

Activity of the novel engineered antimicrobial peptide PLG0206 against staphylococci and enterococci

David Huang¹, Jonathan Steckbeck¹, Dean Shinabarger², Ian Morrissey³, Stephen Hawser⁴, ¹Peptilogics, Pittsburgh, PA, USA.; ²Microbiologics, Kalamazoo, MI, USA; ³Antimicrobial Focus, Sawbridgeworth, UK; ⁴IHMA Europe, Monthey, Switzerland



INTRODUCTION

- PLG0206 is an investigational, engineered cationic antimicrobial peptide designed to overcome the shortcomings of other natural AMPs, such as toxicity and limited activity (1,2). PLG0206 has recently been shown to be well tolerated and safe when administered i.v. in a Phase 1 study (3). The initial proposed indication for this peptide is the treatment of periprosthetic joint infections via irrigation due to a broad spectrum of activity and anti-biofilm properties.
- This study evaluated the activity of PLG0206 and comparator antimicrobials against staphylococci and enterococci, causes of periprosthetic joint infections, from the IHMA repository of isolates collected from various world-wide locations in 2019.

MATERIALS AND METHODS

- Isolates tested included *Enterococcus faecalis* (77), *E. faecium* (75), methicillin-resistant *Staphylococcus aureus* (MRSA, 180), methicillin-susceptible *S. aureus* (MSSA, 121) and 152 coagulase-negative staphylococci (CoNS) comprised of *S. epidermidis* (113), *S. haemolyticus* (31), *S. hominis* (4), *S. lugdunensis* (1), *S. saprophyticus* (2) and *S. simulans* (1).
- Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution methodology (4) in cation-adjusted Mueller Hinton broth (CA-MHB), except for PLG0206 which was tested in MOPS RPMI-1640 medium supplemented with 0.002% Tween-80 due to precipitation of PLG0206 observed in CA-MHB.
- The susceptibility of comparators was determined using the 2022 CLSI breakpoints (5). Multi-drug-resistance (MDR) was defined as resistance to 3 or more of the following antimicrobials: azithromycin, clindamycin, daptomycin, doxycycline, levofloxacin, penicillin and vancomycin.

FIGURE 1. Geographical location of the enterococci and staphylococci tested.

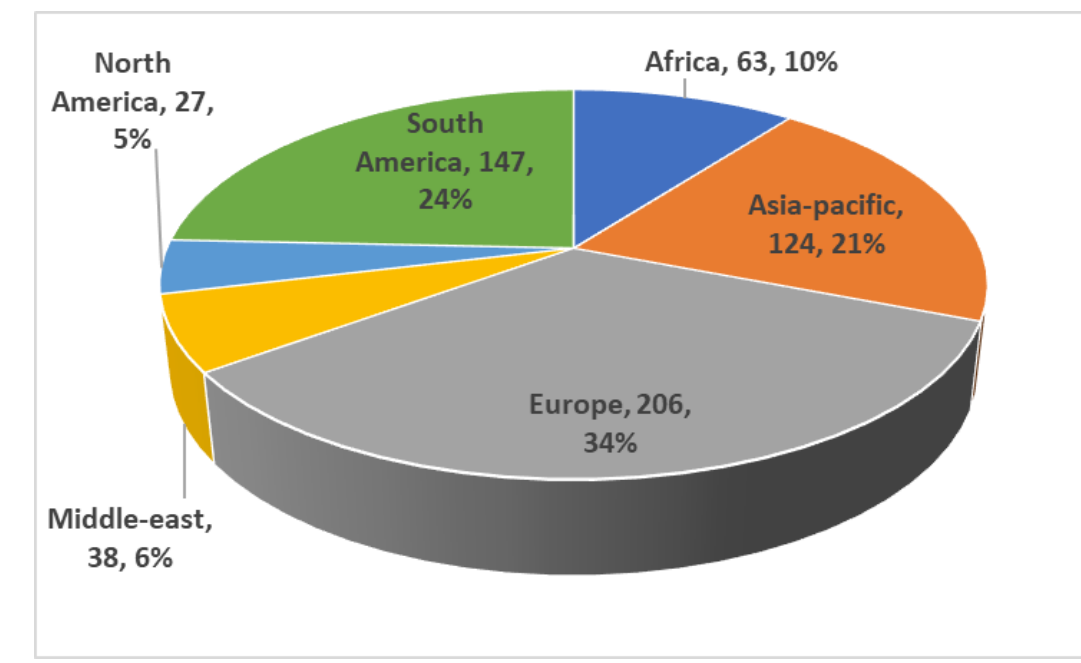


FIGURE 2. Infection source for the enterococci and staphylococci tested.

