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P1664 Star-shaped nano-engineered antimicrobial polypeptide polymers (SNAPPs) against multidrug-resistant pathogens

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Background: Among bacteria that cause healthcare-associated infection (HCAI), the ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumanni*, *Pseudomonas aeruginosa* and Enterobacter) are the most concerning. As many are multidrug resistant (MDR), effective antibiotics are increasingly limited, leaving clinicians to resort to older, more toxic, less effective agents. Star-shaped nano-engineered antimicrobial polypeptide polymers (SNAPPs) have potential for development as alternative antimicrobials as their bacterial targets are distinct from those of conventional antibiotics.

Materials/methods: The susceptibility of clinical isolates representing five of the six ESKAPE pathogens, to the 64-arm SNAPP, G5(S64)–PLL5 was investigated. Bactericidal activity of G5(S64)–PLL5 was determined and the effect of human plasma on bactericidal activity was evaluated.

Results: Potent bactericidal activity was found for all ESKAPE pathogens tested with 90% killing observed at 25μM and 10μM for MDR *K. pneumoniae* (carbapenemase producer) and *E. Coli* (extended-spectrum beta-lactamase producer). For *P. aeruginosa* and methicillin-resistant *S. aureus* (MRSA), 90 % killing was observed at 5 μM. Significantly more potent killing activity was observed for a linezolid-resistant isolate of vancomycin-resistant *E. faecium* (VRE), at 50nM. The addition of human plasma (20% v/v) to assays, reduced the bactericidal activity of G5(S64)–PLL5 against VRE but bactericidal activity was maintained for all other isolates in the presence of plasma.

Conclusions: This study demonstrated potent antibacterial activity of G5(S64)–PLL5 against all ESKAPE pathogens tested including isolates resistant to multiple antibiotics. Linezolid-resistant VRE are an emerging threat for which treatment options are increasingly limited, therefore the finding of SNAPP activity against VRE in the low nM range is encouraging. Further investigations, particularly in *in-vivo* relevant conditions will be important in the further development of SNAPPs as novel antimicrobial agents.