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P0540 Poly-L-lysine based polymers as topical antimicrobial polymers for skin and soft tissue infections

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Background: Skin and soft tissue infections (SSTIs) affect a significant number of hospitalized patients and the most frequent bacterial causes are *Staphylococcus aureus* and *Pseudomonas aeruginosa*. These organisms form biofilms resulting in chronic infection. Increasingly SSTIs involve antibiotic-resistant organisms making treatment even more challenging. There is an unmet need for the discovery of innovative anti-infective agents with novel bacterial targets. Furthermore, effective novel topical treatments with enhance anti-biofilm activity would improve outcomes. Recently enhanced antimicrobial activity was observed for structurally nano-engineered antimicrobial peptide polymers (SNAPPs) arranged in a star-shape and these polymers may have potential for treatment of SSTIs.

Materials/methods: Bactericidal and anti-biofilm activity of poly-L-lysine-based SNAPPs was tested against *S. aureus* strain 25923, methicillin-resistant *S. aureus* (MRSA) strain BH1CC and *P. aeruginosa* strain PAO1. To determine the importance of the star-arrangement to activity, an 8-arm star-shaped SNAPP, G2(8)-PLL20 was compared to its linear equivalent MHA(1)-PLL16. Bactericidal activity was determined using viable plate counting following incubation with SNAPPs. Loss of biofilm viability was measured by resazurin staining of biofilms of each bacteria exposed to both SNAPPs.

Results: Potent bactericidal activity of G2(8)-PLL20 and MHA(1)-PLL160 was observed against all strains, reaching > 3 log reduction in colony forming units at 10µM. Bactericidal activity was concentration-dependent over the range 1-100nM and almost identical patterns were observed for star and linear forms. Loss of biofilm viability of 95 % and 96 % (*S. aureus*), 70 % and 72 % (MRSA) and 47 % and 75 % (PAO1) for linear and star forms respectively. These value were significantly greater than was achieved using the antibiotics rifampicin or gentamicin.

Conclusions: With the emergence of multidrug-resistant (MDR) bacteria, innovative treatment are needed. Thus the finding of antibacterial activity in the low nM range, including against MRSA, for these SNAPPs, is important. Furthermore, their ability to kill biofilms makes these agents promising for treatment of SSTIs. Importantly, it appears that for these SNAPPs, the star-shape is not essential for activity and this will make further chemical modification of these agents for clinical applications, less challenging.