PRESS RELEASE

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Finally understanding the rules

How the joint defence mechanism of two bacteria works

by Charlotte Fuchs

Cooperation exists in board games, among researchers and among bacteria. Working closely together locally, scientists have deciphered how two species of bacteria join forces to avoid being eaten.

Back in 2021, Pierre Stallforth and his team at the Leibniz-Institute for Natural Product Research and Infection Biology (Leibniz-HKI) showed that bacteria of the genera *Pseudomonas* and *Paenibacillus* join forces to protect themselves from their predator, an amoeba. Now, a team led by Pierre Stallforth, Ute Hellmich, and Markus Lakemeyer has been able to show exactly how this defense mechanism works. The study was conducted by the Cluster of Excellence Balance of the Microverse at the University of Jena and has just been published in the renowned journal *JACS*.

Analysis at the molecular level

The cooperation between the two bacteria *Pseudomonas* sp. *SZ40* and *Paenibacillus* sp. *SZ31* is based on a natural product, a lipopeptide called syringafactin. It is produced by *Pseudomonas*, but only becomes dangerous to the amoeba after a modification caused by *Paenibacillus*. *Paenibacillus* cleaves the lipopeptide at an unusual site using two special enzymes, known as DL peptidases. This converts the syringafactin into a substance that is toxic to the amoeba.

"It was very exciting for me to understand the mechanism by which the special class of DL lipopeptides is cleaved and how this can be exploited in the interaction of microbes," reports Hellmich. What is special about these natural products is their unusual site of attack in the spatial structure of the lipopeptides. "Amino acids are normally L-configured in nature, which is why most enzymes are specialised in cleaving this variant," explains Stallforth. D and L forms differ only in their symmetry; they are mirror-image molecules with the same atomic composition. "This means that for many analytical methods, both molecules look the same, even though we know that there is a huge difference between using the left or right hand," Hellmich illustrates.

Multifunctional game mechanics

According to Stallforth, this alteration is not an isolated case, but appears to be a general, albeit very specific, mechanism. "These enzymes are so interesting because we can use them to elucidate the structure of complex natural products by selectively dividing them into smaller fragments." "And that will make it easier for us and other groups to analyse new natural products in the future," adds Lakemeyer. This is a great help for the development of new natural product-based anti-infectives.

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A dream

Like the bacteria, the research team also worked together organically, Hellmich explains enthusiastically. Just as a single species of bacteria cannot defeat the amoeba, researchers also need cooperation and interdisciplinarity. "Individually, none of us would have been able to tackle this problem in this way," Hellmich describes the situation. "Here in Jena, we were able to go from small natural products to protein structures in cells to the ecological context, and we also had an application in biotechnology." That is unique. "I have never experienced anything like Jena at any other location," adds Lakemeyer. "It's just fun when you can look at the same problem from different angles and then also have great colleagues."

The study was a collaboration between Leibniz-HKI and the Universities of Jena and Würzburg. The research networks involved were the Cluster of Excellence *Balance of the Microverse* and the Collaborative Research Centre ChemBioSys.

The exciting dynamics of playing a game at the table instead of the digital version were particularly evident in the local collaboration: “You can sit down together in a café on a Sunday and say, ‘We need to analyze the data now,’” says Lakemeyer, describing his enthusiasm for the collegial collaboration among researchers in Jena.

The team and the sponsors

The following researchers were involved in the work:

Shuaibing Zhang, Ying Huang, Kevin Schlabach, Mai Anh Tran, Raed Nachawati, Anna Komor, Christian Hertweck, and Pierre Stallforth from Leibniz-HKI,

Markus Lakemeyer and Ute Hellmich from Friedrich Schiller University Jena,

Nicole Bader and Hermann Schindelin from Julius Maximilian University of Würzburg.

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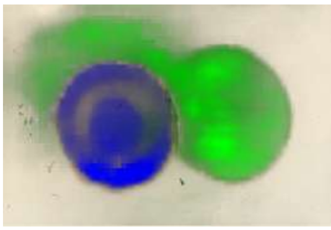
Captions

26_02_MALDI 1.jpg



Visualized using imaging mass spectrometry (MALDI): The lipopeptide syringafactin produced by *Pseudomonas* syringae *SZ57* is shown in blue, while the lipopeptide that has already been modified by *Paenibacillus* sp. *SZ31* and is now toxic to amoebae is shown in green.

Source: Leibniz-HKI

The Leibniz-HKI

The Leibniz Institute for Natural Product Research and Infection Biology was founded in 1992 and has been part of the Leibniz Association since 2003. Scientists at Leibniz-HKI conduct research into the infection biology of human-pathogenic fungi. They investigate the molecular mechanisms of disease onset and the interaction with the human immune system. New natural products from microorganisms are investigated in an ecological context and developed for possible applications as active ingredients. The focus is on new anti-infectives to overcome resistance.

The heads of the Leibniz HKI's research departments are predominantly professors appointed by Friedrich Schiller University Jena. In the junior research group program, young scientists qualify for future leadership positions. Several application-oriented cross-sectional facilities fulfill an integrative function for the institute. Together with the University of Jena, the Leibniz-HKI operates the *Jena Microbial Resource Collection*, a comprehensive collection of microorganisms and natural products.

The Leibniz HKI is a core partner in major research networks that shape the profile of the location. Examples include the Cluster of Excellence *Balance of the Microverse*, the *Jena School for Microbial Communication* graduate school, and the translational Leibniz Center for Photonics in Infection Research. The Leibniz HKI is the seat of the National Reference Center for Invasive Fungal Infections.
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