Electronic Supplementary Material (ESI) for Molecular BioSystems.

Supplementary material

Sequence Context Induced Antimicrobial Activity: Insight to Lipopolysaccharide Permeabilization

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Table S1. Antimicrobial activity (MIC) of WR17 and its analogues.

Peptide name	MIC (μM)		
	P. aeruginosa	***X. campestris***	***B. subtilis***
WR17	9.5	10	20
WG12	>100	75	>100
WK10	>100	>100	>100
KG11	>100	>100	>100
KR12	>100	>100	>100
KK9	>100	>100	>100
KR8	>100	>100	>100

Table S2. LPS neutralization and depth of insertion by the designed peptides.

Peptide name	**Neutralization of LPS at 0.25 EU/ml**	**Neutralization of LPS at 0.5 EU/ml**	**Neutralization of LPS at 1 EU/ml**	**Distance of Trp from LPS head group (Å)**
WR17	5	10	15	7.4
WG12	25	50	50	7.1
KG11	>100	>100	>100	
WK10	>100	>100	>100	
KR12	>100	>100	>100	
KR8	>100	>100	>100	
KK9	>100	>100	>100	

Table S3: Table containing atom-wise interaction details (post-docking analysis) between peptides and LPS moieties.

Key Interaction of Lactoferrampin fragments with LPS moiety from docking studies.

Interactions	**WR17**	**LPS moiety**	**Distance (Å)**
Polar Interactions	**L3.O**	**Acly.O**	**2.7**
	K10.NH	**GlcN II-(1→O)-PO^{2-}-O-PO^{3-}**	**2.1**
	N14.Nδ	**Acly.O**	**2.1**
	N14.Nδ	**GlcN I-(4→O)-PO^{3-}**	**1.8**
	R17.NH1	**GlcN I-(4→O)-PO^{3-}**	**1.7**
Non-Polar Interactions	**L3.Cβ**	**Acyl.C**	**3.9**
	L3.Cδ	**Acyl.C**	**3.9**
	L4.Cδ	**Acyl.C**	**4.0**
	A7.Cβ	**Acyl.C**	**2.9**
	F11.CZ	**GlcN.C**	**3.6**
	K13.Cδ	**KDO.C**	**4.5**

	WG12	**LPS moiety**	**Distance (Å)**
Polar Interactions	**K2.NZ**	**KDO.O/O/OH**	**2.8**
	S5.OG	**Acyl.H**	**2.9**
	S5.CB	**Acyl.O**	**2.0**
	Q8.OE	**Acyl.H**	**3.2**
	Q8.OE	**Acyl.OH**	**1.9**
Non-Polar Interactions	**W1.CE**	**Acyl.C**	**3.2**
	L4.Cδ	**Acyl.C**	**3.8**

	WK10	**LPS moiety**	**Distance (Å)**
Polar Interactions	**Q8.HE**	**Acyl.O**	**1.9**

	E9.OE	**GlcN II-(1→O).N**	**2.3**
Non-Polar Interactions	**W1.Cδ/ W1.Cα**	**Acyl.C/ Acyl.C**	**3.3/3.7**
	K2.Cβ	**Acyl.C**	**3.2**
	S5.Cβ	**Acyl.C**	**4.0**

	KR8	**LPS moiety**	**Distance (Å)**
Polar Interactions	**K4.NZ**	**Acyl.O/ Acyl.O**	**2.3/2.7**
	N5.Oδ	**Acyl.OH/ Acyl.OH**	**1.9/2.0**
	K6.NZ	**Acyl.O**	**2.0**
	K6.NZ	**GlcN I-(4→O)-PO^{3-}**	**2.0**
	R8.NH1	**GlcN II-(1→O).O**	**1.9**
	R8.NH2	**GlcN II-(1→O)-PO^{2-}—O-PO^{3-}**	**2.4**
	R8.NH2	**KDO.O/KDO.O**	**2.5/1.9**
Non-Polar Interactions	**F2.CE**	**Acyl.O**	**3.4**

Table S4. A Summary of Structural Statistics for the 20 Final NMR Structures of peptides in LPS micelle.

