

Title: The preclinical development of a novel antimicrobial peptide with strong antibacterial and anti-inflammatory actity. Systemic and pulmonary delivery with nanoparticles.

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The peptide SET-M33 is currently under preclinical development for the set up of a new antibacterial agent against the most important Gram-negative pathogens (Brunetti et al. 2016, Sci Reports). It is a synthestic molecule produced in tetrabranched form, that makes the peptide particularly stable for *in vivo* use.

SET-M33 has a potent activity against a large panel of Gram-negative bacteria, with MIC90 below 1.5 μM for multiresistant strains of *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Its mechanism of action involves LPS binding and membrane permeation (van der Weide et al. 2017, Biochim Biophys Acta). In *in-vivo* models of *P. aeruginosa* infections the peptide enabled a survival percentage of 60-80% in sepsis and lung infections when injected i.v. or by nebulization. The peptide is also able to neutralize LPS thus inhibiting the expression of inflammatory cytokines. This produces a strong anti-inflammatory effect as demonstrated *in vivo* in models of pulmonary infections (Brunetti et al. 2016, J Biol Chem). Plasma clearance, biodistribution, acute toxicity, synergistic activity with traditional drugs, and resistance selection profiles in comparison with molecules already used in the clinical practice, have been evaluated.

The conjugation of SET-M33 to nanoparticles based on different carriers (dextran, poly-lactide-co-glycolide, and others) is under evaluation for the improved delivery and slow release of the molecule administerd by aereosol or systemically.

Preclinical tests including ADME, safety pharmacology and manufacturing processes are in the last stages of development, thus SET-M33 is expected to enter into clinical trials in the next 18 months.

(Up to 250 words)

Biography

Alessandro Pini is Associate Professor of Biochemistry at the University of Siena, Italy. He has a degree in Biology, a PhD in Biotechnology, and a postgraduate degree in Clinical Biochemistry. He was visiting researcher at the Centre of Protein Engineering, MRC, Cambridge, UK, and at the Swiss Federal Institute for Research (ETH), Zurich, Switzerland.

He is founder and president of the company SetLance, based in Siena. SetLance has a special focus in the identification and early development of peptide-based drugs. He is author of dozens of publications and inventor in 12 patents regarding antibodies and peptides and their applications.

(Up to 100 words)

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