SUPPLEMENTARY DATA

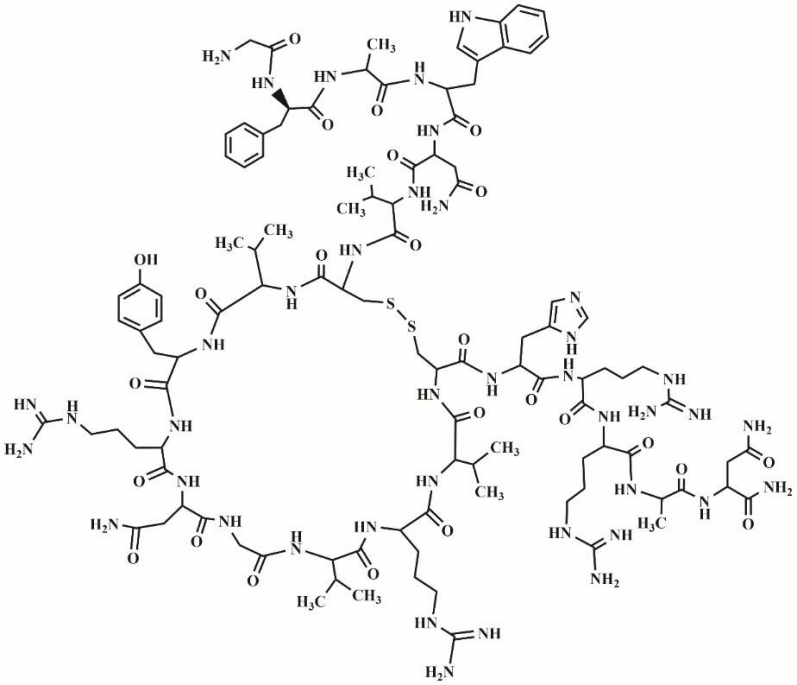

Figure S1-1. The chemical structure of $N6NH_2$.

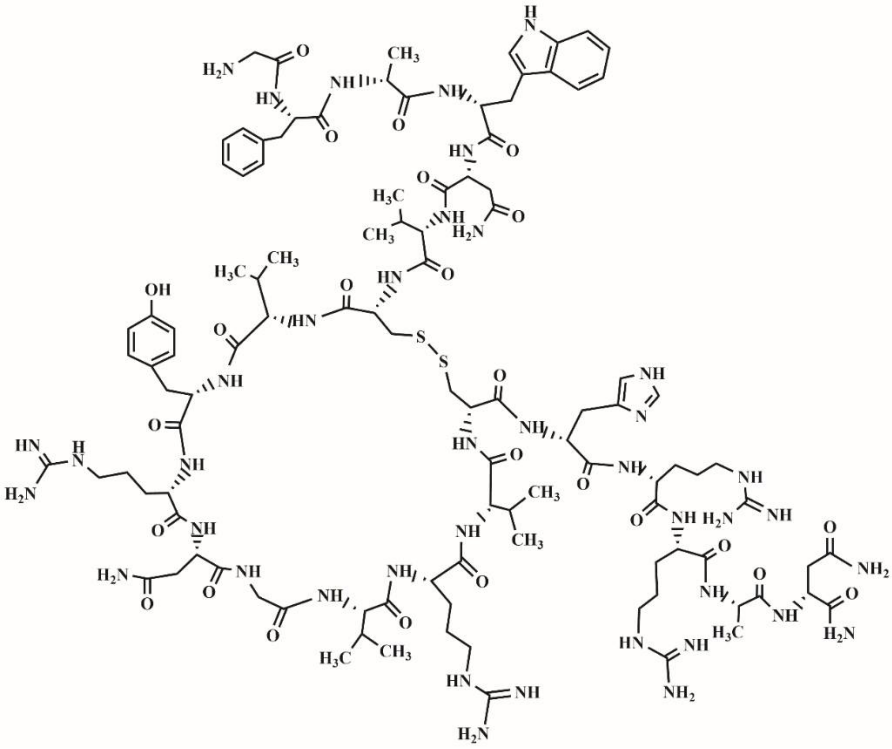

Figure S1-2. The chemical structure of $DN6NH_2$.

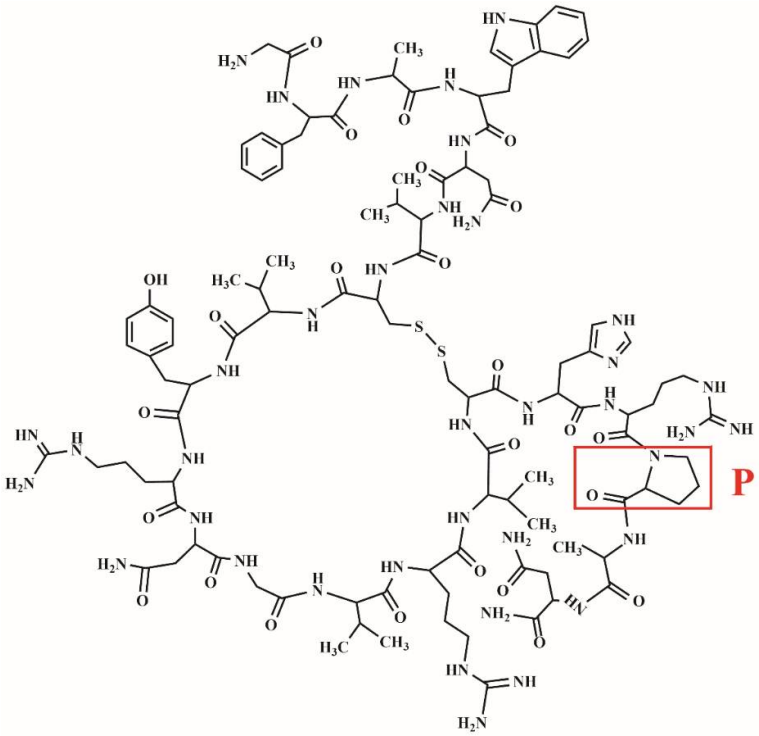

Figure S1-3. The chemical structure of N6PNH2. The red circle represents the position of amino acid replacement group.

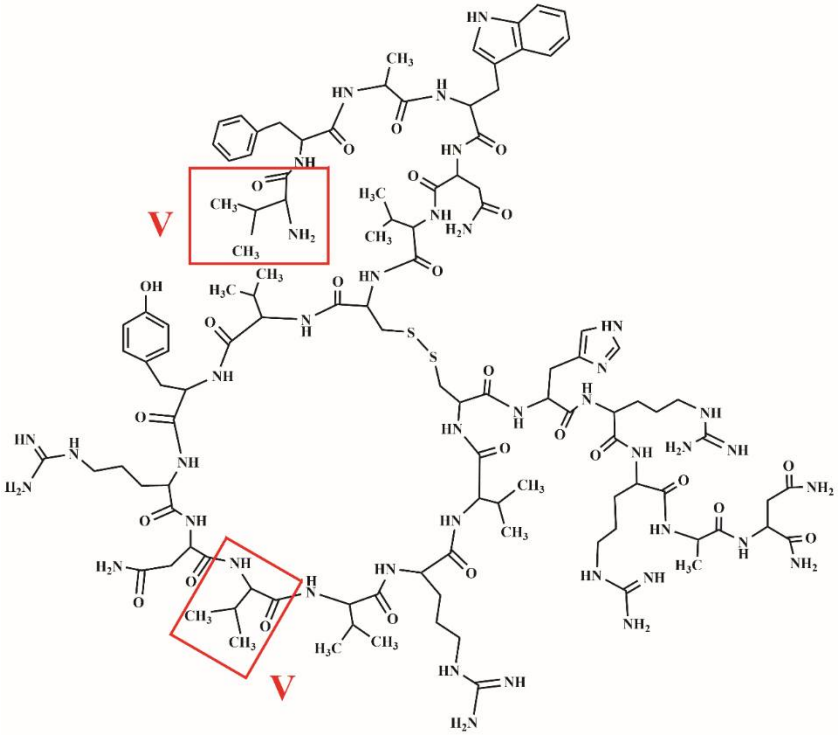

Figure S1-4. The chemical structure of V112N6NH2. The red circle represents the position of amino acid replacement group.

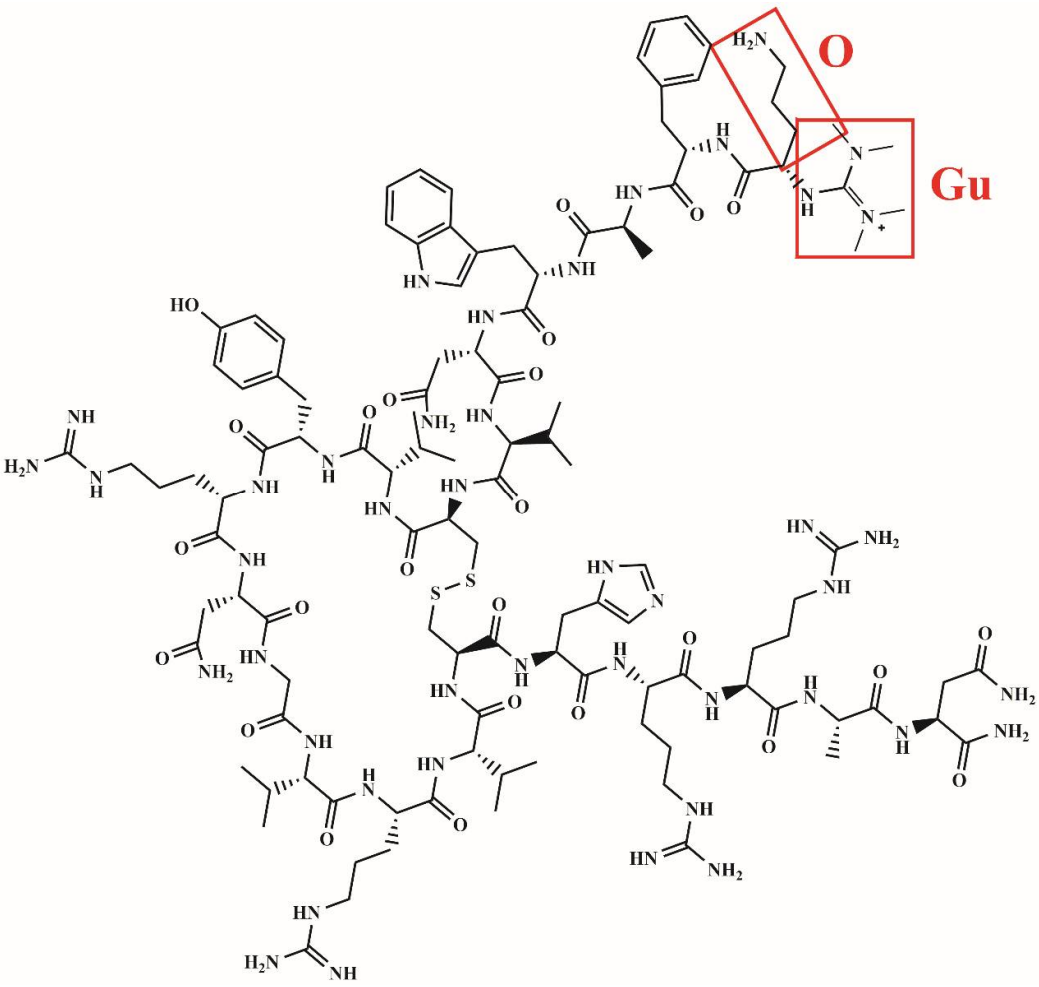

Figure S1-5. The chemical structure of Guo-N6NH2. The red circle represents the position of amino acid added group.

