Tuesday, January 6, 2026

Poster abstract submission

Approval Status Not Started

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Country U.K.

Type of organization Academic / research institution

Poster title
Novel heptapeptide analogues of teixobactin with potent antibacterial activity against pathogenic Gram-positives

Poster abstract

Teixobactin, a depsi-undecapeptide isolated from Eleftheria terrae, is comprised of several amino acid residues in the D-configuration as well as the non-proteinogenic enduracididine. Teixobactin exhibits potent activity against an extensive array of Gram-positive bacteria, including methicillin-resistant S. aureus (MRSA). The MRSA strains, which are resistant to multiple antibiotics, have been designated as high priority pathogen by the WHO.

Following structural simplification and systematic modification of the native teixobactin, we herein report the discovery of novel heptapeptide analogues [1] that display potent in vitro antibacterial activities against several clinical multidrug-resistant S. aureus strains (including MRSA and VRSA) and three other opportunistic Gram-positive pathogens, Enterococcus faecium, S. epidermidis and Cutibacterium acnes (MIC = 4–8 μg/mL). A lead compound, RG266 showed unexpectedly rapid bactericidal activity against the community MRSA strain, S. aureus USA300 JE2 – at 4x MIC, compared to vancomycin the kill rate (to bactericidal level) of RG266 is >8-fold more efficient, with no viable cells remaining after 1 h. These unique antibacterial activities highlight the therapeutic potential of the heptapeptide analogues.

[1] W.C. Chan and R.A. Gangloff. Antibacterial natural product analogues (2025), Priority Patent Application GB2515916.1

Research topic Small molecule therapeutics

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Antimicrobial activity of heptapeptide analogues against multidrug-resistant clinical *S. aureus* strains.

Compound	MIC (µg/mL)						
	S. aureus						
	P1V44	160013	HIP5836	BR5	HIP11714	USA300 JE2	Mu50
RG356	8	4	4	4	4	4	4
Analogue 11	4	4	4	4	4	8	4
Vancomycin	4	4	4	8	>256	2	8