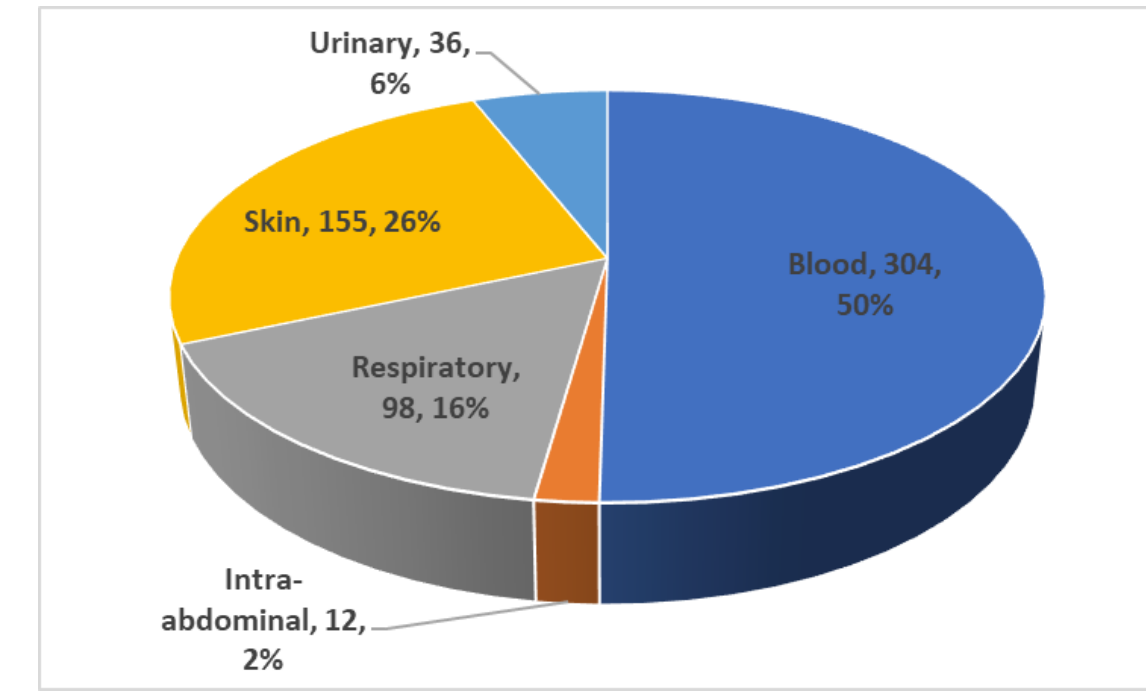


FIGURE 3. Cumulative % MIC distribution for PLG0206 against enterococci and staphylococci