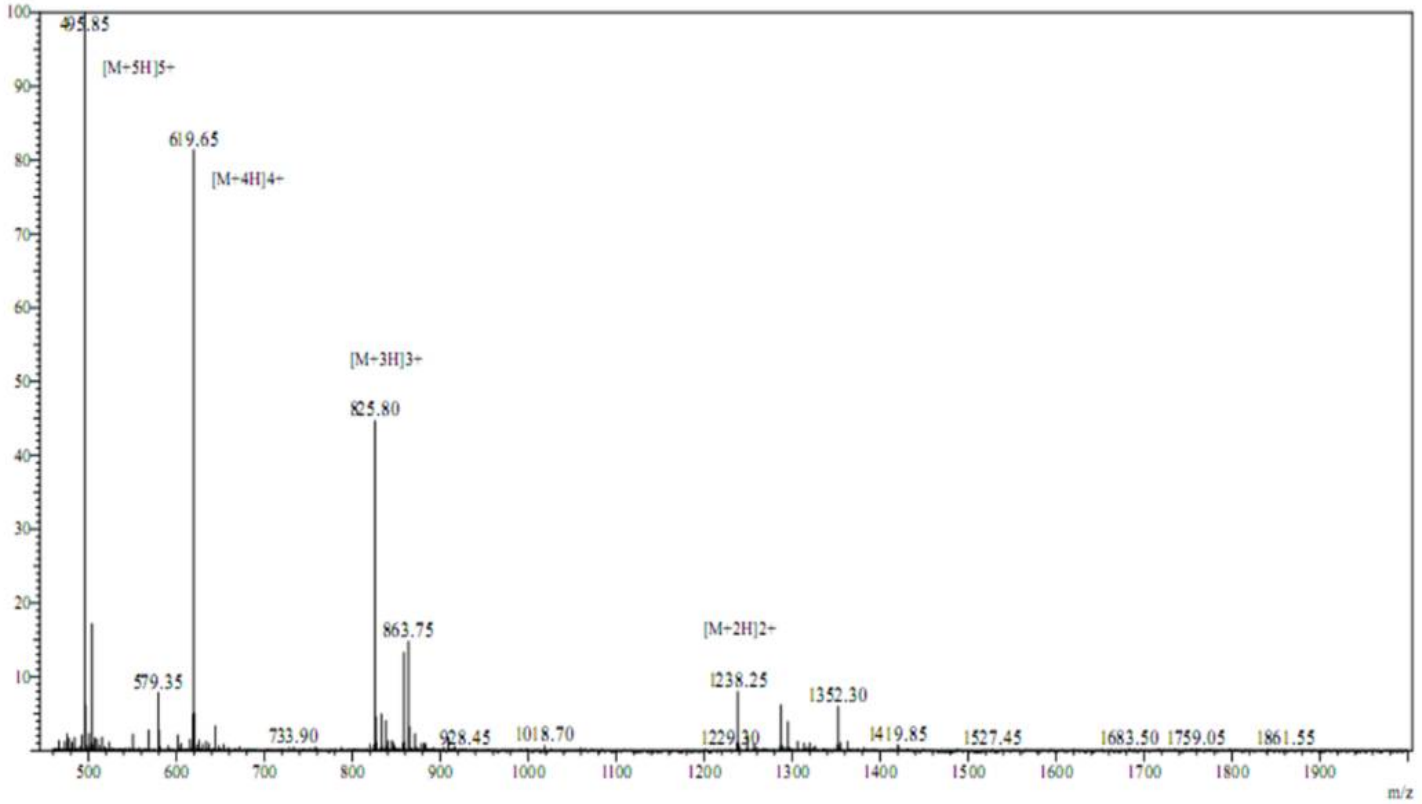

Figure S2-1. The mass spectrometry (MS) analysis of $N6NH_2$.

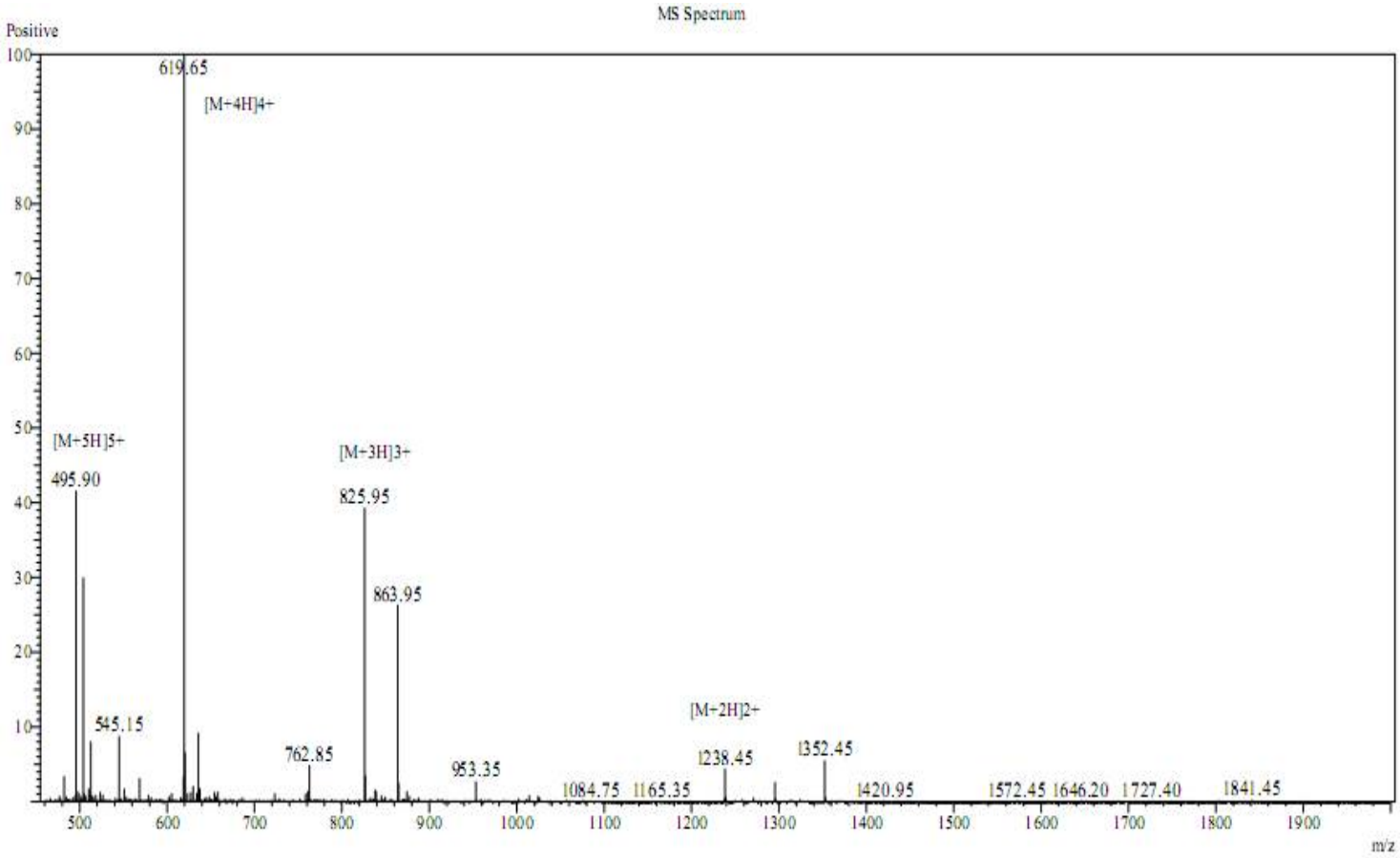

Figure S2-2. The mass spectrometry (MS) analysis of DN6NH2.

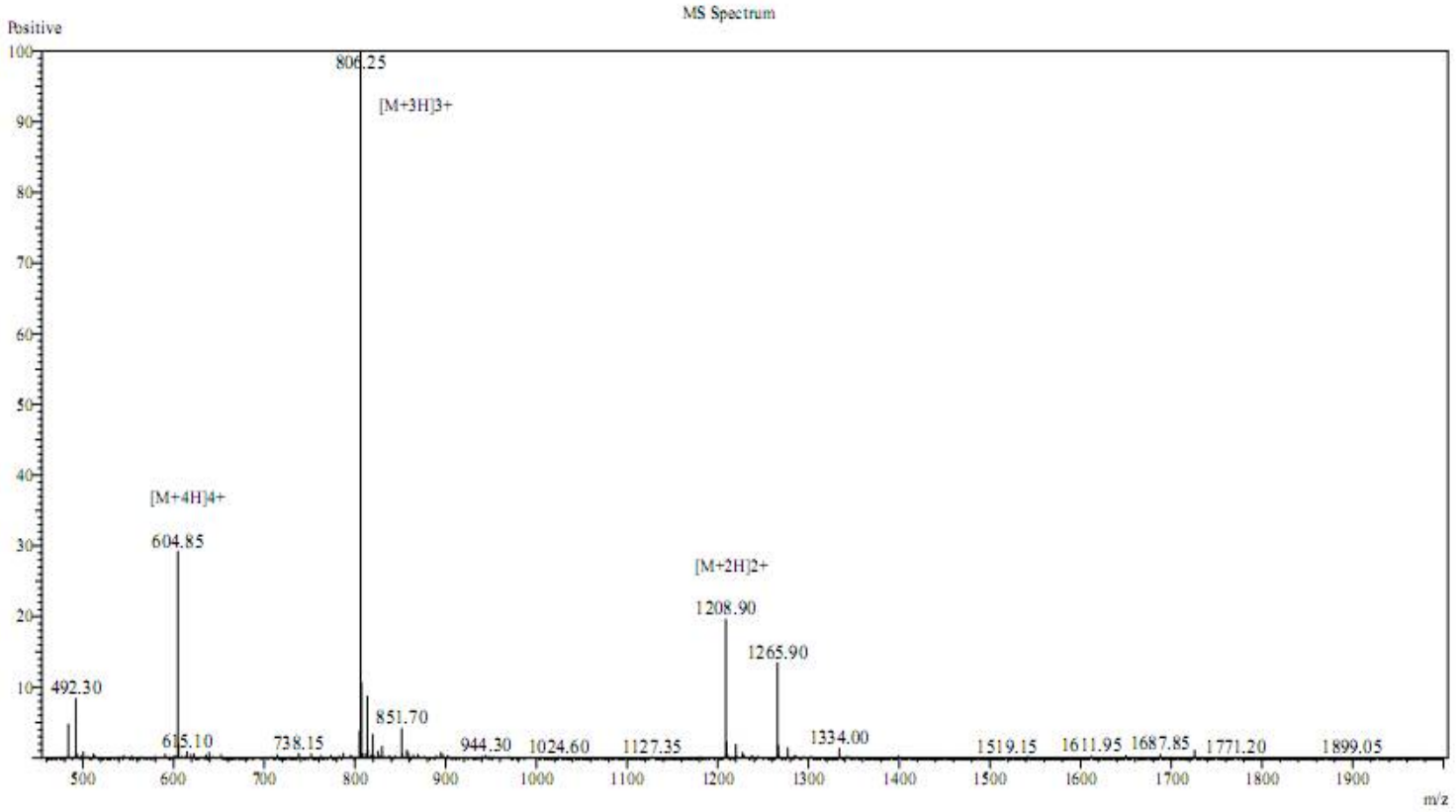

Figure S2-3. The mass spectrometry (MS) analysis of N6PNH2.

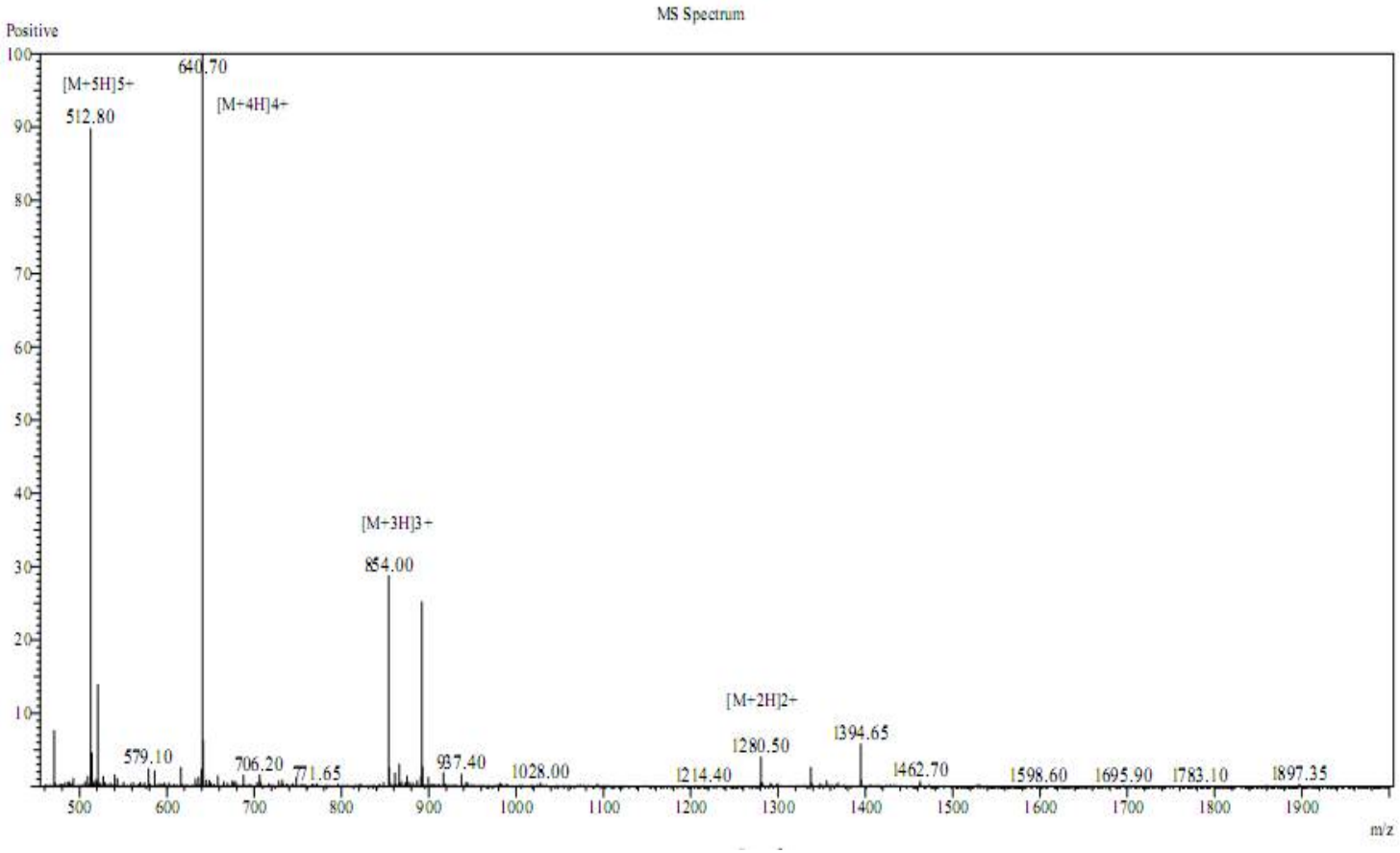

Figure S2-4. The mass spectrometry (MS) analysis of V112N6NH2.

