

## Supporting Information

### Transforming cross-linked cyclic dimers of KR-12 into stable and potent antimicrobial drug leads

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**Table S1: Sequences, net charge, hydropathicity, and molecular weight of linear peptides**

Peptide	Sequence	Net Charge (at neutral pH) <sup>a</sup>	Grand average of hydropat hicity <sup>a</sup>	Molecular Weight (Expecte d) <sup>b</sup>	Molecular Weight (Observed ) <sup>b</sup>
cd4-CCPP	CFLRGPGGKRIV CRIKAFLRG PGGKRIVK RIK	+11	- 0.178	3581.49	3582.11
cd4-CC	CFLRGAGGKRIV CRIKAFLRG AGGKRIVK RIK	+11	0.034	3529.41	3529.91
KR-12 (Q5K, D9A)	KRIVKRIKAFLR	+6	- 0.300	1527.97	1528.01
KR-12	KRIVQRIKDFLR	+ 4	- 0.708	1571.93	1572.13
LL-37	LLGDFFRKSKEKI GKEFKRIV QRIKDFLR NLVPRTES	+6	- 0.724	4493.32	4493.98

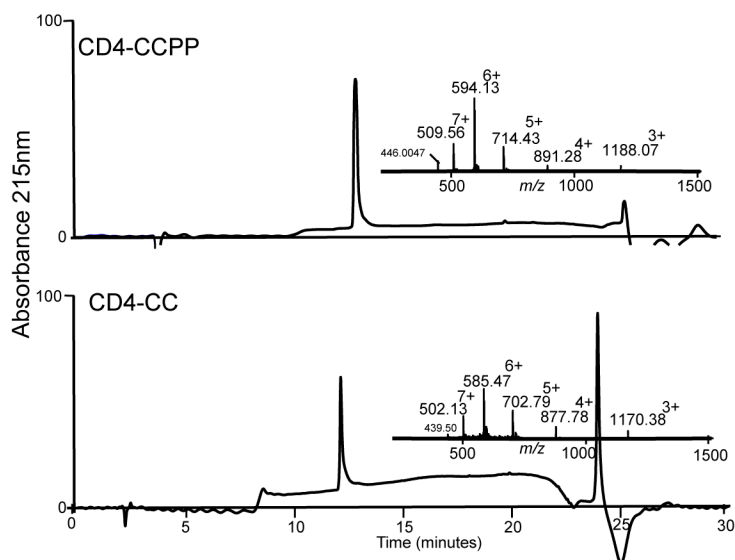
<sup>a</sup>ExPASy ProtParam tool was used to calculate the molecular weight, net charge, and hydropathy index (<http://web.expasy.org/protparam/>)

<sup>b</sup>Observed peptides masses presented as (M+1)<sup>+</sup> have been deconvoluted from (M+2)<sup>2+</sup>, (M+3)<sup>3+</sup> and (M+4)<sup>4+</sup> masses.

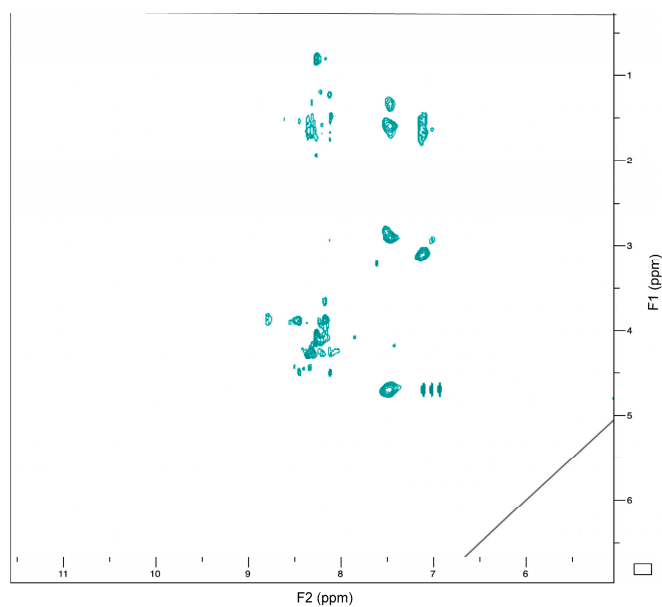
**Table S2: MIC values in two-step microdilution assay, MHB, and TSB**

Peptides	MIC ( $\mu$ M)					
	Control <sup>1</sup>		MHB <sup>2</sup>		TSB <sup>3</sup>	
	<i>B. cereus</i>	<i>B. subtilis</i>	<i>B. cereus</i>	<i>B. subtilis</i>	<i>B. cereus</i>	<i>B. subtilis</i>
LL-37	1.25	1.25	>80	>80	>80	>80
KR-12	2.5	5	>80	>80	>80	>80
KR-12 (Q5K, D9A)	1.25	1.25	>80	>80	> 80	>80
cd4-CCPP	0.312	0.625	>40	>40	>40	>40
cd4-CC	0.625	0.625	>40	>40	>40	>40

<sup>1</sup> The control MICs were determined in a two-step microdilution assay in Tris buffer 10 mM without salts. <sup>2</sup> MHB, Muller-Hinton broth (rich media, unbuffered). <sup>3</sup> TSB, Tryptic Soy broth (rich media, unbuffered).



**Supplementary Figure S1. Purity and identity analysis of cross-linked cyclic dimers using RP-HPLC and MS.** The purity of cross-linked dimers was analyzed at 215 nm and chemical identity was confirmed by LC-MS spectrometer.



**Supplementary Figure S2. NMR Spectroscopy.** TOCSY spectrum of cd4-CCPP displayed a broadening of signals and overlapping resonances which made it difficult to assign chemical shift assignments.