Preclinical development of antimicrobial peptide active against multidrug resistant Gram-negative bacteria

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SET-M33L is a synthetic antimicrobial peptide with a strong activity against different multi-resistant Gram-negative bacteria, including MDR clinical isolates of *P. aeruginosa*, *K. pneumoniae*, *A. baumanii* and other enterobacteriaceae.[1] SET-M33L is synthesized in a tetra-branched form, a well-defined structure that makes the molecule highly resistant to proteases, overcoming the problem of peptides short half-life.[2] In vivo models of *P. aeruginosa* infections, gave rates of survival of 60-80% in sepsis and lung infections when M33 was injected i.v. and completely healed skin infections when administered topically. [3, 4] Unlike colistin, SET-M33L did not select resistant mutants in bacterial cultures and also proved non genotoxic and less toxic in animals than antimicrobial peptides already used in clinical practice. We also report its potent anti-inflammatory activity by reducing expression of a number of cytokines involved in inflammation triggered by LPS from *P. aeruginosa*, *K. pneumonia* and *E. coli*. All the characterizations described in this study make the antimicrobial peptide SET-M33L a good candidate to become a new antibacterial agent for the treatment of severe infections due to MDR pathogens, and especially indicated against *P. aeruginosa* and *K. pneumoniae*.

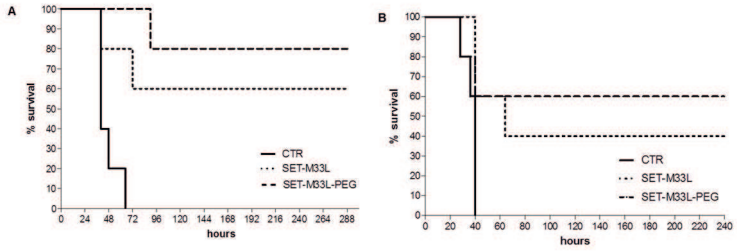

Figure 1. In vivo antibacterial activity of SET-M33L and SET-M33L-PEG peptides in sepsis animal model (A) and lung infection (B).

References

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