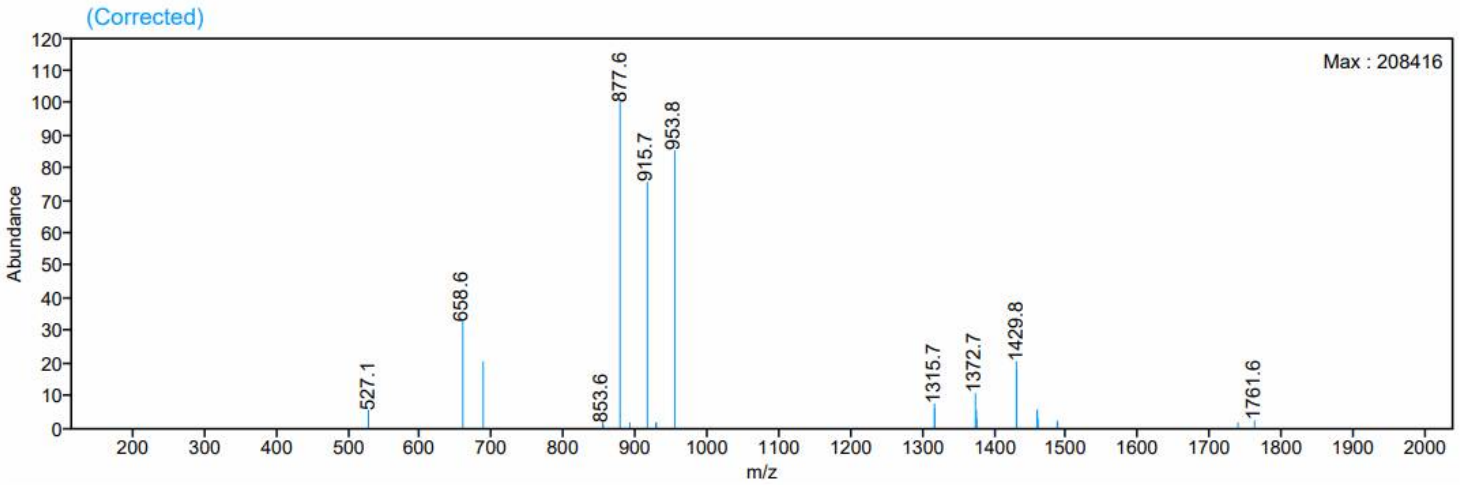

Figure S2-5. The mass spectrometry (MS) analysis of Guo-N6NH2.

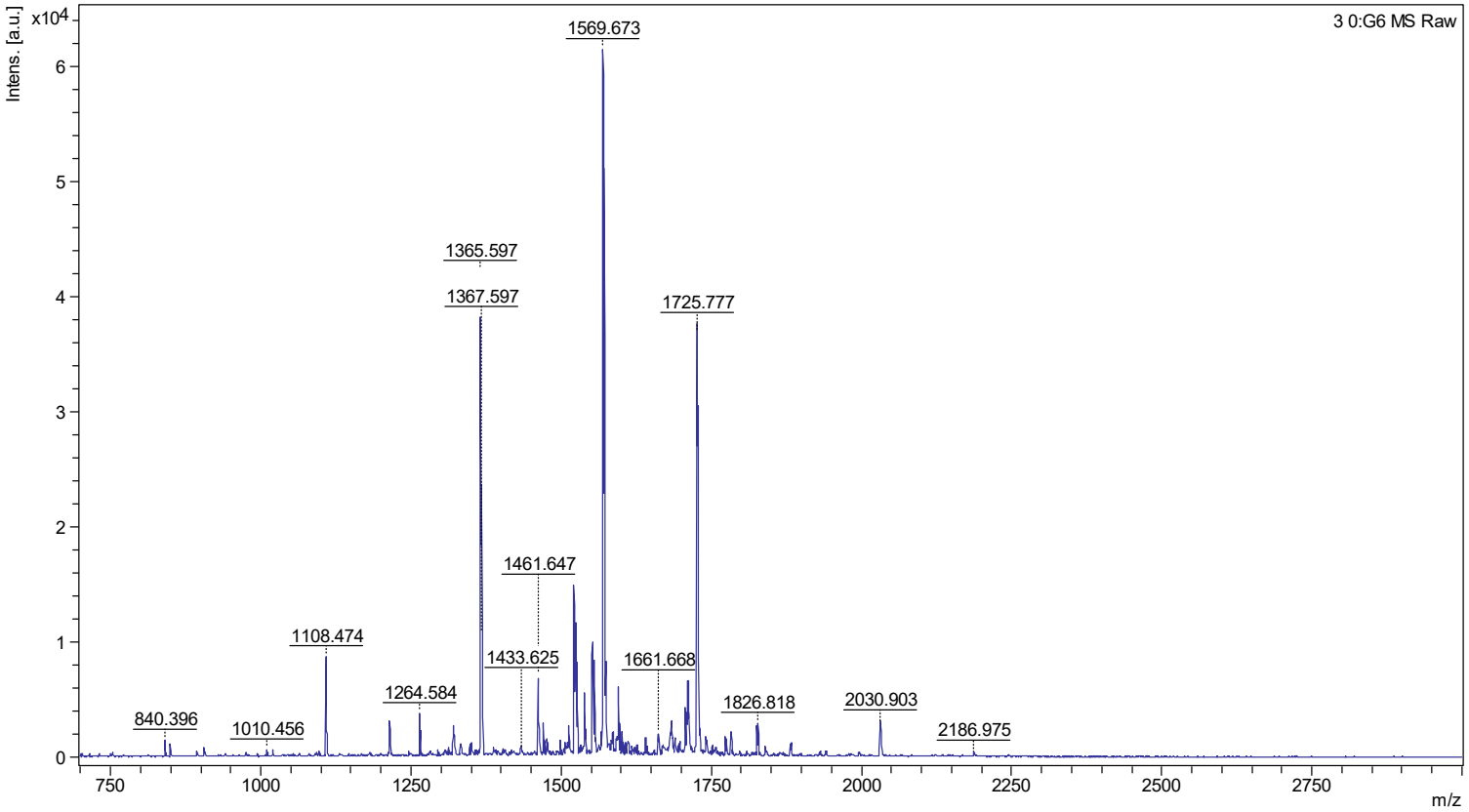

Figure S3. The mass spectrometry (MS) analysis of N6NH$_2$ treated by trypsin. It was confirmed by MALDI-TOF MS (Ultraflextreme, Brucker, Germany) at the Laboratory of Proteomics, Institute of Biophysics, Chinese Academy of Sciences.

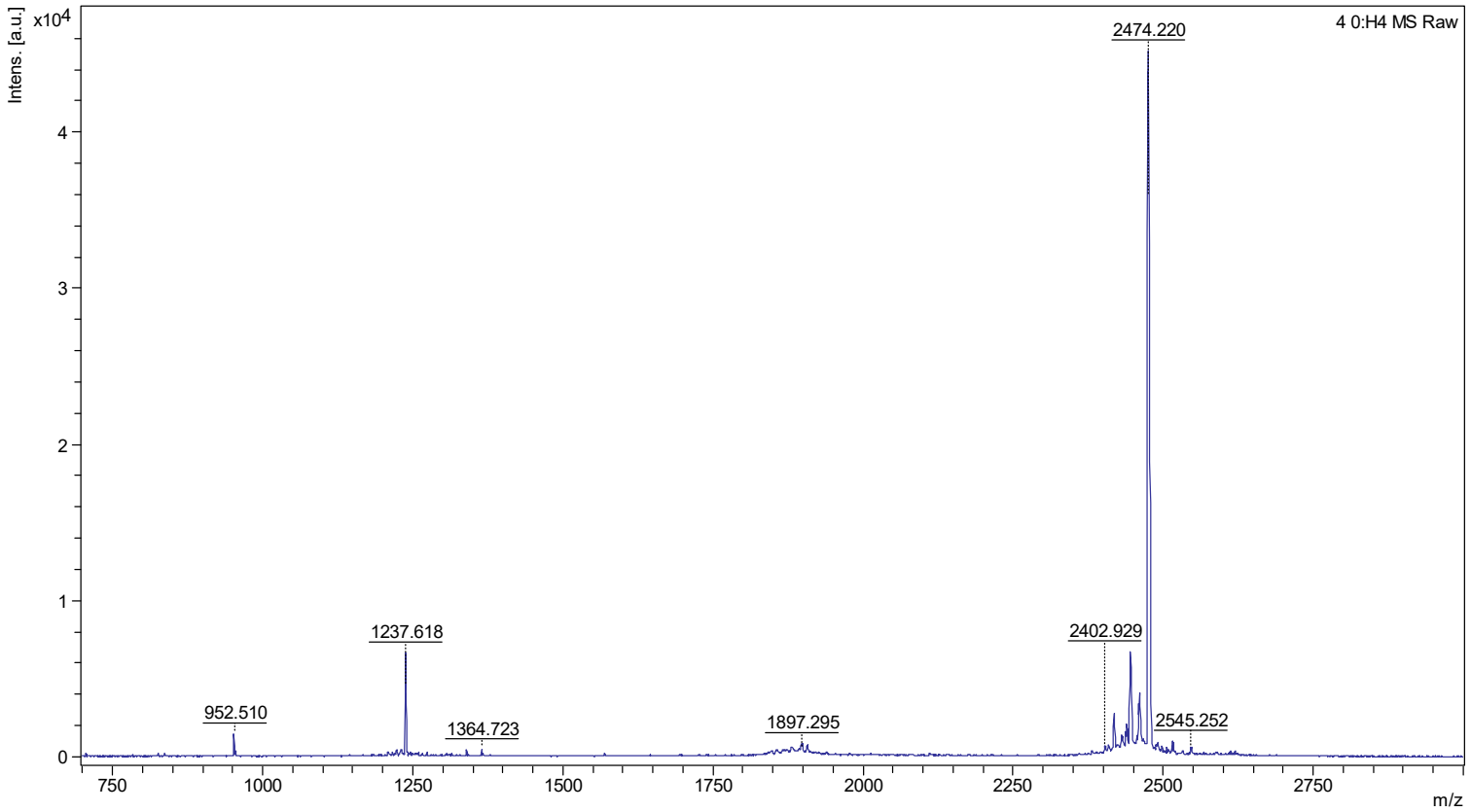

Figure S4. The MS analysis of DN6NH$_2$ treated by trypsin. It was confirmed by MALDI-TOF MS (Ultraflextreme, Brucker, Germany) at the Laboratory of Proteomics, Institute of Biophysics, Chinese Academy of Sciences.

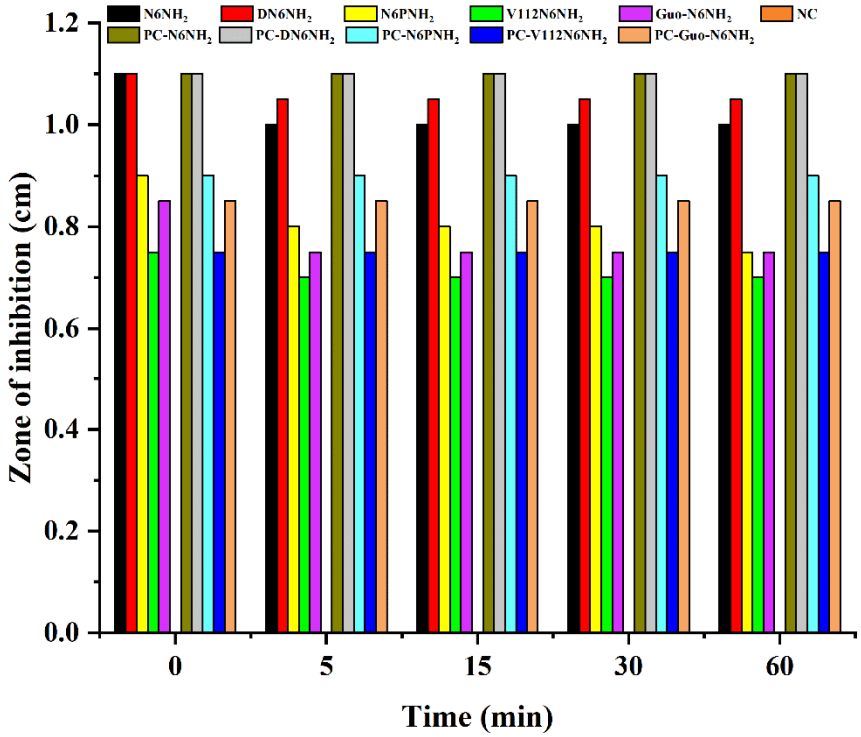

Figure S5. The stability of $N6NH_2$ analogues in simulated gastric fluid (SGF). NC, negative control; PC, positive control.