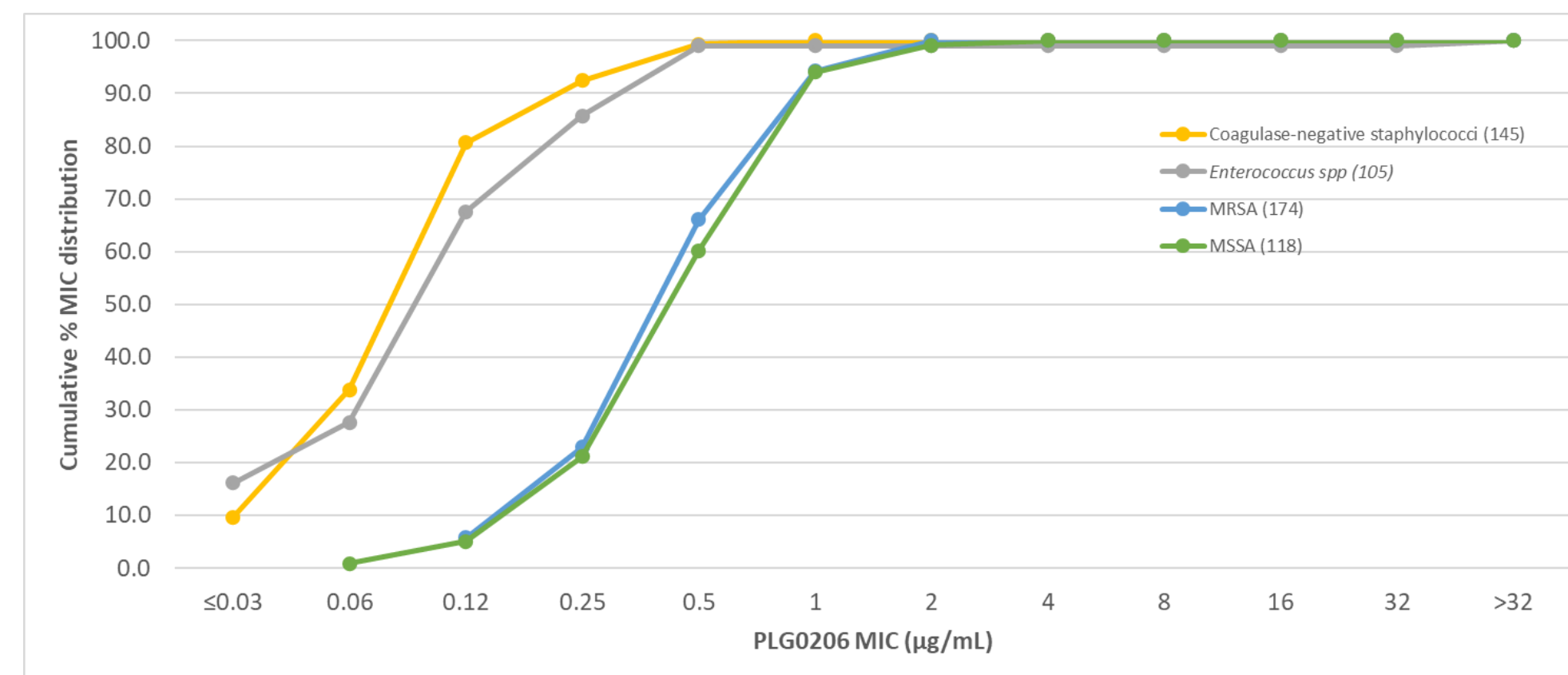


TABLE 1: Summary activity of PLG0206 and comparators against enterococci

Antimicrobial	<i>E. faecium</i> (n=46)					<i>E. faecalis</i> (n=59)				
	MIC ₅₀	MIC ₉₀	%S	%I	%R	MIC ₅₀	MIC ₉₀	%S	%I	%R
PLG0206	0.06	0.25	-	-	-	0.12	0.5	-	-	-
Daptomycin	2	2	100.0	-	0.0	1	2	98.3	1.7	0.0
Doxycycline	2	16	63.0	8.7	28.3	8	8	42.4	50.8	6.8
Levofloxacin	>32	>32	10.9	4.3	84.8	1	>32	67.8	1.7	30.5
Linezolid	1	2	97.8	0.0	2.2	1	2	91.5	6.8	1.7
Penicillin	>32	>32	15.2	-	84.8	2	8	96.6	-	3.4
Vancomycin	0.5	>32	71.7	0.0	28.3	1	2	98.3	1.7	0.0

MIC_{50/90}: concentration (µg/mL) required to inhibit 50/90% of the bacteria tested;
%S/I/R: % susceptible/intermediate/resistant according to CLSI breakpoints

TABLE 2: Summary of activity of PLG0206 and comparators against coagulase-negative staphylococci.

Antimicrobial	Coagulase-neg staph (n=145)*					<i>S. epidermidis</i> (n=108)					<i>S. haemolyticus</i> (n=30)				
	MIC ₅₀	MIC ₉₀	%S	%I	%R	MIC ₅₀	MIC ₉₀	%S	%I	%R	MIC ₅₀	MIC ₉₀	%S	%I	%R
PLG0206	0.12	0.25	-	-	-	0.12	0.25	-	-	-	0.12	0.25	-	-	-
Azithromycin	>32	>32	34.5	0.0	65.5	>32	>32	38.0	0.0	62.0	>32	>32	16.7	0.0	83.3
Clindamycin	0.12	>32	70.3	0.7	29.0	0.12	>32	69.4	3.7	26.9	0.12	>32	50.0	6.7	43.3
Daptomycin	0.5	0.5	100.0	-	-	0.5	0.5	100.0	-	-	0.5	0.5	100.0	-	-
Doxycycline	0.25	4	92.4	4.1	3.4	0.25	4	92.6	5.6	1.9	0.25	1	93.3	0.0	6.7
Levofloxacin	1	16	50.3	4.8	44.8	0.25	8	55.6	6.5	38.0	8	32	23.3	0.0	76.7
Linezolid	0.5	1	97.9	-	2.1	0.5	1	98.1	-	1.9	1	1	96.7	-	3.3
Penicillin	8	>32	7.6	-	92.4	4	32	9.3	-	90.7	>32	>32	0.0	-	100.0
Vancomycin	1	2	100.0	0.0	0.0	1	2	100.0	0.0	0.0	1	2	100.0	0.0	0.0

MIC_{50/90}: concentration (µg/mL) required to inhibit 50/90% of the bacteria tested
%S/I/R: % susceptible/intermediate/resistant according to CLSI breakpoints
*Includes 108 *S. epidermidis*, 30 *S. haemolyticus*, 4 *S. hominis*, 2 *S. saprophyticus* & 1 *S. simulans*

