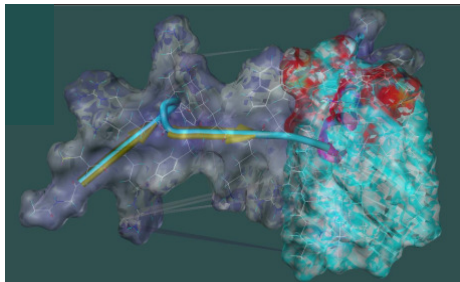


Synthetic Antimicrobial and LPS-Neutralizing Peptides (SALP) for Prevention and Treatment of Sepsis

Reference Number: TO 14-00020

Challenge

Sepsis is one of the leading causes for mortality in industrialized countries. In the US



Modelling of the interaction of a SALP (left) with lipid A as the endotoxic principle of LPS (right).

approximately 750.000 patients per year contract sepsis, 215.000 of these patients die. The estimated costs for treatment are 17 billion US Dollar per year (Angus DC, Crit Care Med 2001). Still, existing therapies do not address one of the major underlying triggers for sepsis: free lipopolysaccharides (LPS), released from bacteria by the action of the immune system or simply by cell division. Despite of recently improved diagnostic and therapeutic options, there is a major need for new and efficient active agents, which not only kill the bacteria, but additionally neutralize free endotoxins.

Technology

The technology meets this medical need by disclosing new synthetic peptides (SALPs) which both kill bacteria and efficiently neutralize free LPS. These SALPs were designed and synthesized based on the insight of comprehensive biophysical studies of natural occurring antimicrobial proteins (e.g. porcine NK-lysin or human granulysin) in which the essential parameters for LPS-neutralization were determined. Among these parameters are the surface potential of the LPS head group, the fluidity of the lipid A acyl chains and the lipid A aggregate structure.

Commercial Opportunity

The new SALPs are offered for in-licensing or co-development.

Developmental Status

Toxicity of new SALPs was tested *in vitro* using human erythrocytes and mononuclear cells. No toxicity was observed in therapeutically relevant concentrations. Antibacterial activity was determined by microdilution susceptibility assays following the recommendations of the Clinical Standards Institute.

LPS-neutralizing activity was tested *in vitro* (cytokine secretion of human mononuclear cells) and *in vivo*. The results from a murine model for endotoxic shock prove that SALPs efficiently neutralize LPS *in vivo* and reduce mortality as good or even better as the accepted 'gold standard' polymixin B.

Currently, additional preclinical experiments are conducted to explore SALP-properties in other *in vitro* and *in vivo* models of sepsis. A GLP-compliant ADME/Tox study is scheduled for 2010.

Patent Situation

A priority establishing European Patent application has been filed in 2008. In the extended European search report novelty and inventive step are acknowledged for the claims. A PCT-application has been filed in 2009.

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