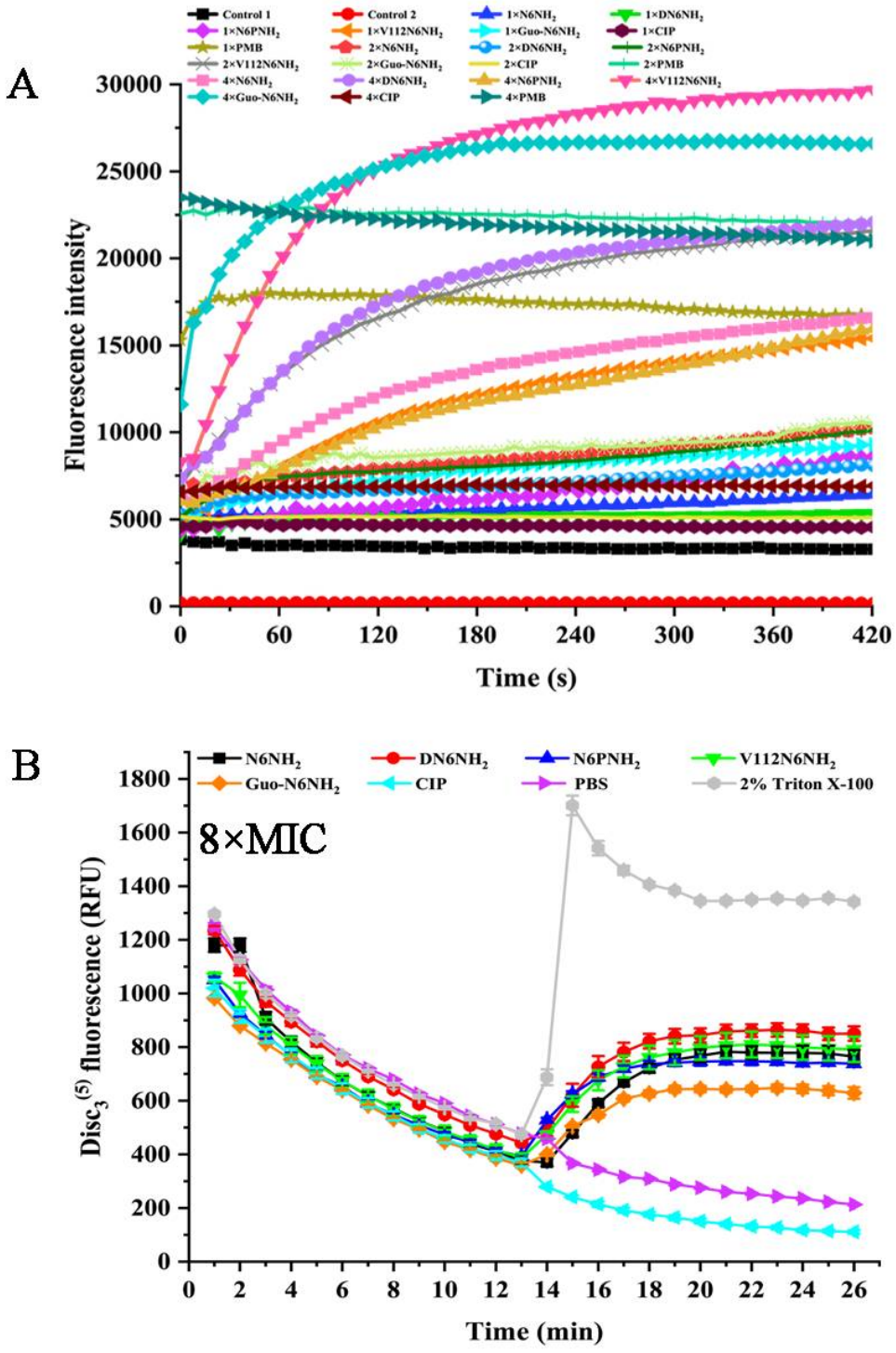

Figure S6-1. Interaction of $N6NH_2$ and its analogues with cell membrane. (**A**) $N6NH_2$ and its analogues outer membrane penetration test. (**B**) Effects of 8×MIC $N6NH_2$ and its analogues on bacterial cytoplasmic membrane potential.

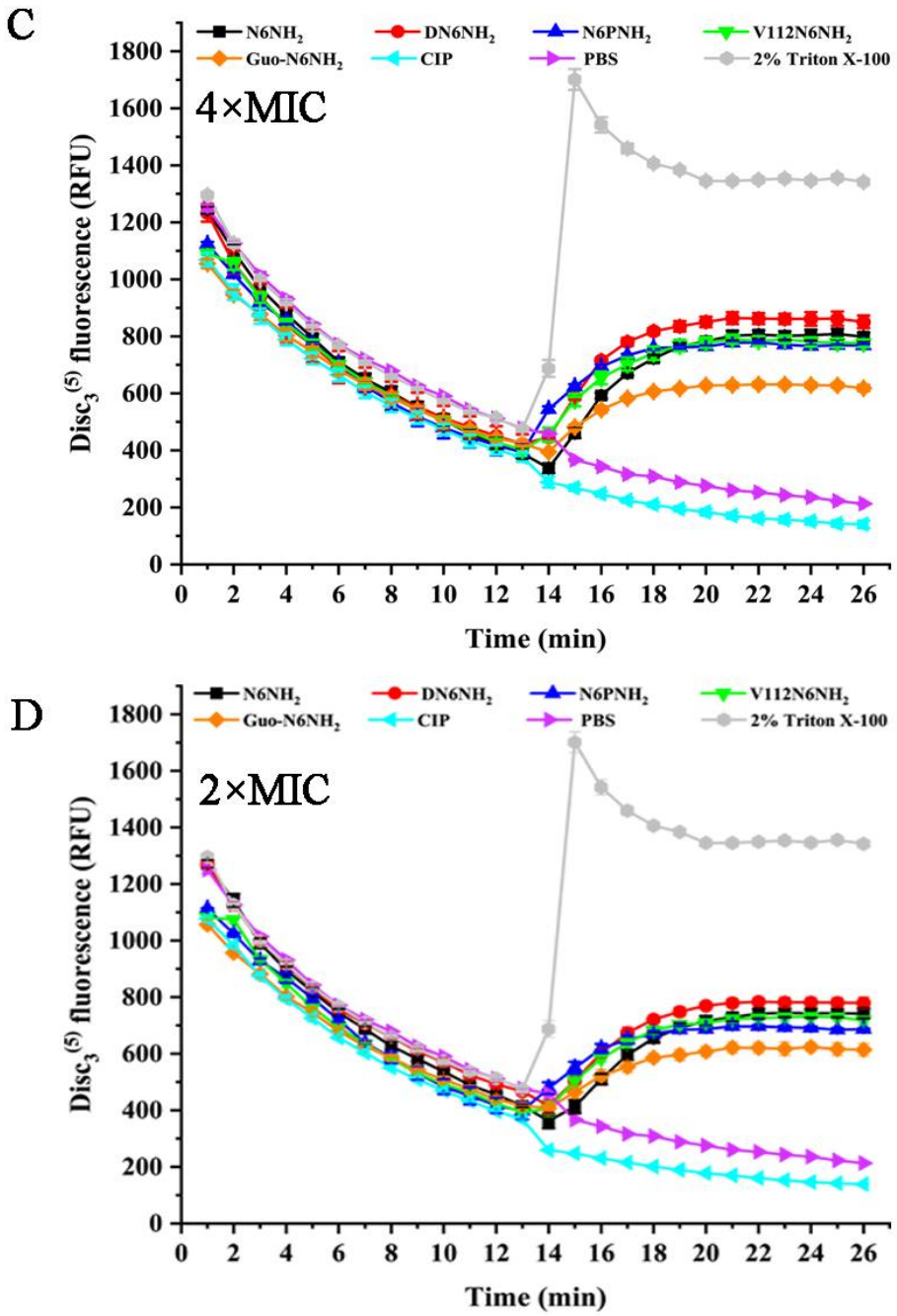

Figure S6-2. Interaction of $N6NH_2$ and its analogues with cell membrane. (**C-D**) Effects of 4×MIC or 2×MIC $N6NH_2$ and its analogues on bacterial cytoplasmic membrane potential.

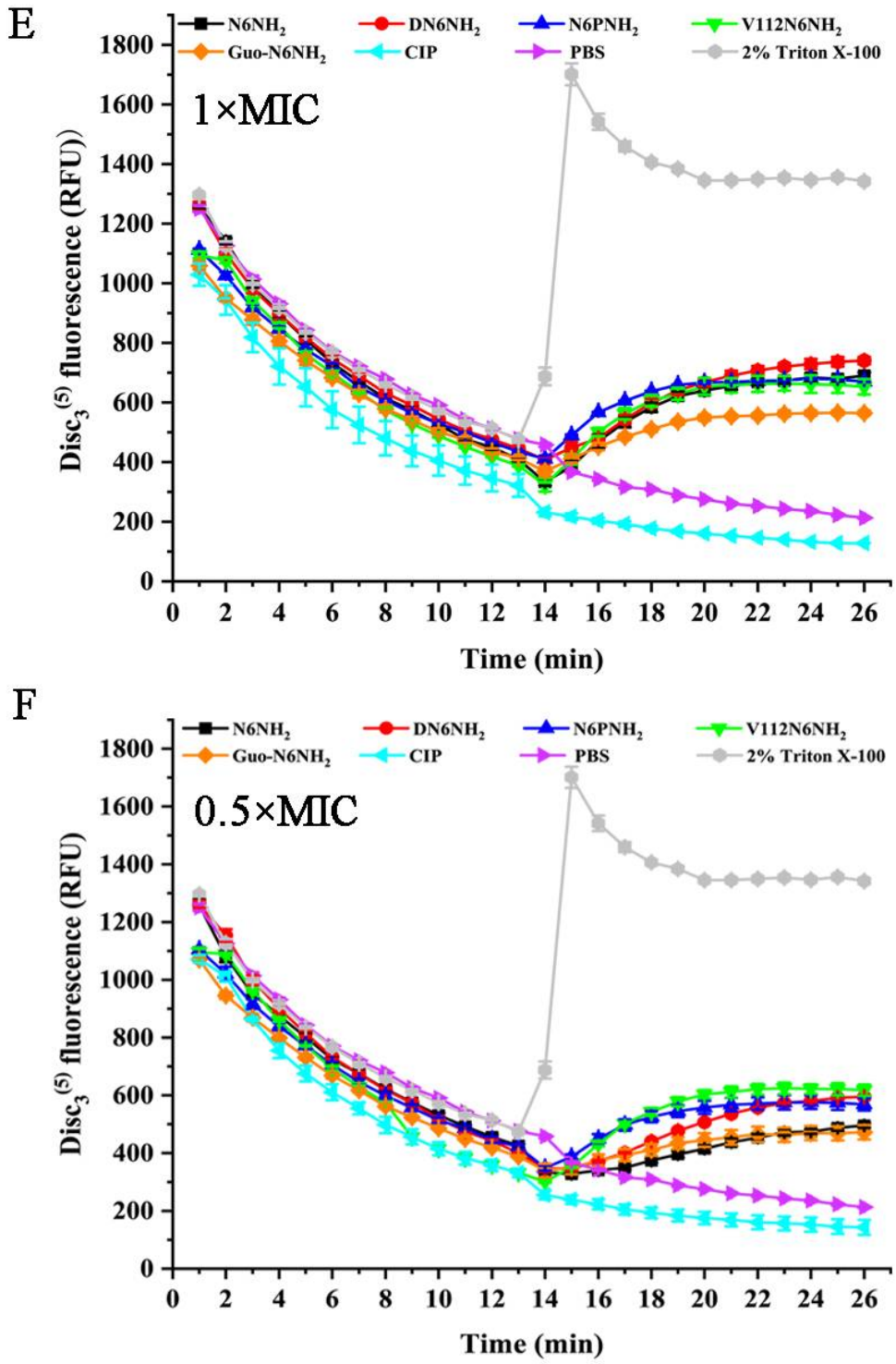

Figure S6-3. Interaction of $N6NH_2$ and its analogues with cell membrane. (**E-F**) Effects of 1×MIC or 0.5×MIC $N6NH_2$ and its analogues on bacterial cytoplasmic membrane potential.

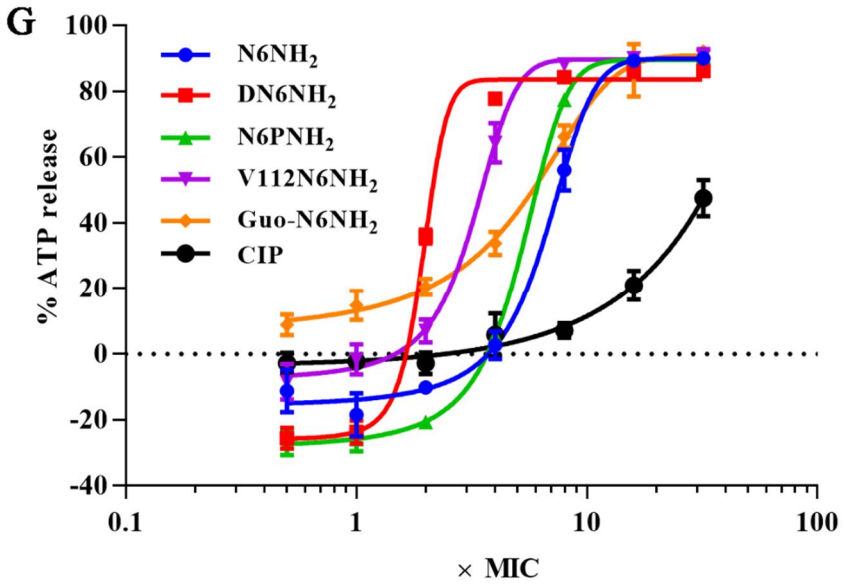

Figure S6-4. Interaction of $N6NH_2$ and its analogues with cell membrane. (**G**) Extracellular ATP release.

