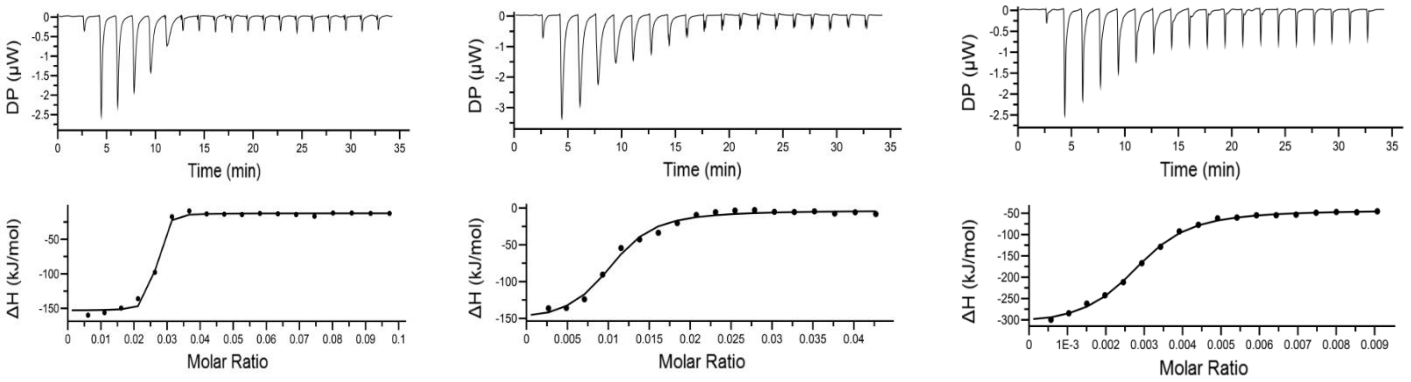
Supplementary figure legend

Figure S1 Binding of C16-KWKW with lipids from *P. acnes*, *S. aureus* and *E. coli*, melittin was used as control. A significant binding can be observed between 150 μg/mL C16-KWKW and 4 mg/mL lipid extracted from *P. acnes*, whereas C16-KWKW bound very weakly to other lipids at the same concentration. In contrast, 200 μg/mL melittin shows binding with lipids from all the three strains at 4 mg/mL, and the binding difference was not significant. N=5. Each experiment was repeated independently 5 times.

Figure S2 Tryptophan fluorescence emission spectra of the lipopeptides using various liposome models. The lipid extracted from *P. acnes* treated with C16-KWKW or C10-KWKW at 150 μg/mL showed a significant blueshift in the maximum emission spectrum, while the blueshift in other lipids was not obvious. In contrast, melittin produced a significant blueshift with all three lipids at the same concentration. N=5. Each experiment was repeated independently 5 times.



C16-KWKW - *P. acnes* **C16-KWKW - *S. aureus*** **C16-KWKW - *E. coli***



Melittin - *P. acnes* **Melittin - *S. aureus*** **Melittin - *E. coli***

Figure S1 Binding of C16-KWKW with lipids from *P. acnes*, *S. aureus* and *E. coli*, melittin was used as control. A significant binding can be observed between 150 μg/mL C16-KWKW and 4 mg/mL lipid extracted from *P. acnes*, whereas C16-KWKW bound very weakly to other lipids at the same concentration. In contrast, 200 μg/mL melittin shows binding with lipids from all the three strains at 4 mg/mL, and the binding difference was not significant. N=5. Each experiment was repeated independently 5 times.

