Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/researchers-discover-novel-antibiotic-substance-human-nose

Researchers discover novel antibiotic substance from the human nose

For the first time, the active substance epifadin has been isolated at the University of Tübingen – Epifadin is produced by specific bacteria in the nose and on the skin of humans, has an antibiotic effect, and is the first example of a previously unknown antimicrobial compound class.

Researchers at the University of Tübingen have discovered a novel antibiotic substance from the human nose that can be used against pathogenic bacteria. Named epifadin, the molecule is produced from specific strains of the bacterial species *Staphylococcus epidermidis*, which occur on the mucous membrane of the inside wall of the nose. Strains that produce epifadin can also be isolated on the surface of the skin. Epifadin constitutes a new, previously unknown class of antimicrobial compounds that kills microorganisms and could be used as a lead structure for the development of novel antibiotics.

The human nose, skin and intestine are colonized by both benign and pathogenic bacteria. These microorganisms live together in what are called microbiomes. If the microbiome becomes unbalanced, pathogens can increase and we become ill. The bacterium *Staphylococcus epidermidis* occurs naturally in the dermal and nasal microbiomes of almost all humans. The newly-identified strain is believed to produce the active substance epifadin in order to survive against competing microorganisms. Epifadin not only works against the bacteria that are locally in competition with *Staphylococcus epidermidis*, it is also effective against bacteria from other habitats such as the intestine and certain fungi. The researchers found that it is especially effective against the potential pathogens *Staphylococcus aureus*, a hospital-acquired infection which is particularly dangerous in antibiotic-resistant form (MRSA).

Back in 2016 the same working group headed by Dr Bernhard Krismer and Professor Andreas Peschel together with Professor Stephanie Grond and Professor Heike Brötz-Oesterhelt at the University of Tübingen discovered an unknown antibiotic substance with a unique structure – Lugdunin. Epifadin is now the second discovery of this kind that this working group has made in the human microbiome.

In experiments, the active substance epifadin reliably killed the pathogen *Staphylococcus aureus*, destroying hostile bacterial cells by damaging their cell membrane. The chemical structure of epifadin is extremely unstable and the substance is only active for a very few hours, so epifadin has a mainly local effect. This reduces the likelihood of collateral damage to the microbiome that is common with current treatments with broad-spectrum antibiotics. More research is needed to discover whether epifadin or its derivates can be used for therapy. For instance, epifadin-producing *Staphylococcus epidermidis* might be colonized in the nasal mucosa and other places on our skin and thereby suppress the growth of pathogens such as *Staphylococcus aureus*. This could prevent bacterial infections – using natural means that our bodies already have.

Researchers from the Cluster of Excellence "Controlling Microbes to Fight Infections" CMFI at the University of Tübingen tracked the active substance and its structure down ten years ago, when they first managed to isolate the strain. Complex natural substances such as epifadin are formed by microorganisms from single components using enzymes – this is called 'biosynthesis'. Initial attempts to reproduce this biosynthesis indicated early on that it was an extremely novel molecule. It took several years of close cooperation on chemical analysis and synthesis at the University of Tübingen's Institute of Organic Chemistry before they succeeded in accumulating and storing the active substance in a way that enabled complete isolation of the pure substance.

Study leader Bernhard Krismer from the Interfaculty Institute of Microbiology and Infection Medicine Tübingen (IMIT) recalls: "The data from the laboratory was extremely interesting, but difficult to interpret because of the instability. Despite the difficulties, I thought it was still worth continuing research into it. Tenacity and a high tolerance of frustration have finally led to success."

Andreas Peschel, Professor of Microbiology at the University of Tübingen and speaker of the Cluster of Excellence CMFI, adds: "The development of new antibiotics has stagnated for decades. But we need them more than ever, because in recent years we've registered a rapid rise in multiresistant bugs worldwide. It is hard to get control of these infections and our reserve antibiotics no longer have such a strong effect. We urgently need new active substances and treatment methods."

Follow-up studies will investigate the effect of the active substance on the basis of its structure. Here too, the perishability of

epifadin makes extensive chemical and biological analysis more difficult. So, to begin with, they will use chemical synthesis in the laboratory to produce artificial molecules with a similar structure and antimicrobial effect as epifadin that are stable and easier to work with.

Publication:

Benjamin O. Torres Salazar, Taulant Dema, Nadine A. Schilling, Daniela Janek, Jan Bornikoel, Anne Berscheid, Ahmed M. A. Elsherbini, Sophia Krauss, Simon J. Jaag, Michael Lämmerhofer, Min Li, Norah Alqahtani, Malcolm J. Horsburgh, Tilmann Weber, José Manuel Beltrán-Beleña, Heike Brötz-Oesterhelt, Stephanie Grond, Bernhard Krismer & Andreas Peschel. (2023) Commensal production of a broad spectrum and short-lived antimicrobial peptide polyene eliminates nasal Staphylococcus aureus. Nature Microbiology. DOI: doi.org/10.1038/s41564-023-01544-2.

Press release

18-Dec-2023
Source: University of Tübingen

Further information

Dr. Bernhard Krismer
University of Tübingen
Interfaculty Institute of Microbiology and Infection Medicine Tübingen (IMIT) / Infection Biology
Tel.: +49 (0)7071 29 74640
E-Mail: b.krismer(at)uni-tuebingen.de

Prof. Dr. Stephanie Grond
University of Tübingen
Institute of Organic Chemistry
E-Mail: stephanie.grond(at)uni-tuebingen.de

- Eberhard Karls University of Tübingen