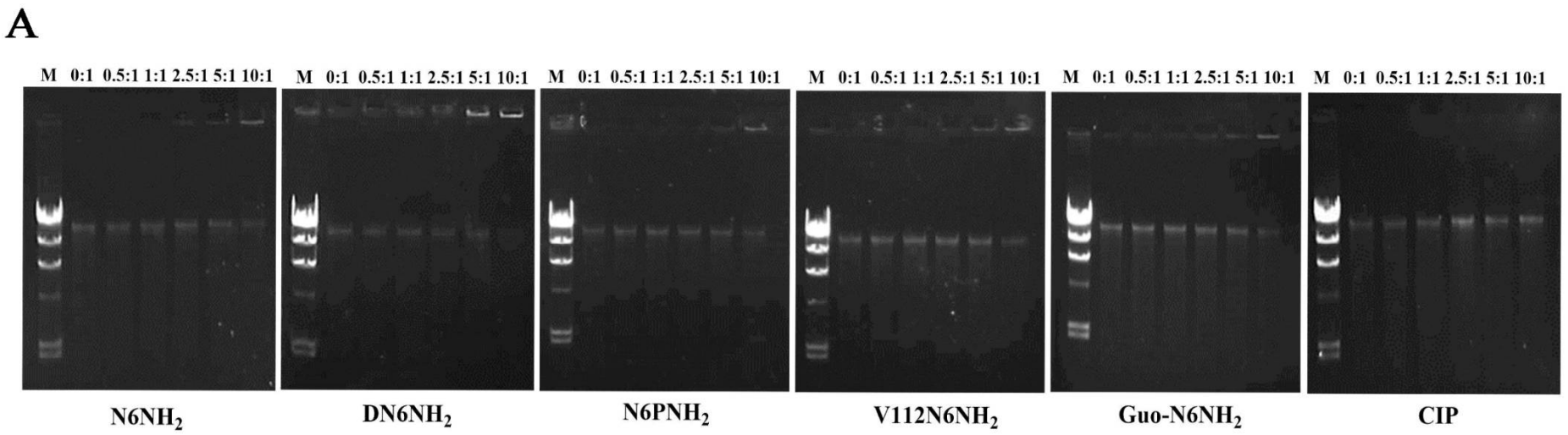

Figure S7-1. Interaction of $N6NH_2$ and its analogues with genomic DNA. (**A**) Gel block analysis of interaction between $N6NH_2$ analogues and genomic DNA of *A. veronii* ACCC61732.

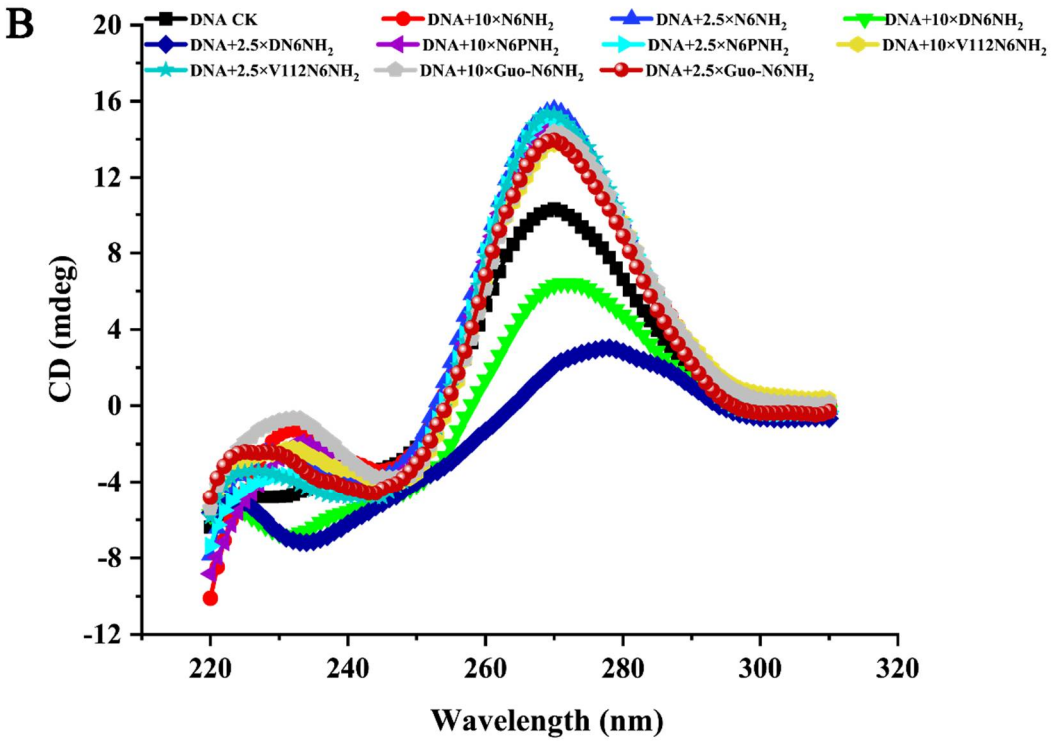

Figure S7-2. Interaction of $N6NH_2$ and its analogues with genomic DNA. (**B**) CD analysis of the effect of $N6NH_2$ and its analogues on DNA structure.

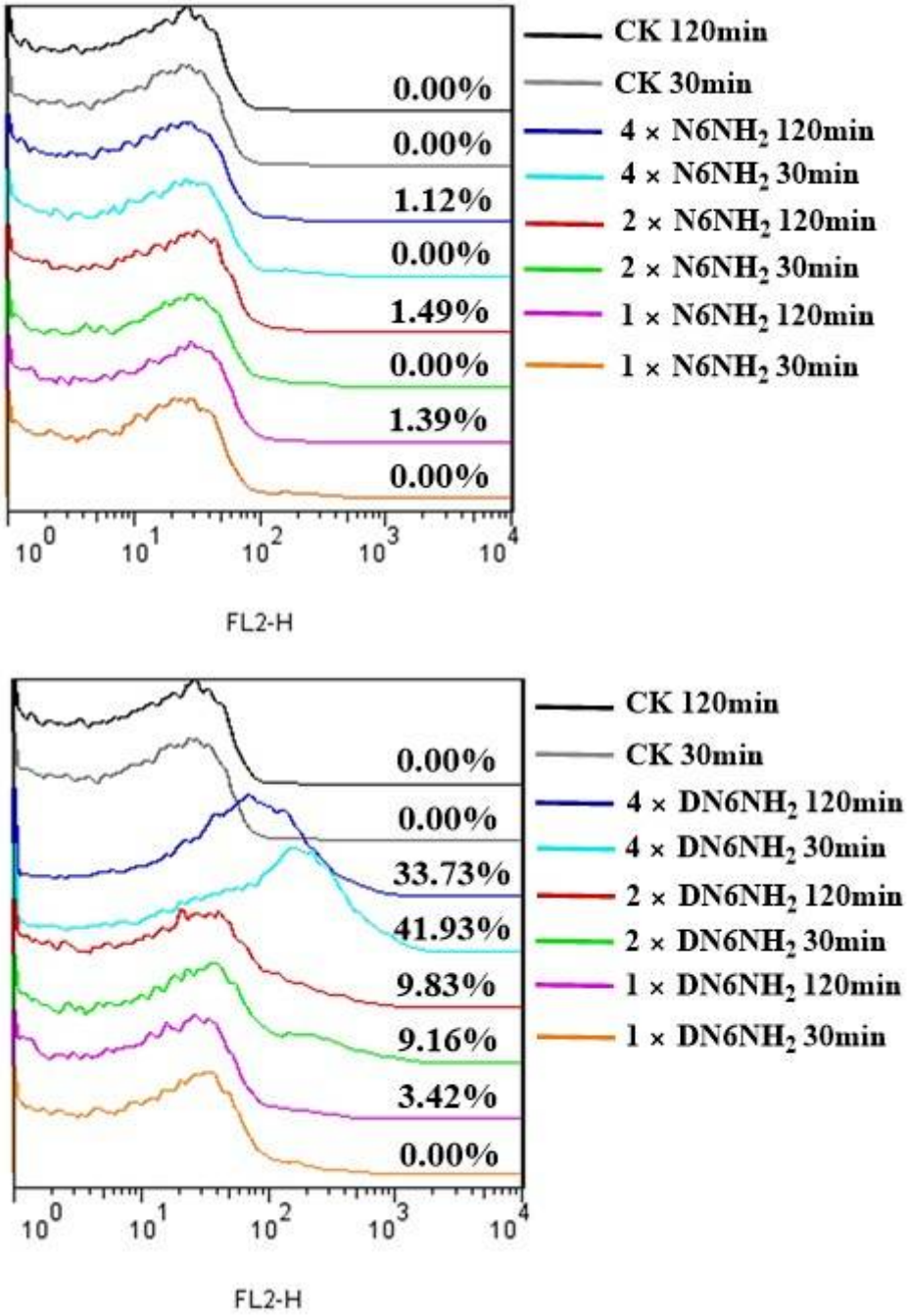

Figure S8-1. FACS analysis of the membrane penetration capacity of $N6NH_2$ and $DN6NH_2$ against *A. veronii* ACCC61732.

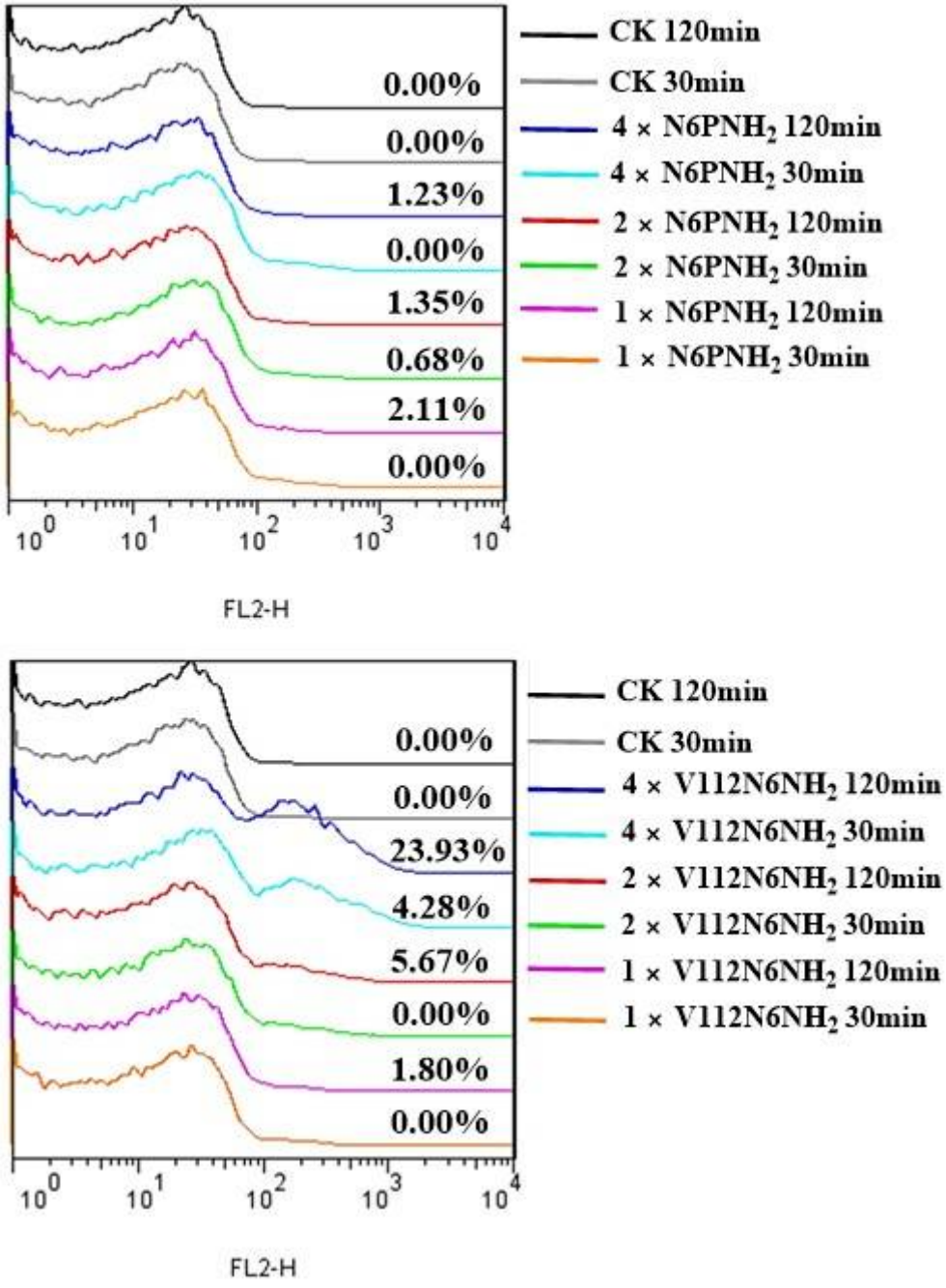

Figure S8-2. FACS analysis of the membrane penetration capacity of $N6PNH_2$ and $V112N6NH_2$ against *A. veronii* ACCC61732.

