Monday, January 5, 2026

Poster abstract submission

Approval Status Not Started

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Poster title
IntraBacterial Delivery of Antimicrobial Agents

Poster abstract

Antimicrobial resistance (AMR) is increasingly driven by failure of antimicrobial agents to reach intracellular targets, due to reduced uptake and active efflux in both Gram-positive and Gram-negative bacteria. As a result, promising intracellular antibacterial strategies fail to due to poor access. Here, we introduce single-chain polymer nanoparticles (SCNPs) as a versatile platform for the controlled intrabacterial delivery of antimicrobial peptides and antibiotics, to effectively fight pathogenic bacteria.

SCNPs are prepared via intramolecular crosslinking of individual polymer chains, yielding uniform 5–10 nm nanocarriers with tunable surface functionality, through a highly scalable process. We demonstrate that bacterial uptake of SCNPs is strongly ligand-dependent: nanocarriers functionalized with small, neutral organic groups efficiently enter the bacterial cytoplasm, whereas positively charged variants remain membrane-associated. Uptake studies in E. coli revealed an optimal internalization at intermediate glucose ligand densities, highlighting the importance of precise surface engineering of the SCNPs. Successful internalization was further confirmed in S. aureus, P. aeruginosa and A. baumannii.

Exploiting this uptake mechanism, we decided to focus on intracellular delivery of short peptides targeting nucleoid-associated proteins (NAPs), such as H-NS, HU, and MvaT. These NAPs are central regulators of DNA organization and gene expression. Peptide-functionalized SCNPs induced pronounced growth inhibition in E. coli and P. aeruginosa. Notably, activity was observed in P. aeruginosa despite the absence of H-NS, indicating functional targeting with conserved NAP-mediated processes rather than sequence-specific targeting.

In addition, SCNP-mediated delivery significantly enhanced the antibacterial activity of penicillin-G in E. coli, demonstrating that this platform extends beyond peptides to small-molecule antibiotics.

Together, these results establish SCNPs as a powerful strategy to overcome bacterial uptake barriers and enable intracellular targeting of conserved bacterial functions, opening new avenues for antimicrobial development, as well as repurposing of antibiotics.

Research topic

Small molecule therapeutics

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