Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/pseudomonas-aeruginosa-bakterien-stellen-ein-molekuel-her-das-zellen-des-immunsystems-laehmt

Pseudomonas aeruginosa Bacteria produce a molecule that paralyzes immune system cells

Bacteria of the species Pseudomonas aeruginosa are antibiotic-resistant hospital germs that can enter blood, lungs and other tissues through wounds and cause life-threatening infections. In a joint project, researchers from the Universities of Freiburg and Strasbourg in France have discovered a mechanism that likely contributes to the severity of P. aeruginosa infections. At the same time, it could be a target for future treatments. The results were recently appeared in the journal EMBO Reports.

Many bacterial species use sugar-binding molecules called lectins to attach to and invade host cells. Lectins can also influence the immune response to bacterial infections. However, these functions have hardly been researched so far. A research consortium led by Prof. Dr. Winfried Römer from the Cluster of Excellence CIBSS - Centre for Integrative Biological Signalling Studies at the University of Freiburg and Prof. Dr. Christopher G. Mueller from the IBMC - Institute of Molecular and Cell Biology at the CNRS/University of Strasbourg has investigated the effect of the lectin LecB from P. aeruginosa on the immune system. It found that isolated LecB can render immune cells ineffective: The cells are then no longer able to migrate through the body and trigger an immune response. The administration of a substance directed against LecB prevented this effect and led to the immune cells being able to move unhindered again.

LecB barricades the path for immune cells

As soon as they perceive an infection, cells of the innate immune system migrate to a nearby lymph node, where they activate T and B cells and trigger a targeted immune response. LecB, according to the current study, prevents this migration. "We assume that LecB not only acts on the immune cells themselves in this process, but also has an unexpected effect on the cells lining the inside of the blood and lymph vessels," Römer explains. "When LecB binds to these cells, it triggers extensive changes in them." Indeed, the researchers observed that important structural molecules were relocated to the interior of the cells and degraded. At the same time, the cell skeleton became more rigid. "The cell layer thus becomes an impenetrable barrier for the immune cells," Römer said.

An effective agent against LecB

Can this effect be prevented? To find out, the researchers tested a specific LecB inhibitor that resembles the sugar building blocks to which LecB otherwise binds. "The inhibitor prevented the changes in the cells, and T-cell activation was possible again," Mueller said, summarizing the promising results of the current study. The inhibitor was developed by Prof. Dr. Alexander Titz, who conducts research at the Helmholtz Institute for Pharmaceutical Research Saarland and Saarland University.

Further studies are needed to determine how clinically relevant the inhibition of the immune system by LecB is to the spread of P. aeruginosa infection and whether the LecB inhibitor has potential for therapeutic application. "The current results provide further evidence that lectins are a useful target for the development of new therapies, especially for antibiotic-resistant pathogens such as P. aeruginosa," the authors conclude.

A cooperation across the Rhine

The results stem from a cooperation between the universities of Freiburg and Strasbourg. The two first authors of the study were or are currently doctoral candidates at both universities and were/are supported by the Franco-German University of Applied Sciences. The project is thus an example of a successful cross-border research project on the Upper Rhine.

About the Cluster of Excellence CIBSS

The Cluster of Excellence CIBSS - Centre for Integrative Biological Signalling Studies at the University of Freiburg aims to gain a comprehensive understanding of biological signalling processes across scales - from the interactions of single molecules and cells to the processes in organs and whole organisms. The researchers are using the knowledge they have gained to develop strategies for controlling signals in a targeted manner. Thanks to these technologies, they not only unlock new insights in research, but also enable innovations in medicine and plant sciences.

About the French research lab

The CNRS laboratory on the campus of the University of Strasbourg studies the development of the adaptive immune system and how pathogens escape an immune response. Among other things, the laboratory develops cell culture models that allow the study of the interplay of infection mechanisms and immunological defenses in humans.

Publication:
Janina Sponsel, Yubing Guo, Lutfir Hamzam, Emma Partiot, Quentin Muller, Julien Rottura, Raphael Gaudin, Dirk Hauck, Alexander Titz, Vincent Flacher, Winfried Römer, Christopher G. Mueller (2023): Pseudomonas aeruginosa LecB suppresses the immune response by inhibiting transendothelial migration. In: *EMBO Reports*. DOI: 10.15252/embr.202255971.

Press release

01-Mar-2023
Source: Albert-Ludwigs-Universität Freiburg

Further information

- University of Freiburg
- CIBSS Centre for Integrative Biological Signalling Studies