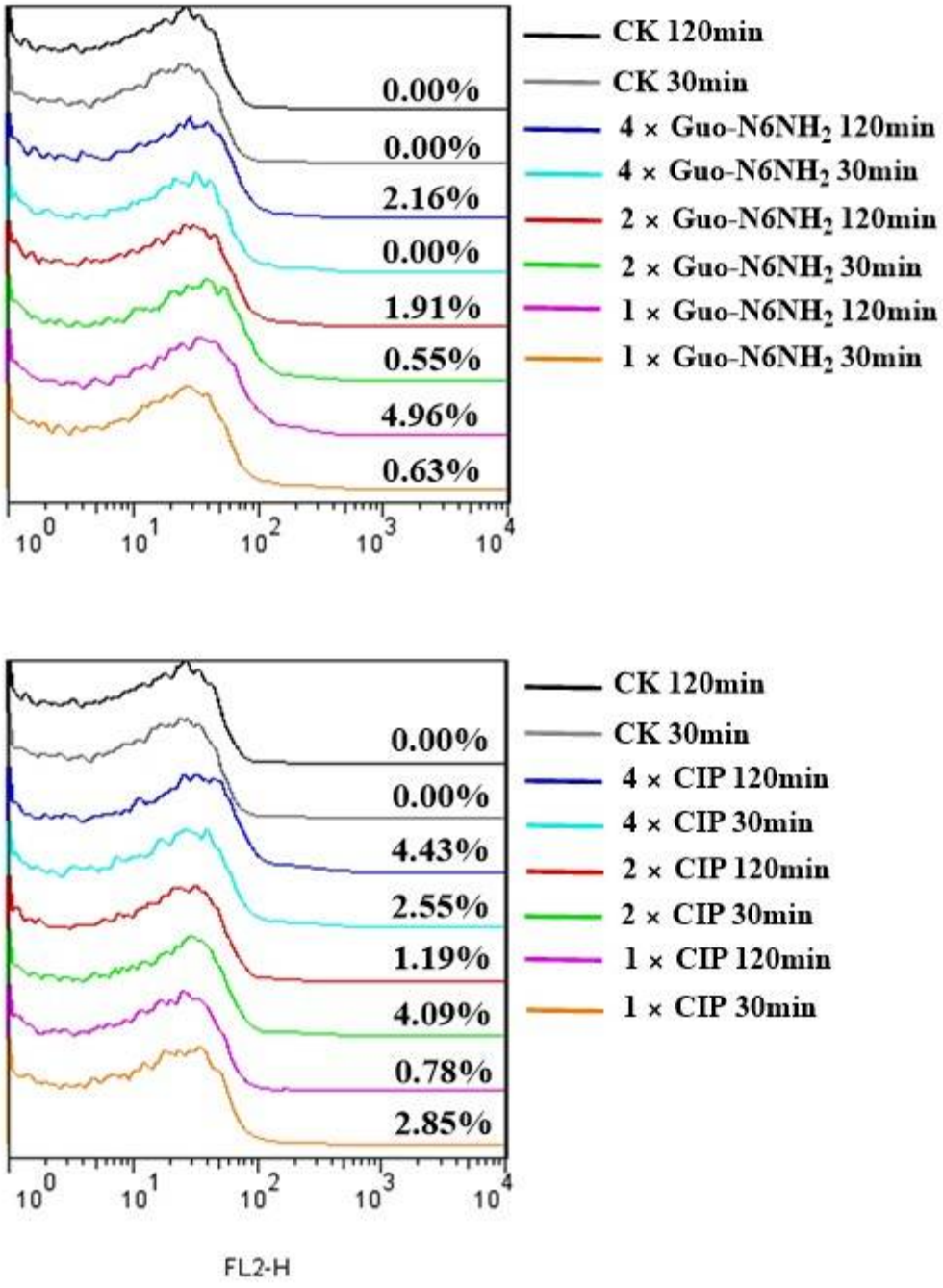

Figure S8-3. FACS analysis of the membrane penetration capacity of Guo-N6NH2 and CIP against *A. veronii* ACCC61732.

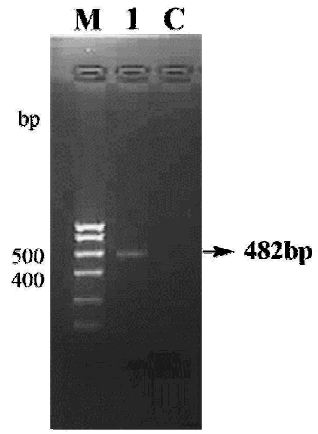

Figure S9. Identification of *vac* J gene of *A. veronii* ACCC61732. Lane M: *Trans* DNA Marker I. Lanes 1: *vac*J gene. Lane C: negative control.

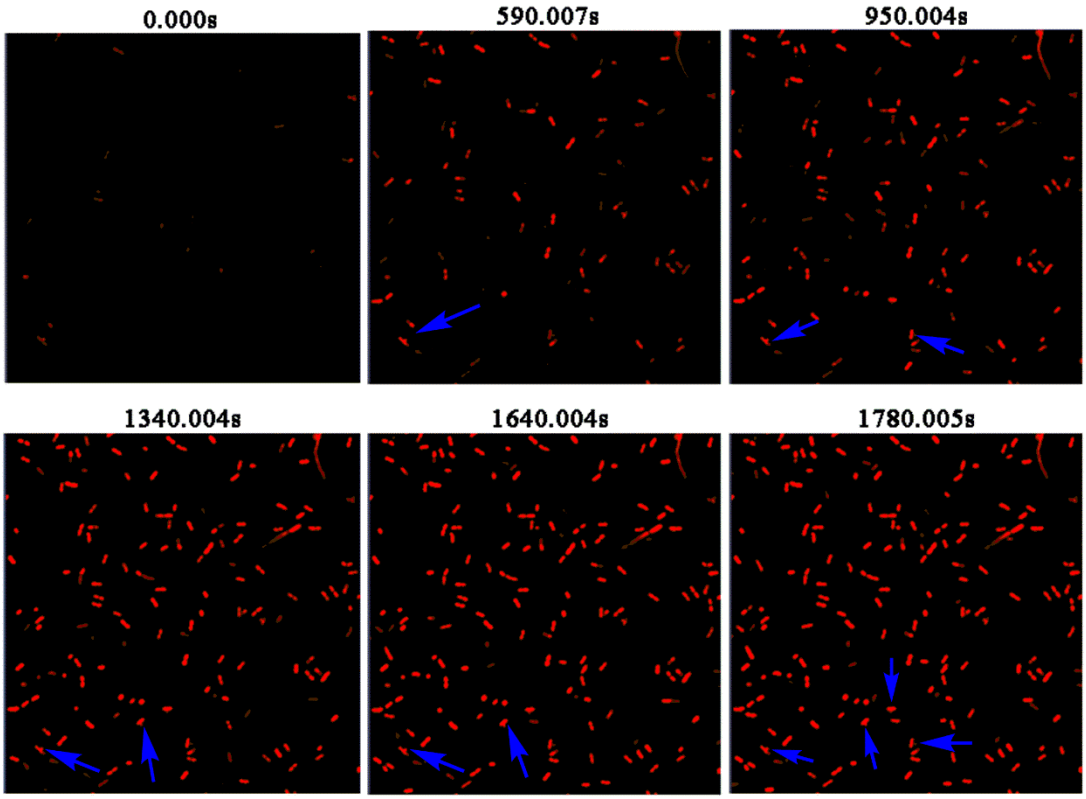

Figure S10. Outer membrane vesicles (OMVs) of *A. veronii* ACCC61732 treated with V112N6NH$_2$. The cells were observed using CLSM.

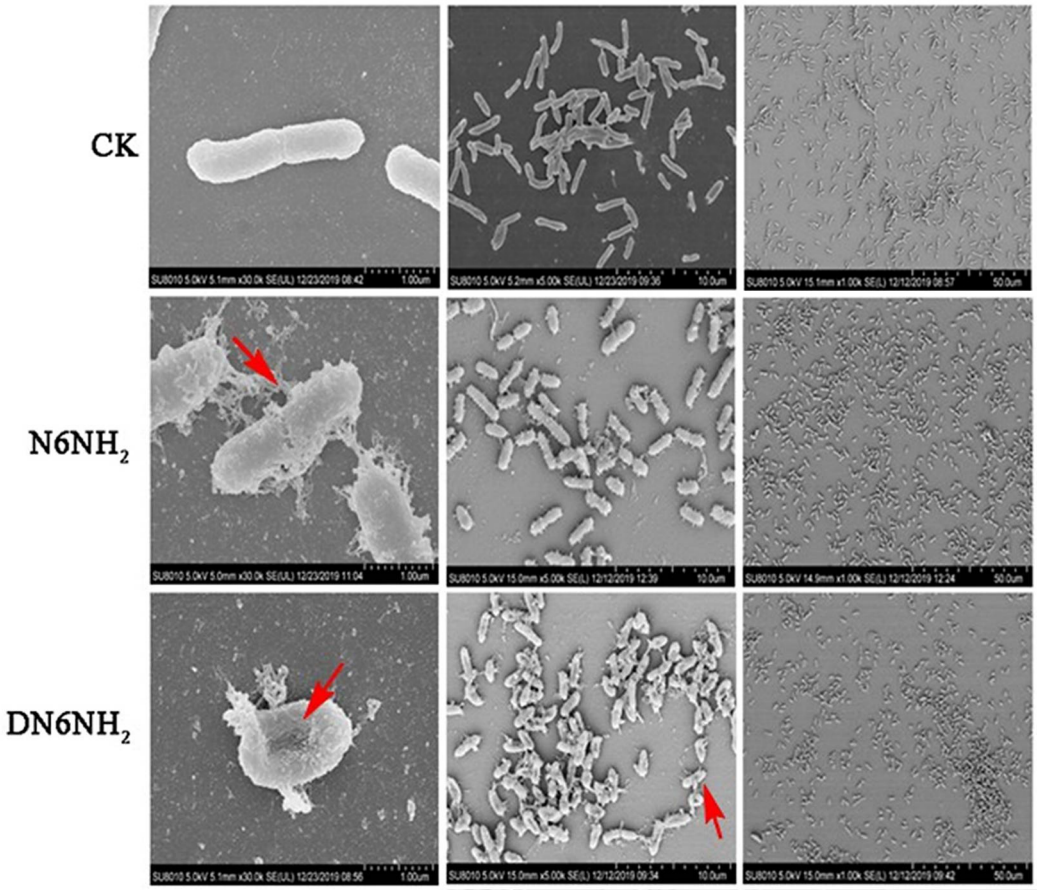

Figure S11-1. Effects of $N6NH_2$ or $DN6NH_2$ on biofilms of *A. veronii* ACCC61732 by using SEM.

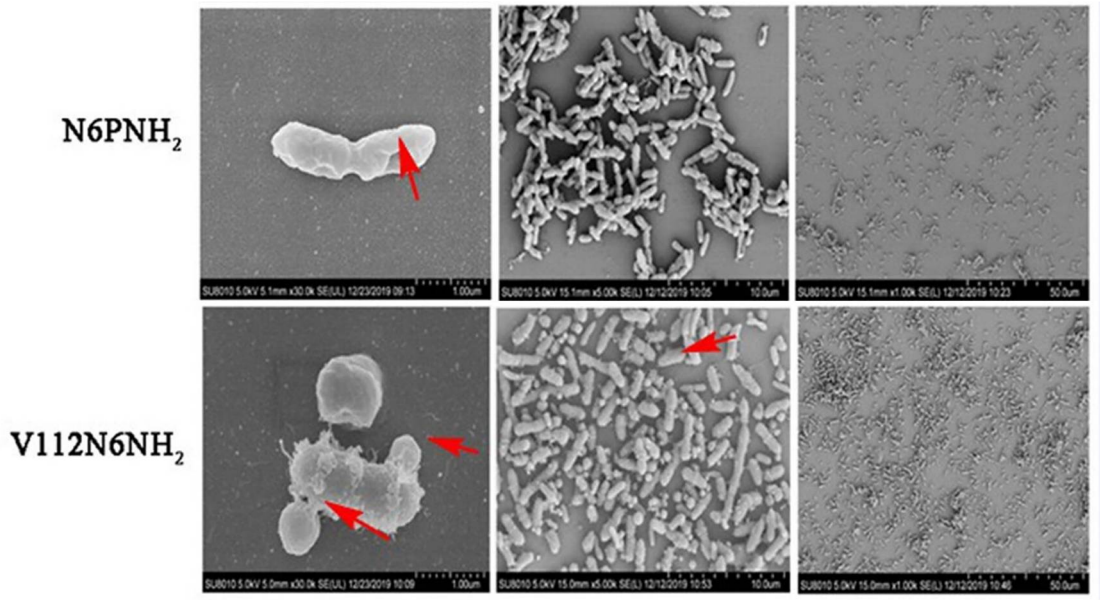

Figure S11-2. Effects of $N6PNH_2$ or $V112N6NH_2$ on biofilms of *A. veronii* ACCC61732 by using SEM.