Distance restrains	WR17	WG12	WK10	KR8
Intra-residue (i–j = 0)	36	20	29	15
Sequential (|i–j| = 1)	52	41	32	17
Medium-range (2≤|i–j|≤4)	57	53	40	1
Long-range (|i–j| ≥5)	0	0	0	0
Total	145	114	101	33
Angular restraints				
Φ	16	11	9	7
Ψ	16	11	9	7
Distance restraints from violations (≥ 0.3 Å)	0	0	0	0
Deviation from mean structure (Å) Average back bone to mean structure N-ter region "*Trp1-Gly12*" of WR17	 1.43± 0.53 0.05± 0.01	 0.10± 0.05	 0.34± 0.13	 1.06± 0.25
Average heavy atom to mean structure	2.23± 0.65	0.55± 0.08	1.21± 0.29	2.13± 0.42
Ramachandran plot for mean structure				
% Residues in the most favourable and additionally allowed regions	100	100	100	100
% Residues in the generously allowed Region	0	0	0	0
% Residues in the disallowed region	0	0	0	0

Fig. S1: Selected amide region of two dimensional ^{1}H-^{1}H NOESY spectrum of WR17, WG12, WK10, KR12 and KR8 in water at pH 4.5. The lack of NOEs indicates that the peptides did not adopt any folded conformation in water. NOESY experiments were carried out at 500 MHz and 298 K, with a mixing time of 150 ms.

