A New Class of Antibiotics Against Gram-Positive Bacteria

Among Gram-positive bacteria are some of the most dangerous pathogens for humans. Especially Methicillin-resistant Staphylococcus aureus (MRSA) is responsible for a high percentage of hospital-acquired and deadly infections.

We have identified a naturally human-associated bacterial antibiotic producer strain (S. lugdunensis IVK28 wild type), which may act as a probiotic cure before patients enter hospital. Its application could avoid costly decolonization of human commensal bacteria before surgery.

From this bacterium we furthermore isolated a previously unknown class of peptide related structures with high potential as new antibiotics. Total chemical synthesis has been established.

The main compound Lugdunin shows very high potential against MRSA and other highly-resistant species like Enterococcus faecalis, E. faecium (VRE), Streptococcus pneumoniae and Listeria monocytogenes.

A patent application covering the chemical structures, the genetic background of the producer strain and the bioactivity of the new substances has been filed.

Innovation

A new class of antibiotics with high activity against a wide range of Gram-positive pathogens

Market Potential

Replacement of usual antibiotics, e.g. mupirocin and reduction of duration of hospitalization stays

Applications

- Human and veterinary medicine: Potential use as a drug against a broad spectrum of Gram-positive bacteria
- Potential use as a probiotic – colonization of skin and mucosa with the producer could reduce the titer of S. aureus drastically.

Advantages

- Very rapid killing of pathogenic bacteria even in the non-growing state. Application of 1x MIC leads to complete killing of bacteria in vitro.
- Efficiency of the pure compound already shown in a topical mouse model
- Preliminary data suggest, that molecular target might be a biochemical structure so far not targeted by established antibiotics.
- Low toxicity: First data point to a low cytotoxic potential against human cells.

Proof of Concept

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Requested Cooperation/IP Status

Industrial licensing partner/ Patent application filed, priority date 2015-03-23
**Proof of Concept**

**Overall Structure of Lugdunin (C₄₀H₆₂N₈O₆S) and Activity against Pathogens**

Lugdunin kills highly pathogenic *S. aureus* (MRSA) after a single-dose treatment, demonstrating the compound’s bactericidal mode of action.

Furthermore, *S. aureus* does not select for spontaneous resistance when lugdunin is applied at subinhibitory concentrations over 30 days.

**Bactericidal Mode of Action**

![Graph showing bactericidal mode of action](image)

**No Resistance Development**

![Graph showing no resistance development](image)

**Efficacy in an Animal Model**

Topical application of the antibiotic leads to eradication of *Staphylococcus aureus* in an animal model (mouse).

(*) P<0.05

**No Toxicity on Human Neutrophils**

Determination of potential cytotoxic effects on neutrophil granulocytes shows no significant effect (monitored after 3 h of incubation by the release of lactate dehydrogenase (LDH)).

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**Reference**