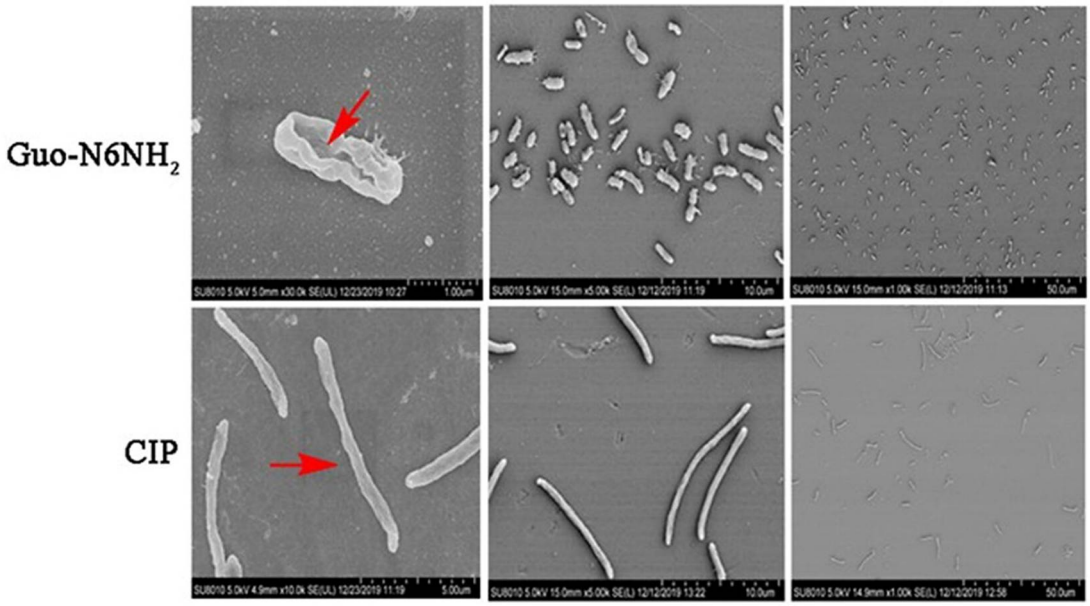

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Figure S11-3. Effects of Guo-N6NH$_2$ or CIP on biofilms of *A. veronii* ACCC61732 by using SEM.

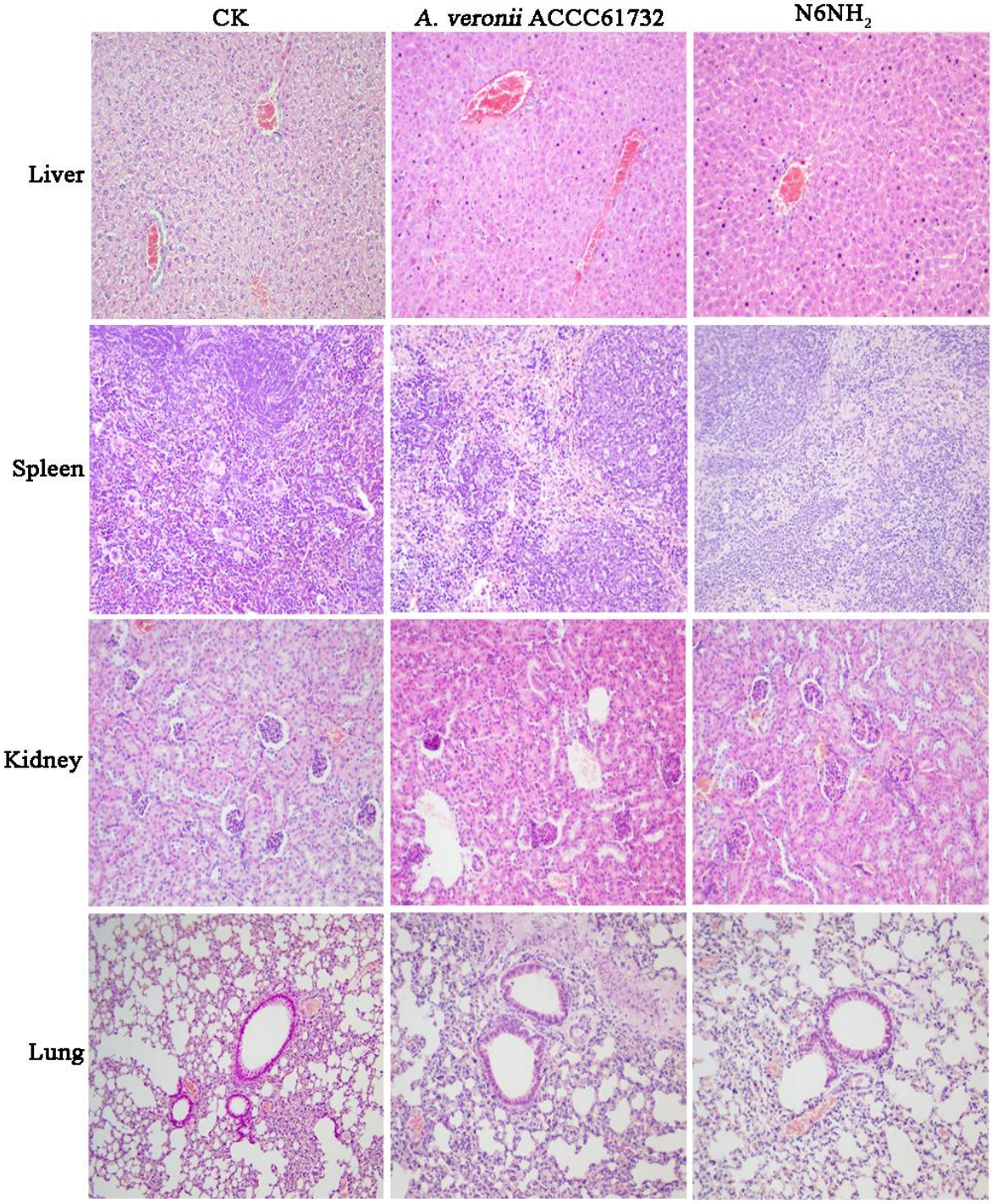

Figure S12-1. Effects of $N6NH_2$ and its analogues on organ injury in mice. Mice were infected intraperitoneally with *A. veronii* ACCC61732 (6×10^8 CFU/mL, 200 μL) and treated with $N6NH_2$ (5 μmol/kg). The livers, spleens, kidneys and lungs were harvested from mice sacrificed at 24 h after infection.

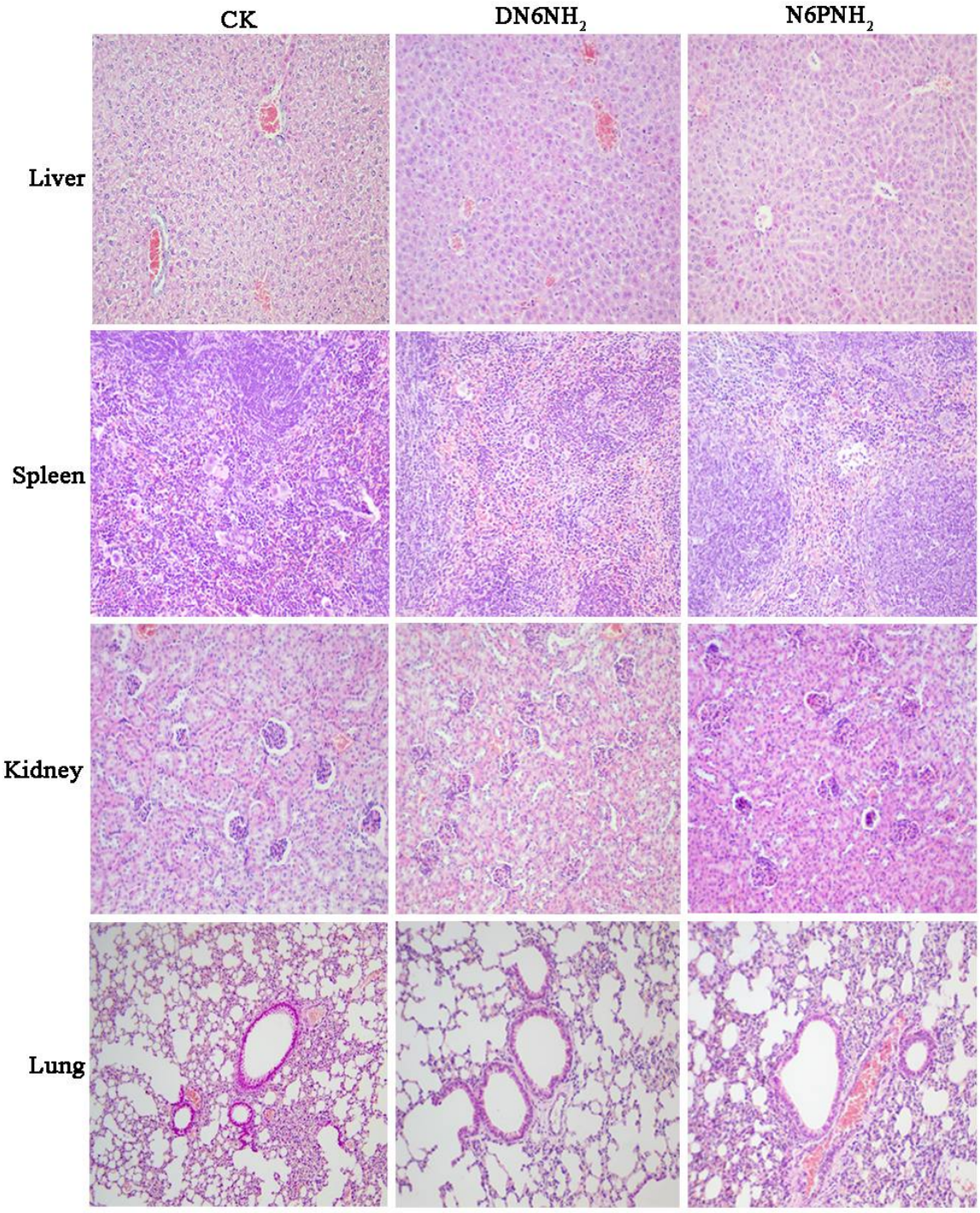

Figure S12-2. Effects of $N6NH_2$ and its analogues on organ injury in mice. Mice were infected intraperitoneally with *A. veronii* ACCC61732 (6×10^8 CFU/mL, 200 μL) and treated with $DN6NH_2$ and $N6PNH_2$ (5 μmol/kg). The livers, spleens, kidneys and lungs were harvested from mice sacrificed at 24 h after infection.

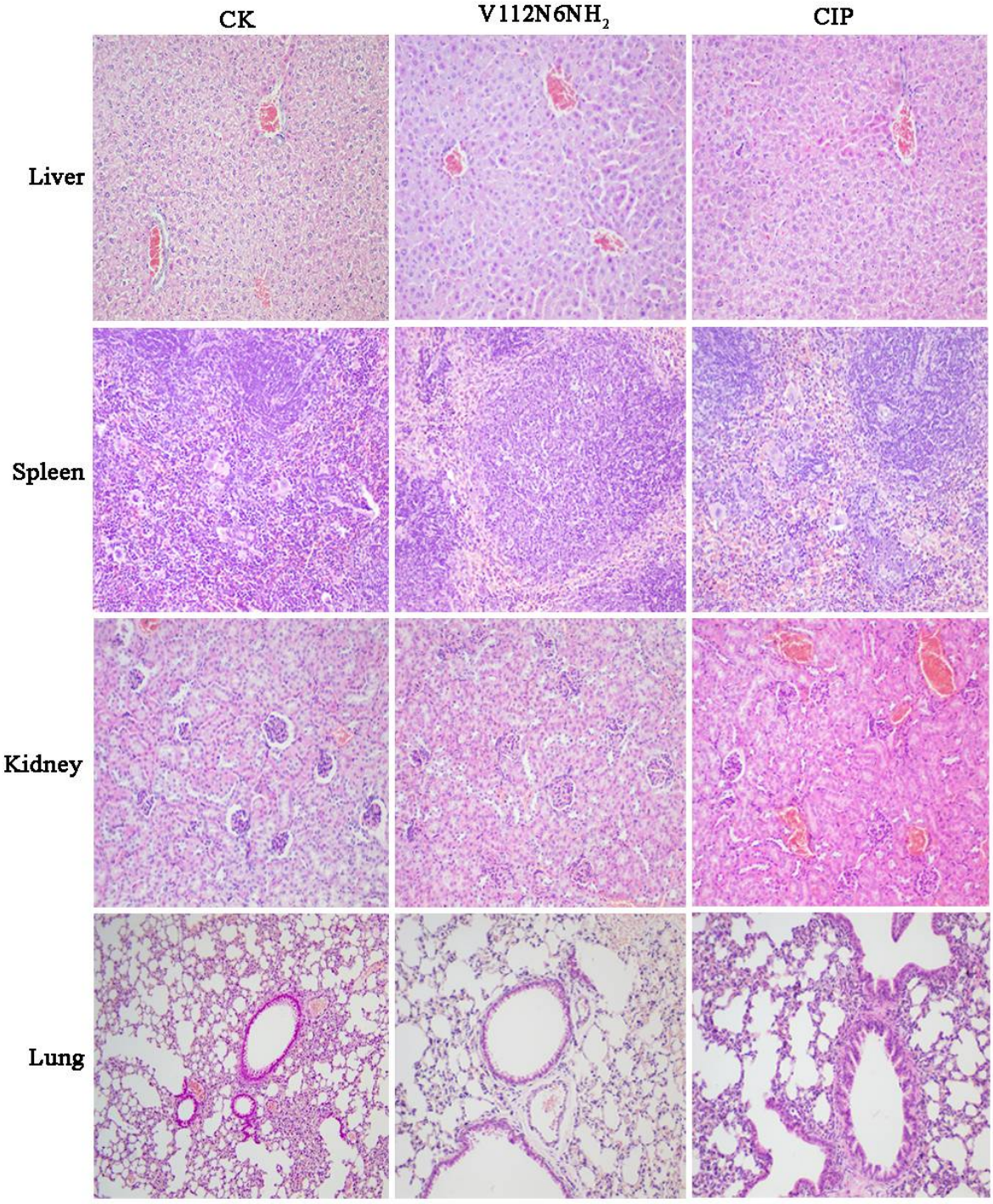

Figure S12-3. Effects of $N6NH_2$ and its analogues on organ injury in mice. Mice were infected intraperitoneally with *A. veronii* ACCC61732 (6×10^8 CFU/mL, 200 μL) and treated with $V112N6NH_2$ (5 μmol/kg) and CIP (1 μmol/kg). The livers, spleens, kidneys and lungs were harvested from mice sacrificed at 24 h after infection.