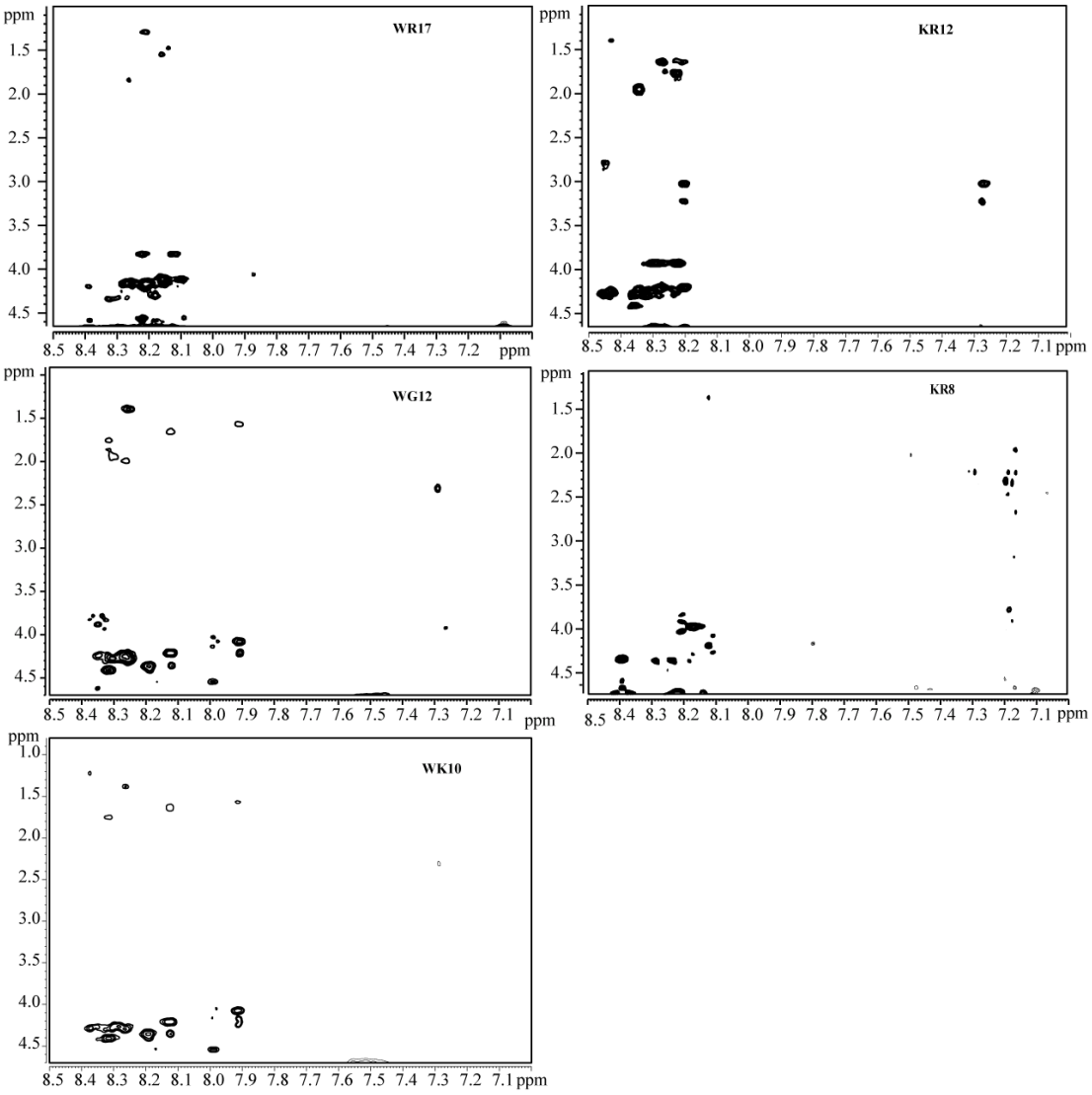

Fig. S2: Selected amide region of two dimensional ^{1}H-^{1}H *tr*NOESY spectrum of KG11and KK9 in presence of LPS. The lack of NOEs indicates that the peptides did not adopt any folded conformation in the presence of LPS.

