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P1663 Star-shaped nano-engineered antimicrobial polypeptide polymers (SNAPPs) as novel agents against carbapenemase-producing Klebsiella pneumoniae

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Background: Carbapenemase-producing enterobacteriaceae (CPE) are a group of Gram-negative opportunistic pathogens that cause increasingly challenging healthcare-associated infections. They are resistant to all β-lactam antibiotics including the last result group, the carbapenems. Among CPE, *Klebsiella pneumoniae* infections are among the most commonly reported and are associated with multi-drug resistance (MDR). Patients with CPE infection have a poor prognosis due to severely limited treatment options. Star-shaped nano-engineered antimicrobial polypeptide polymers (SNAPPs) are active against several Gram-negative bacteria and may have potential for development against CPE.

Materials/methods: We determined the efficacy of two SNAPPs, G5(64)PLL5 (64 arms) and G4(32)PLL40 (32 arms), against representative CPEs (*K. pneumoniae*) using a bactericidal assay.

Results: Concentration-dependent killing of carbapenemase-producing *K. pneumoniae* was shown in the range 0-50 μM for the 64-arm SNAPP and in the range 0-500 nM for the 32-arm SNAPP. Time-dependent killing was observed for both SNAPPs with 100 % killing after only 15 min incubation with 500 nM of the 32-arm SNAPP. Both SNAPPs demonstrated variable killing of six CPE clinical isolates recovered from patients with infection and of carbapenemase-positive and -negative reference strains (64-98 % killing at 500 μM, G5(64)PLL5 and 32-98 % killing at 250 nM G4(32)PLL40). Bactericidal activity was maintained over pH range 5.0-8.0 but was reduced in the presence of human plasma.

Conclusions: Our findings suggest that SNAPPs have potent and rapid *in-vitro* bactericidal activity against clinically significant CPEs. However, further investigation of their selective bacterial toxicity under *in-vivo*-like conditions are required. These agents have potential for development as novel alternative anti-infective agents.