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Competition among pathogens

Research at the University of Konstanz has identified a molecule that allows the bacterium *Pseudomonas aeruginosa* to inhibit its rival, *Staphylococcus aureus* - Possible basis for the development of new antibiotics

Bacteria of the species *Pseudomonas aeruginosa* and *Staphylococcus aureus* are among the most common hospital germs, causing a variety of infections in humans, some of them deadly. Through interaction as partners or rivals they can substantially influence the development and progression of polymicrobial infections. In a study conducted by Dr Thomas Böttcher and doctoral researcher Dávid Szamosvári, the scientists were able to identify a molecule - an unsaturated quinolone *N*-oxide - which they suspect is one of the main agents in these interactions. It allows *Pseudomonas aeruginosa* to inhibit the growth of *Staphylococcus aureus*. The molecule could therefore be used as a basis for a new generation of tailor-made antibiotics. The science journal "Angewandte Chemie" will publish the research findings in one of its June 2017 issues, showcasing Böttcher and Szamosvári's work on the front cover. An online preview of the article is available for reading now.

Patients suffering from cystic fibrosis usually acquire an infection with *Staphylococcus aureus*. Often, during the later stages of the disease, the *Staphylococcus aureus* bacteria are largely replaced by *Pseudomonas aeruginosa*. Both pathogens can cause similar diseases, often share the same environment and therefore compete for the same resources. They defend themselves by producing various substances to ward off their rivals. *Pseudomonas aeruginosa* produces more than 50 different substances from the quinolone compound class. Of these, approximately 16 different quinolone *N*-oxides (AQNOs) are known, which are produced and released by *Pseudomonas aeruginosa*.

In order to elucidate the importance of these AQNOs, Thomas Böttcher's working group synthesised several of these naturally occurring substances and examined their biological activity. "In doing this we were able to demonstrate that there is a compound whose activity against *Staphylococcus aureus* is about ten to twenty times more potent than that of any of the other known structures. Besides inhibiting *Staphylococcus* growth, this substance is also capable of modulating the behaviour of lesser *Staphylococcus* concentrations", explains Dávid Szamosvári, who completed this project as part of his doctoral thesis.

Pseudomonas aeruginosa thus modulates both the growth and the ability of *Staphylococcus aureus* to cause disease. It can even disable the dangerous antibiotic-resistant MRSA (Methicillin-resistant *Staphylococcus aureus*) strains of the bacteria.

In the last instance, the inhibition of *Staphylococcus aureus* growth through the quinolone *N*-oxide molecule is a result of an attack on various steps of the bacterial respiratory chain. The cell's energy budget is shut down, leading to arrested or severely slowed growth. "We haven't got an antibiotic agent capable of exploiting this concept yet, which is why the extremely effective inhibitor we have identified serves as an important starting point for the development of new synthetic substances that can be used as tailor-made antibiotics", says Thomas Böttcher.

Original publication:

Dávid Szamosvári and Thomas Böttcher: An unsaturated quinolone *N*-oxide of *Pseudomonas aeruginosa* modulates growth and virulence of *Staphylococcus aureus*, 13 June 2017, Issue 25 International Edition: <https://doi.org/10.1002/anie.201702944>
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- Dávid Szamosvári holds a doctoral scholarship from the Konstanz Research School Chemical Biology (KoRS-CB).
- More information on antibiotic resistance: joint report of the Academy of Sciences and Humanities in Hamburg and the German National Academy of Sciences Leopoldina www.degruyter.com/isbn/9783110306675, as well as the WHO's "Antimicrobial Resistance: Global Report on Surveillance" http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748_eng.pdf

Note to editors:

You can download a photo here:

https://cms.uni-konstanz.de/fileadmin/pi/fileserver/2017/048_B%C3%B6ttcher/048_2017_Boettcher.jpg

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