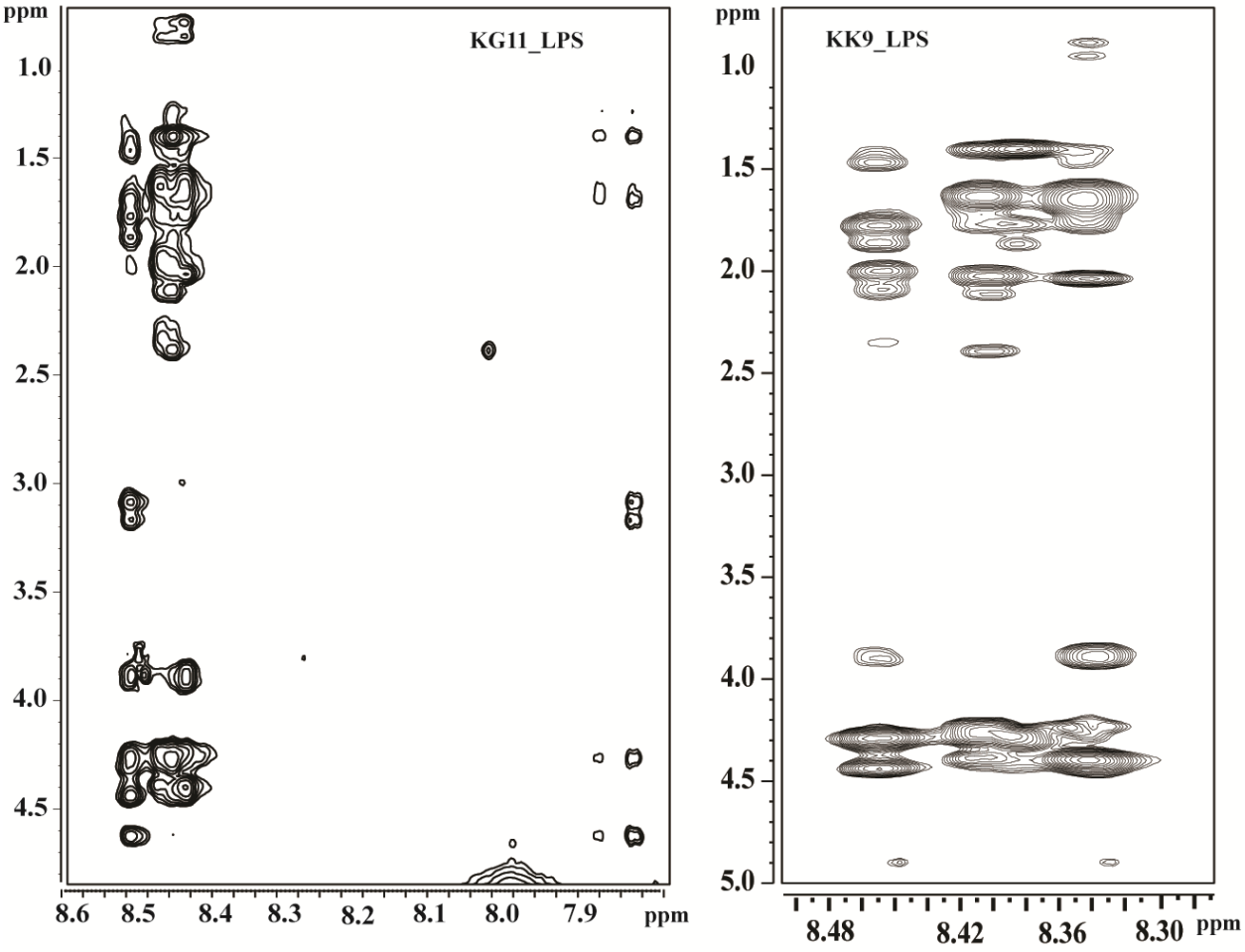

Fig. S3: SASA plots for peptides with LPS moiety as a function of time from MD simulation.

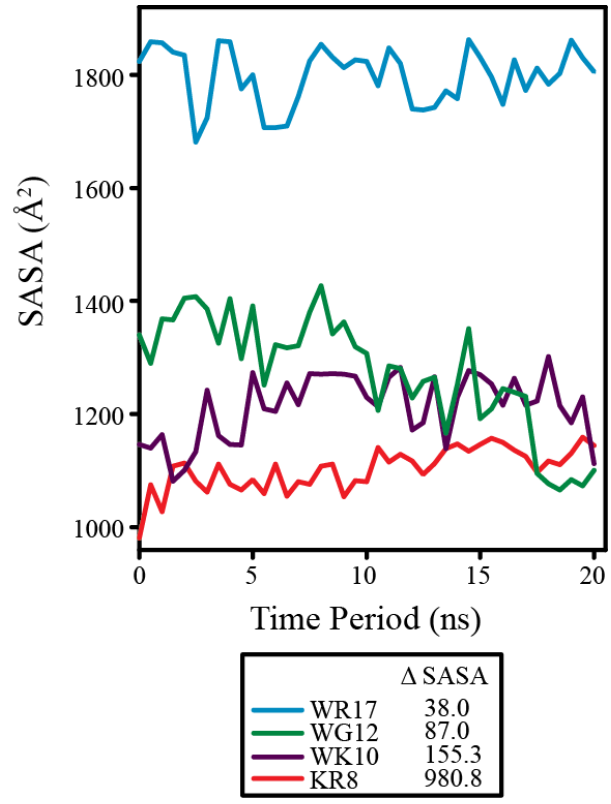

Fig. S4: Distance measurement plot between atoms involved in forming polar contacts. Lys10 and Arg17 (of WR17) are forming strong hydrogen bonds with a phosphate group of LPS, which are consistent throughout the simulation time course.