TABLE 3: Summary activity of PLG0206 and comparators against *Staphylococcus aureus*

Antimicrobial	MRSA (n=174)					MSSA (n=118)				
	MIC ₅₀	MIC ₉₀	%S	%I	%R	MIC ₅₀	MIC ₉₀	%S	%I	%R
PLG0206	0.5	1	-	-	-	0.5	1	-	-	-
Azithromycin	4	>32	48.9	1.1	50.0	1	>32	77.1	1.7	21.2
Clindamycin	0.12	>32	77.6	0.0	22.4	0.12	0.12	97.5	0.0	2.5
Daptomycin	0.25	0.5	99.4	-	-	0.25	0.5	100.0	-	-
Doxycycline	0.06	1	95.4	3.4	1.1	0.06	1	98.3	1.7	0.0
Levofloxacin	4	32	48.3	0.6	51.1	0.25	4	89.8	0.0	10.2
Linezolid	1	2	100.0	-	0.0	1	2	100.0	-	0.0
Penicillin	32	>32	1.7	-	98.3	4	32	13.6	-	86.4
Vancomycin	1	1	100.0	0.0	0.0	1	1	100.0	0.0	0.0

MIC_{50/90}: concentration (µg/mL) required to inhibit 50/90% of the bacteria tested
%S/I/R: % susceptible/intermediate/resistant according to CLSI breakpoints

TABLE 4: Summary of activity of PLG0206 and comparators against multi-drug-resistant Gram-positive cocci.

Antimicrobial	<i>S. epidermidis</i> (n=40)				<i>S. haemolyticus</i> (n=22)				<i>E. faecium</i> (n=38)				MRSA (n=67)			
	MIC ₅₀	MIC ₉₀	%S	%R	MIC ₅₀	MIC ₉₀	%S	%R	MIC ₅₀	MIC ₉₀	%S	%R	MIC ₅₀	MIC ₉₀	%S	%R
PLG0206	0.12	0.25	-	-	0.12	0.25	-	-	0.06	0.25	-	-	0.5	1	-	-
Azithromycin	>32	>32	0.0	0.0	100.0	>32	>32	4.5	0.0	95.5	>32	>32	-	-	1.5	1.5
Clindamycin	>32	>32	25.0	2.5	72.5	8	>32	36.4	4.5	59.1	>32	>32	-	-	41.8	0.0
Daptomycin	0.5	0.5	100.0	-	-	0.5	0.5	100.0	-	-	2	2	100.0	-	-	-
Doxycycline	0.25	4	95.0	0.0	5.0	0.25	1	95.5	0.0	4.5	4	16	55.3	10.5	34.2	6.0
Levofloxacin	4	16	20.0	10.0	70.0	16	32	4.5	0.0	95.5	>32	>32	0.0	2.6	97.4	1.5
Linezolid	0.5	1	95.0	-	5.0	1	1	95.5	-	4.5	1	2	97.4	0.0	2.6	-
Penicillin	16	>32	0.0	-	100.0	>32	>32	0.0	-	100.0	>32	>32	0.0	-	100.0	-
Vancomycin	1	2	100.0	0.0	0.0	1	2	100.0	0.0	0.0	>32	65.8	0.0	34.2	1	1

MIC_{50/90}: concentration (µg/mL) required to inhibit 50/90% of the bacteria tested
%S/I/R: % susceptible/intermediate/resistant according to CLSI breakpoints

RESULTS SUMMARY

- 18 *E. faecalis*, 29 *E. faecium*, 9 *S. aureus* and 7 CoNS were unable to grow in RPMI, so all antimicrobial data presented exclude these isolates.
- PLG0206 was most active against CoNS and enterococci but good activity was also observed against *S. aureus* (Figure 3).
- PLG0206 had lower MIC₅₀ and MIC₉₀ values than the comparator antimicrobials against enterococci (Table 1).
- PLG0206 had a lower MIC₅₀/MIC₉₀ values than the comparator antimicrobials against CoNS, except clindamycin where the same MIC₅₀ was obtained (Table 2).
- PLG0206 showed equal activity against MRSA and MSSA (Figure 3, Table 3).
- Identical MIC₅₀ and MIC₉₀ values were obtained for PLG0206 when tested against MDR isolates (Table 4) compared to the populations as a whole (Tables 1-3).

CONCLUSIONS

- PLG0206 was the most potent antimicrobial overall (based on MIC₅₀ and MIC₉₀) against enterococci and CoNS and compared well with the comparators against MRSA and MSSA.
- These data support the evaluation of this novel antimicrobial peptide as a treatment option for periprosthetic joint infections, including those caused by MDR strains.

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