Antimicrobial, endotoxine-neutralizing peptides for wound healing and treatment of bacterial skin and soft-tissue infections

Challenge
Severe bacterial infections represent an ever-increasing threat worldwide, which is aggravated by the continued appearance of multi-resistant bacteria and the lack of efficacious antidotes. This applies not only for systemic, but also non-systemic infections like COPD and severe skin and soft-tissue infections (SSTI), which are not necessarily life-threatening, but still significantly impact a patient's quality of life. Non-systemic bacterial infections causing chronic inflammations do represent a particular challenge for public health systems, emphasizing the urgent need for new therapeutic treatment options.

Technology
Antimicrobial peptides represent a promising class of agents for the treatment of bacterial infections. Recent studies convincingly showed that Pep19-2.5 (also known as Aspidasept), a synthetic antimicrobial and LPS-neutralizing peptide (SALP), efficiently neutralizes pathogenicity factors of Gram-negative and Gram-positive bacteria and protects against sepsis. An international group of scientist led by the FZB now demonstrated the potential of Pep19-2.5 and the structurally related compound Pep19-4LF for their therapeutic use in wound healing and against SSTI.

Commercial Opportunity
Proprietary peptides and compositions are available for in-licensing and/or co-development.

Developmental Status
Pep19-2.5 and Pep19-4LF are the result of nearly 20 years of research. Both SALPs possess antimicrobial and anti-inflammatory activity and are capable of efficiently neutralizing bacterial endotoxins. Pep19-2.5 has been successfully tested (e.g. in various animal models) regarding its therapeutic use against sepsis. In this context, also the compound's general tolerability was proven.

The possible use of Pep19-2.5 and Pep19-4LF in wound healing and against SSTI has been comprehensively tested in vitro, ex vivo, as well as in the context of a healing attempt.

Both SALPs inhibit the bacterial endotoxin-induced maturation and migration of monocyte-derived dendritic cells (MoDCs), thereby preventing sustained and excessive inflammatory responses, which otherwise may contribute to chronic inflammation and delayed wound healing. In TLR2/6-activated keratinocytes, the peptides considerably reduced the release of IL-8, a key pro-inflammatory mediator. In a scratch assay, both peptides markedly promoted cell migration and accelerated artificial wound healing attempt: wound before and after daily treatment w/ Pep19-2.5

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closure at concentrations as low as 1 ng/ml (= equipotent to TGF-β).

Finally, two healing attempts have been conducted. The first study concerned a male patient, who - due to a cured tumor - had an extensive open wound in his back (see picture). Over 6 years, all therapeutic approaches (incl. operative reconstruction, different antibiotics and salve formulations) have failed. Regular application of Pep19-2.5 (1% in DAC base cream), however, led to a complete healing of the wound after just 6 months.

The second healing attempt has been conducted with a female patient, suffering from a wide-spread exacerbated atopic dermatitis (AD). A defined part of the affected region was treated with Pep19-2.5 (1% in DAC base cream), while the remaining part remained untreated. After only 48h the treated part was free of symptoms.

**Patent Situation**
The proprietary peptides are subject of patent application WO 2009/124721 (priority date: 09.04.2008), which has been granted in EP, US and JP.

Particular compositions and formulations of SALPs, as well as their use for treatment of e.g. non-systemic infections are covered by separate patent application WO 2017/140770 (priority date: 19.02.2016).

**Further Reading**