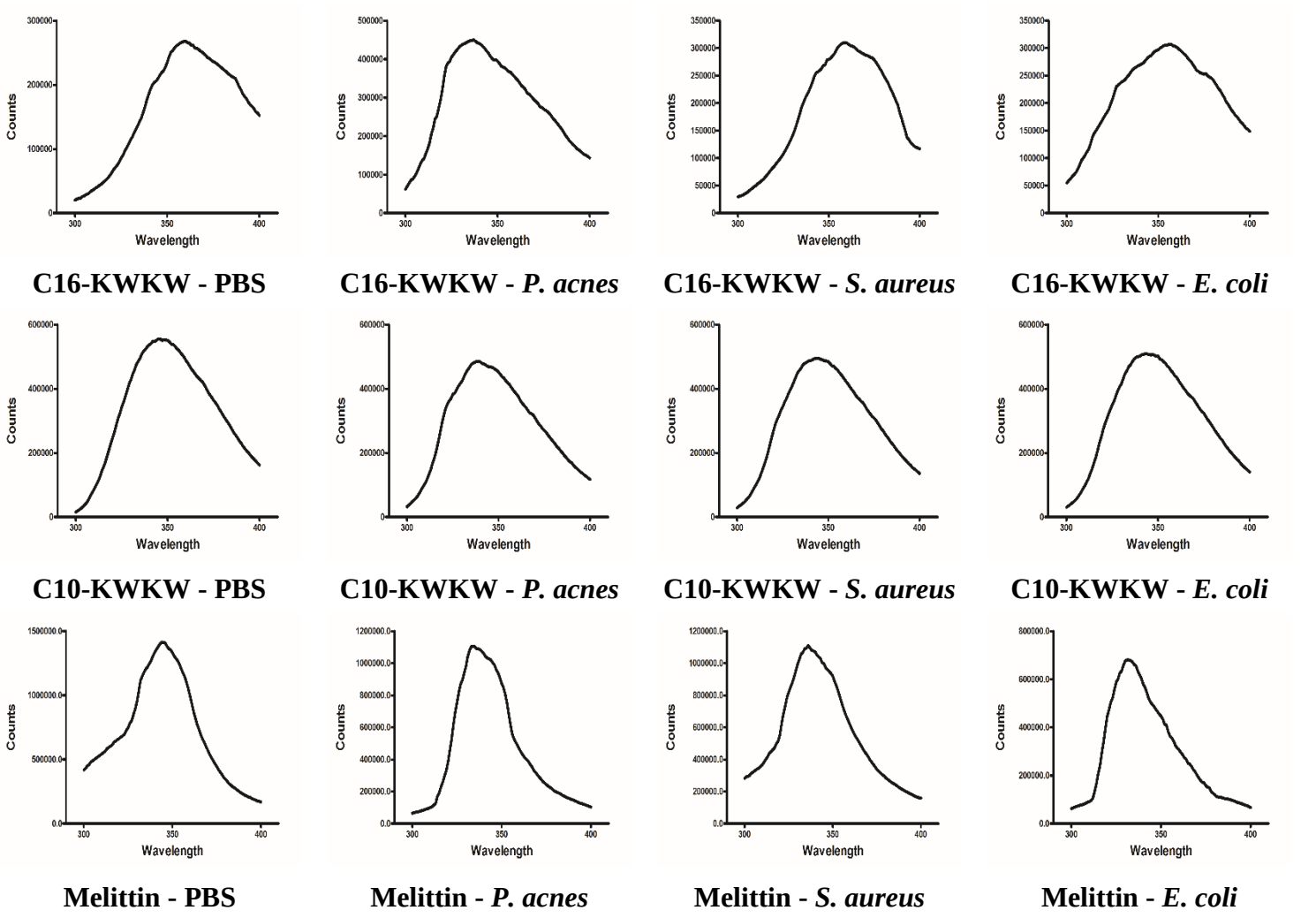


Figure S2 Tryptophan fluorescence emission spectra of the lipopeptides using various liposome models. The lipid extracted from *P. acnes* treated with C16-KWKW or C10-KWKW at 150 μg/mL showed a significant blueshift in the maximum emission spectrum, while the blueshift in other lipids was not obvious. In contrast, melittin produced a significant blueshift with all three lipids at the same concentration. N=5. Each experiment was repeated independently 5 times.