Table S1. Synergism of $N6NH_2$ analogues and antibiotics.

Combination	Variety	*A. veronii* ACCC61732			
		MIC[a] (μg/mL)	MIC[c] (μg/mL)	FIC	FICI
$N6NH_2$-CIP	$N6NH_2$+CIP	4+0.125	4+0.0078	1+ 0.0625	1.0625
$N6NH_2$-OFX	$N6NH_2$+OFX	4+0.25	4+0.0156	1+ 0.0625	1.0625
$N6NH_2$-NOR	$N6NH_2$ +NOR	4+0.5	4+0.5	1+1	2
$N6NH_2$-ENRO	$N6NH_2$+ENRO	4+0.25	4+0.25	1+1	2
$N6NH_2$-RIF	$N6NH_2$ +RIF	16+0.5	8+0.125	0.5+0.25	0.75[b]
$N6NH_2$-VAN	$N6NH_2$+VAN	16+16	16+1	1+0.0625	1.0625
$N6NH_2$-PMB	$N6NH_2$+PMB	16+8	8+2	0.25+0.25	0.5[a]
$N6NH_2$-STRE	$N6NH_2$+STRE	16+64	8+32	0.5+0.5	1[b]
$N6NH_2$-DOXY	$N6NH_2$+DOXY	16+1	8+0.5	0.5+0.5	1[b]
$N6NH_2$-KANA	$N6NH_2$+KANA	16+8	8+0.5	0.5+0.125	0.625[b]
$N6NH_2$-CHLO	$N6NH_2$+CHLO	16+0.25	16+0.0156	1+0.625	1.0625

Note: MIC[a] indicates the MIC of drug used alone; MIC[c] indicates the MIC of drug used in combination; [a]Synergic effect.; [b]Additive effect; CIP: ciprofloxacin; OFX: ofloxacin; NOR: norfloxacin; ENRO: enrofloxacin; RIF: rifampicin; VAN: vancomycin; PMB: polymyxin B; STRE: streptomycin sulfate; DOXY: doxycycline hyclate; KANA: kanamycin sulfate; CHLO: chloramphenicol.

Table S2. Synergism of $DN6NH_2$ and antibiotics.

Combination	Variety	*A. veronii* ACCC61732			
		MIC[a] (μg/mL)	MIC[c] (μg/mL)	FIC	FICI
$DN6NH_2$-CIP	$DN6NH_2$+CIP	4+0.125	4+0.0078	1+0.0625	1.0625
$DN6NH_2$-OFX	$DN6NH_2$+OFX	4+0.25	4+0.0078	1+0.0625	1.0625
$DN6NH_2$-NOR	$DN6NH_2$ +NOR	4+0.5	2+0.0625	0.5+0.125	0.625[b]
$DN6NH_2$-ENRO	$DN6NH_2$+ENRO	4+0.25	1+0.25	0.25+1	1.25
$DN6NH_2$-RIF	$DN6NH_2$ +RIF	4+0.5	2+0.25	0.5+0.5	1[b]
$DN6NH_2$-VAN	$DN6NH_2$+VAN	4+16	4+1	1+0.0625	1.0625
$DN6NH_2$-PMB	$DN6NH_2$+PMB	4+8	4+0.5	1+0.0625	1.0625
$DN6NH_2$-STRE	$DN6NH_2$+STRE	4+64	2+8	0.5+0.125	0.625[b]
$DN6NH_2$-DOXY	$DN6NH_2$+DOXY	4+1	4+0.0625	1+0.0625	1.0625
$DN6NH_2$-KANA	$DN6NH_2$+KANA	4+8	2+1	0.5+0.125	0.625[b]
$DN6NH_2$-CHLO	$DN6NH_2$+CHLO	4+0.25	4+0.0156	1+0.625	1.0625

Note: MIC[a] indicates the MIC of drug used alone; MIC[c] indicates the MIC of drug used in combination; [b]Additive effect; CIP: ciprofloxacin; OFX: ofloxacin; NOR: norfloxacin; ENRO: enrofloxacin; RIF: rifampicin; VAN: vancomycin; PMB: polymyxin B; STRE: streptomycin sulfate; DOXY: doxycycline hyclate; KANA: kanamycin sulfate; CHLO: chloramphenicol.

Table S3. Synergism of $N6PNH_2$ and antibiotics.

Combination	Variety	*A. veronii* ACCC61732			
		MIC[a] (μg/mL)	MIC[c] (μg/mL)	FIC	FICI
$N6PNH_2$-CIP	$N6PNH_2$+CIP	16+0.125	16+0.0078	1+0.0625	1.0625
$N6PNH_2$-OFX	$N6PNH_2$+OFX	16+0.25	16+0.0156	1+0.0625	1.0625
$N6PNH_2$-NOR	$N6PNH_2$ +NOR	16+0.5	16+0.0313	1+0.0625	1.0625
$N6PNH_2$-ENRO	$N6PNH_2$+ENRO	16+0.25	16+0.0156	1+0.0625	1.0625
$N6PNH_2$-RIF	$N6PNH_2$ +RIF	16+0.5	8+0.25	0.5+0.5	1[b]
$N6PNH_2$-VAN	$N6PNH_2$+VAN	16+16	16+1	1+0.0625	1.0625
$N6PNH_2$-PMB	$N6PNH_2$+PMB	16+8	8+4	0.5+0.5	1[b]
$N6PNH_2$-STRE	$N6PNH_2$+STRE	16+64	16+4	1+0.0625	1.0625
$N6PNH_2$-DOXY	$N6PNH_2$+DOXY	16+1	16+0.0625	1+0.0625	1.0625
$N6PNH_2$-KANA	$N6PNH_2$+KANA	16+8	16+0.5	1+0.0625	1.0625
$N6PNH_2$-CHLO	$N6PNH_2$+CHLO	16+0.25	16+0.0156	1+0.625	1.0625

Note: MIC[a] indicates the MIC of drug used alone; MIC[c] indicates the MIC of drug used in combination; [b]Additive effect; CIP: ciprofloxacin; OFX: ofloxacin; NOR: norfloxacin; ENRO: enrofloxacin; RIF: rifampicin; VAN: vancomycin; PMB: polymyxin B; STRE: streptomycin sulfate; DOXY: doxycycline hyclate; KANA: kanamycin sulfate; CHLO: chloramphenicol.

Table S4. Synergism of $V112N6NH_2$ and antibiotics.

Combination	Variety	*A. veronii* ACCC61732			
		MIC[a] (μg/mL)	MIC[c] (μg/mL)	FIC	FICI
$V112N6NH_2$-CIP	$V112N6NH_2$+CIP	16+0.125	16+0.0078	1+0.0625	1.0625
$V112N6NH_2$-OFX	$V112N6NH_2$+OFX	16+0.25	16+0.0156	1+0.0625	1.0625
$V112N6NH_2$-NOR	$V112N6NH_2$ +NOR	16+0.5	16+0.0625	1+0.125	1.125
$V112N6NH_2$-ENRO	$V112N6NH_2$+ENRO	16+0.25	16+0.0156	1+0.0625	1.0625
$V112N6NH_2$-RIF	$V112N6NH_2$ +RIF	16+0.0625	16+0.0313	1+0.0625	1.0625
$V112N6NH_2$-VAN	$V112N6NH_2$+VAN	16+16	16+1	1+0.0625	1.0625
$V112N6NH_2$-PMB	$V112N6NH_2$+PMB	16+8	1+4	0.0625+0.5	0.5625[b]
$V112N6NH_2$-STRE	$V112N6NH_2$+STRE	16+64	16+4	1+0.0625	1.0625
$V112N6NH_2$-DOXY	$V112N6NH_2$+DOXY	16+1	16+0.0625	1+0.0625	1.0625
$V112N6NH_2$-KANA	$V112N6NH_2$+KANA	16+8	16+0.5	1+0.0625	1.0625
$V112N6NH_2$-CHLO	$V112N6NH_2$+CHLO	16+0.25	16+0.0156	1+0.0156	1.0625

Note: MIC[a] indicates the MIC of drug used alone; MIC[c] indicates the MIC of drug used in combination; [b]Additive effect; CIP: ciprofloxacin; OFX: ofloxacin; NOR: norfloxacin; ENRO: enrofloxacin; RIF: rifampicin; VAN: vancomycin; PMB: polymyxin B; STRE: streptomycin sulfate; DOXY: doxycycline hyclate; KANA: kanamycin sulfate; CHLO: chloramphenicol.

Table S5. Synergism of Guo-N6NH$_2$ and antibiotics.

Combination	Variety	*A. veronii* ACCC61732			
		MIC[a] (μg/mL)	MIC[c] (μg/mL)	FIC	FICI
Guo-N6NH$_2$-CIP	Guo-N6NH$_2$+CIP	8+0.125	8+0.0078	1+0.0625	1.0625
Guo-N6NH$_2$-OFX	Guo-N6NH$_2$+OFX	8+0.25	8+0.0156	1+0.0625	1.0625
Guo-N6NH$_2$-NOR	Guo-N6NH$_2$ +NOR	8+0.5	4+0.25	0.5+0.5	1[b]
Guo-N6NH$_2$-ENRO	Guo-N6NH$_2$+ENRO	8+0.25	8+0.0156	1+ 0.0625	1.0625
Guo-N6NH$_2$-RIF	Guo-N6NH$_2$ +RIF	16+0.5	8+0.25	0.5+0.5	1[b]
Guo-N6NH$_2$-VAN	Guo-N6NH$_2$+VAN	16+16	16+1	1+0.0625	1.0625
Guo-N6NH$_2$-PMB	Guo-N6NH$_2$+PMB	16+8	4+2	0.25+0.25	0.5[a]
Guo-N6NH$_2$-STRE	Guo-N6NH$_2$+STRE	16+64	8+32	0.5+ 0.5	1[b]
Guo-N6NH$_2$-DOXY	Guo-N6NH$_2$+DOXY	16+1	16+0.0625	1+ 0.0625	1.0625
Guo-N6NH$_2$-KANA	Guo-N6NH$_2$+KANA	16+8	16+0.5	1+0.0625	1.0625
Guo-N6NH$_2$-CHLO	Guo-N6NH$_2$+CHLO	16+0.25	16+0.0156	1+ 0.625	1.0625

Note: MIC[a] indicates the MIC of drug used alone; MIC[c] indicates the MIC of drug used in combination; [a]Synergic effect.; [b]Additive effect; CIP: ciprofloxacin; OFX: ofloxacin; NOR: norfloxacin; ENRO: enrofloxacin; RIF: rifampicin; VAN: vancomycin; PMB: polymyxin B; STRE: streptomycin sulfate; DOXY: doxycycline hyclate; KANA: kanamycin sulfate; CHLO: chloramphenicol.

Table S6. MIC values of N6NH2 and its analogues against *A. veronii* ACCC61732 under different conditions.

Peptide	Control[a]	Temperature (°C)						pH value					Physiological salt (mM)						Enzyme		
		4	20	40	60	80	100	2	4	6	8	10	50	100	200	300	400	500	Pepsin	Trypsin	Proteinase K
N6NH$_2$	4	4	4	4	4	4	8	4	4	4	4	4	4	4	8	8	8	8	4	> 128	> 128
DN6NH$_2$	4	4	4	4	4	4	8	2	2	4	4	4	4	4	4	4	4	4	4	4	4
N6PNH$_2$	16	16	16	16	16	16	32	8	16	16	8	8	8	8	16	16	16	32	16	> 128	> 128
V112N6NH$_2$	16	16	16	16	16	16	32	16	16	16	16	8	8	16	16	16	32	32	16	> 128	> 128
Guo-N6NH$_2$	8	8	8	8	8	8	16	8	8	8	4	4	8	8	8	8	8	16	8	> 128	> 128

Note: [a] The control MIC values were determined in the absence of these temperature, acid and alkali, physiological salt, and enzyme condition.

Table S7. Effects of $N6NH_2$ and its analogues on inner membrane of *A. veronii* ACCC61732.

Peptides	Time (h)	Permeability (%)		
		1 × MIC	2 × MIC	4 × MIC
$N6NH_2$	0.5	0	0	0
	2	1.39	1.49	1.12
$DN6NH_2$	0.5	0	9.16	41.93
	2	3.42	9.83	33.73
$N6PNH_2$	0.5	0	0.68	0
	2	2.11	1.35	1.23
V112N6NH2	0.5	0	0	4.28
	2	1.8	5.67	23.93
Guo-N6NH2	0.5	0.63	0.55	0
	2	4.96	1.91	2.16
CIP	0.5	2.85	4.09	2.55
	2	0.78	1.19	4.43

Table S8. Primers of the *vacJ* gene.

Primer	Sequence (5'→3')	Product (bp)
*vacJ*F	AGTGGTACATGCCTATGC	482
*vacJ*R	GGTAGAAGTCCTTGGTCAG	