

Supplementary Materials

# Antimicrobial Peptides Can Generate Tolerance by Lag and Interfere with Antimicrobial Therapy

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**Table S1.** MICs in *E. coli* wild type and PolB resistant strain. MIC values are in  $\mu$ M.

Peptide/Strain	<i>E. coli</i> wt	PolB
Pleurocidin	0.06	0.06
Polymyxin B	0.01	> 0.2
Dermaseptin	2	2
LL-37	3	3

**Table S2.** MICs in *E. coli* wild type and evolved. MIC values are in  $\mu$ M.

Antibiotic	<i>E. coli</i> wt	PolB	Pleu	LL-37	DMS
Ampicillin	17	17	17	17	17
Kanamycin	1.4	1.4	1.4	1.4	2.8
Ciprofloxacin	42	42	42	42	42
Nalidixic Acid	11	11	11	11	11

**Table S3.** Summary of relevant mutations in Pleu and LL-37 evolved strains.

Gene	Treatment	Position	Reference Sequence	Mutation	Reference (Sequencing Bioproject)
yejK-yejL (b2186 -b2187)	Pleu	2284069	GA	G	--
		66527	C	A	--
araD (b0061)		66530	G	GCGACCGAGAC	--
				C / GCGCCCGAGAC CCGCA	
gltP (b4077)		4296267	GCATCCGACATCAACGCCTGATGCGACGC TTAACGCGTCTTATCAGGCCTACGCCAGA CAGCGCAATAGCCTGATTAGCGTGATTTT GTAGGTCGGATAAGGCGTTTA	G	PRJNA476486
		4296272	ATGC	A	--
		4296060	C	T	PRJNA747892
mlaC (b3192)		3337787	CG	C	--
mlaF (b3195)		3339509	A	C	--
rhaD (b3902)		4093986	T	G	--
		4093989	A	ACGCATGCGGAT	--
				C	
sspA (b3229)		3377363	T	TG	--
glcE (b4468)		3125885	A	G	--
hcr-hcp (b0872-b0873)		912151	C	T	--
	66535	T	A	--	
araD (b0061)	66540	T	G	--	
	66541	C	T	--	
gltP (b4077)	4296267	GCATCCGACATCAACGCCTGATGCGACGC TTAACGCGTCTTATCAGGCCTACGCCAGA	G	PRJNA476486	

		CAGCGCAATAGCCTGATTTAGCGTGATTTT GTAGGTCGGATAAAGGCGTTTA		
	4296272	ATGC	A	--
		CCGCGTCTTATCAGGCCTACGCCAGACAG		
	4296078	CGCAATAGCCTGATTTAGCGTGATTTTGTA GGTCGGATAAAGGCGTTTATGCCGCATCCG ACATCAACGCCTGATGCGACGCTTAA GGGGTGATTAGCTCAGCTGGGAGAGCACC TCCCTTACAAGGAGGGGGTCGGCGGTTTCG	C	PRJNA663118
<b>valU (b2401)</b>	2520930	ATCCCGTCATCACCCACCAACTACTTTATG TAGTCTCCGCCGTGTAGCAAGAAATTGAG	G	PRJNA758726
		AAGT		
<b>mhpC (b0349)</b>	371761	G	GTAGATTT	
	371760	G	T	
			AGTCATACTTTT	
<b>flhD – insB1 (b1892-b1893)</b>	1978507	A	GTTTT	
	1978503	G	T	
	1978504	G	A	
	1299499	G	A	
<b>ychE (b1242)</b>	1299500	G	T	
	1299502	A	ATAATCAATTGT TAAATTATT	
<b>emrY (b2367)</b>	2481016	T	G	