

**Press Release No. 10/2019**

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5 February 2019

Novel enzyme discovered in intestinal bacteria

At the University of Konstanz, in cooperation with Harvard University, a key enzyme for formation of harmful hydrogen sulphide in the human gut by Bilophila bacteria has been discovered.

In the human intestinal system, a complex community of microorganisms, the intestinal microbiome, metabolizes food components that have not readily been digested. However, there are also microbial degradation processes occurring in the colon that may have negative effects on the human host. In the research team Microbial Ecology, headed by biologist Dr David Schleheck, a key enzyme was discovered in cooperation with Harvard University (USA). This enzyme is involved in the degradation of the substrate taurine, which is abundant in the colon, by the intestinal bacterium *Bilophila wadsworthia*. This process generates toxic hydrogen sulphide. Increased hydrogen sulphide production is thought to be associated with higher permeability of the intestinal barrier, higher susceptibility to infections and colon cancer. Moreover, *Bilophila wadsworthia* can act as a pathogen, for example in appendicitis. The results were published in the current issue of the Proceedings of the National Academy of Sciences of the United States of America (PNAS).

Taurine is introduced into the human digestive system primarily through a high-fat diet, but also through meat. A high-fat diet leads to increased production of bile acids, one of which is taurocholate, supporting the digestion of fat. In the large intestine, however, the *Bilophila* bacteria degrade the taurocholate to taurine, and use the taurine for anaerobic energy generation in the absence of atmospheric oxygen, producing the toxic hydrogen sulphide. This special type of energy metabolism by *Bilophila*, the “bile-acid loving” organism, had already been described 20 years ago by the research group of biologist Professor Alasdair Cook at the University of Konstanz. In this pathway, a sulphur-containing group of taurine is split off and reduced to hydrogen sulphide. However, until today it was unknown which enzyme in the strictly anaerobic *Bilophila* bacteria is responsible for this cleavage. The discovery of a novel glycy radical enzyme has now enabled David Schleheck’s research team to close this knowledge gap.

This enzyme was first identified at the Proteomics Centre of University of Konstanz. By means of a total-proteome analysis, the researchers compiled a complete list of the proteins present in the bacterial cells during growth with taurine. “We found that an unknown glycy radical enzyme is produced in very large quantities during growth with taurine, but not during growth with reference substrates,” reports David Schleheck, whose research team is funded by the Heisenberg Programme of the German Research Foundation (DFG). “This enzyme function did fit exactly into the gap of our understanding of the *Bilophila* taurine degradation pathway. We have thus

discovered a novel enzyme that can catalyse a cleavage of such sulphur-containing groups,” explains David Schleheck.

A crucial factor is that the enzyme is extremely oxygen-sensitive. This means that it can react only under strictly anoxic conditions, that is, in a strictly oxygen-free environment, and hence, it can only be examined in the laboratory under such strictly anoxic conditions. Biologist and co-author Karin Denger, who had already been a member of the Cook team: “Back then, we had discovered similar taurine degradation pathways in a wide range of other bacteria. But at that time we did not realize that the pathway in *Bilophila* bacteria is so different.”

David Schleheck, co-author Anna Burrichter and Karin Denger, who is now a member of the collaborating research team of chemist Professor Spiteller at the University of Konstanz, were also able to win two specialists for glyceryl radical enzymes from Harvard University as collaboration partners for their study, Professor Emily Balskus and Dr Spencer Peck, whose work was funded by the Bill & Melinda Gates Foundation. They were able to produce the *Bilophila* enzyme also recombinantly in *Escherichia coli*, purify it and, above all, subsequently reactivate the enzyme system and thus confirm its enzyme function. “With this methodology, we will be able to work on similar sulphur-group cleaving enzymes in the future, since we have found a large number of such enzymes in many important intestinal bacteria, but the functions of these enzymes are still completely unknown,” says David Schleheck.

Apart from its harmful effects, hydrogen sulphide formation in the intestine might also be beneficial for human health, at least at much lower concentrations, since hydrogen sulphide can also act as a signalling compound in humans. “Doctoral student Anna Burrichter recently described the bacterial production of hydrogen sulphide from a component of the vegetable diet, from sulfoquinovose,” says David Schleheck, “while now we were able to elucidate the bacterial formation of hydrogen sulphide from the substrates taurocholate and taurine. For a better understanding of the complex symbiosis of intestinal microbiome and the human host, and of the role of hydrogen sulphide, it is important to know all the pathways that can lead to hydrogen sulphide production, particularly in dependence of the dietary conditions of the host.” As David Schleheck points out, other intestinal bacterial degradation pathways are already being studied in his group.

Key facts:

- Original publication: Spencer C. Peck, Karin Denger, Anna Burrichter, Stephania M. Irwin, Emily P. Balskus, and David Schleheck: A glyceryl radical enzyme enables hydrogen sulfide production by the human intestinal bacterium *Bilophila wadsworthia*. PNAS published ahead of print February 4, 2019. DOI: <https://doi.org/10.1073/pnas.1815661116>
- Key enzyme discovered in *Bilophila* bacteria for hydrogen sulphide production in the human intestine
- Hydrogen sulphide production and *Bilophila* bacteria are associated with intestinal inflammation and colon cancer
- Collaboration with Harvard University (USA)
- Funded by the Heisenberg Programme of the German Research Foundation (DFG), the Konstanz Research School Chemical Biology (KoRS-CB), the Konstanz Young Scholar Fund (YSF), and the Bill & Melinda Gates Foundation.

Note to editors:

You can download photos here:

https://cms.uni-konstanz.de/fileadmin/pi/files/2019/Bilder/Neuartiges_Enzym_in_Darmbakterien_entdeckt_Potraet.jpg

Caption:

David Schleheck, