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A novel synthetic antimicrobial peptide for the cure of Gram-negative infections. Mechanism of action, efficacy in *vivo*, toxicity, biodistribution and resistance selection

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A synthetic antimicrobial peptide was identified some years ago as possible candidate for the development of a new antibacterial drug (Pini et al, 2010, FASEB J, 24:1015-22). The peptide showed a MIC 90 below 1.5 μM for *Pseudomonas aeruginosa* and *Klebsiella pneumonia*. In models in *vivo* of *P. aeruginosa* lethal infections the peptide, and its pegylated form, allowed a survival percentage ranging between 65-80% in sepsis and lung infections when injected IV, and completely resolved skin infections when administered topically. Plasma clearance demonstrated different kinetics for both peptides, with a higher persistence for the pegilated one after two hours from injection. Bio-distribution in organs did not show significant uptake differences between the two peptides. Contrary to colistin, the molecule here described did not select resistant mutants in bacterial cultures. Moreover it resulted not genotoxic and with an in *vivo* toxicity comparable to antimicrobial peptides already used in clinic. The characterizations here reported are part of a preclinical development plan that should bring the molecule to clinical trials in the next years.

Biography

Alessandro Pini is Professor of Biochemistry at the University of Siena, Italy. He is founder and president of SetLance srl (www.setlance.com) a start-up company based in Siena with a special focus in the identification and early development of peptide based-drug. He is author of dozens of publications and inventor in 10 patents.

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