ascenion Technologietransfer for academic research
A company of the LifeScience Foundation

REFERENCE NUMBER TO 02-00387

NOVEL DAROBACTIN DERIVATIVES - HIGHLY ACTIVE ANTIBACTERIALS AGAINST GRAM-NEGATIVE BACTERIA

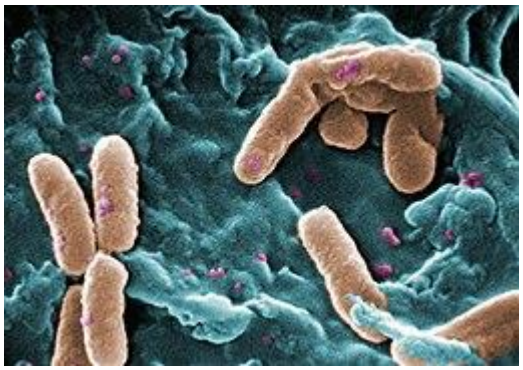
Keywords: darobactin, peptide antibiotics, ESKAPE, *Pseudomonas aeruginosa, Gram-negative pathogens,* biosynthesis gene cluster

INVENTION NOVELTY

The invention relates to novel darobactin derivatives with exceptional antibiotic activity against Gram-negative pathogens and an innovative heterologous expression system for efficient scalable production of darobactins.

VALUE PROPOSITION

The increasing resistance of bacterial pathogens against available antibiotics is one of the major public health issues and is leading to rising human mortality rates worldwide. Thus, the WHO sees urgent priority for discovery and development of new antibiotics against the ESKAPE pathogens (***E****nterococcus faecium*, ***S****taphylococcus aureus*, ***K****lebsiella pneumoniae*, ***A****cinetobacter baumannii*, ***P****seudomonas aeruginosa*, ***E****nterobacter*-species) responsible for many nosocomonsial infections and often multi-resistant. Recently, the new natural peptide antibiotic darobactin A was described, selectively killing difficult to treat Gram-negative pathogens such as *Pseudomonas aeruginosa*. Since the pharmacological properties of darobactin A are not sufficient for direct therapeutic application in humans and the yield from its natural producer *Photorhabdus khanii* is low, limiting options for optimization and upscaling, novel approaches for effective production and modification are needed.



Scanning electron micrograph of Pseudomonas aeruginosa bacteria.(source: wikimedia)

TECHNOLOGY DESCRIPTION

The invention relates to novel darobactin derivatives with antibiotic activity against Gram-negative pathogens in the nanomolar range, which is significantly increased compared to darobactin A. The novel darobactins show favorable pharmacological properties but no cytotoxicity. Furthermore, a synthetic darobactin biosynthesis gene cluster is provided for the heterologous and scalable production of darobactin A and novel darobactin derivatives in *Escherichia coli* BL21 (DE). The establishment of a production platform for darobactin in *Escherichia coli* BL21 (DE3) allows for rapid genetic manipulation and generation of darobactins with further improved pharmaceutical properties.

COMMERCIAL OPPORTUNITY

The technology is offered for co-development and licensing.

DEVELOPMENT STATUS

Antibiotic activity has been investigated against a broad panel of Gram-negative pathogens including resistant strains. PK/PD studies in a mouse model are in preparation.

PATENT SITUATION

The international PCT application PCT/EP2022/054063 was filed in February 2022 and recently published (WO2022/175443).

FURTHER READING

Groß et al. 2021. Improved broad-spectrum antibiotics against Gram-negative pathogens via darobactin biosynthetic pathway engineering. Chemical Science DOI: 10.1039/d1sc02725e

Seyfert et al. 2022. Activity and cryo-EM structure guided biosynthetic pathway engineering yields non-natural darobactin antibiotics with superior activity against Gram-negative pathogens. preprint chemrxiv.org

HZI HELMHOLTZ Zentrum für Infektionsforschung

Ascenion GmbH
Herzogstraße 64
D-80803 München
info@ascenion.de
www.ascenion.de

Licensing Contact
Dr. Sabina Heim
Senior Technology Manager
T: +49 531 618120-90
heim@ascenion.de