

## Technology Offer

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

Reference Number TO 14-00097

### 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.



Healing attempt: wound before and after daily treatment w/ Pep19-2.5

### Technology

Antimicrobial peptides represent a promising class of agents for the treatment of bacterial infections. Recent studies convincingly showed that Pep19-2.5 (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.

### Development 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 closure at concentrations as low as 1 ng/ml (= equipotent to TGF- $\beta$ ).

Four healing attempts have been successfully conducted on patients, suffering from atopic dermatitis, an open wound after radiation therapy as well as inflammations of skin or mucous membranes, using a daily topical application of Pep19-2.5 (either 0,1% or 1% in DAC base cream).

Most recently, the required documents for conducting an investigator-initiated phase I/II trial on wound healing have been submitted to the BfArM.

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### Patent Situation

The proprietary peptides are subject of patent application WO 2009/124721, which has been granted in EP, JP and US. 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. Applications are pending in EP, JP and US.

### Further Reading

Martin et al. (2015) Peptide 19-2.5 inhibits heparan sulfate-triggered Inflammation in murine cardiomyocytes stimulated with human sepsis serum. PlosOne 10:e0127584

Pfalzgraff et al. (2016) Synthetic antimicrobial and LPS-neutralising peptides suppress inflammatory and immune responses in skin cells and promote keratinocyte migration. Sci Rep 6:31577

Martin et al. (2016) The synthetic antimicrobial peptide 19-2,5 attenuates septic cardiomyopathy and prevents down-regulation of SERCA2 in polymicrobial sepsis. Sci Rep 6:37277

Pfalzgraff et al. (2018) Antimicrobial peptides and their therapeutic potential for bacterial skin infections and wounds. Front Pharmacol 9: 281

Kuhlmann et al. (2018) Peptide drug stability: The anti-inflammatory drugs Pep19-2.5 and Pep19-4LF in cream formulation. Eur J Pharm Sci 115: doi 10.1016

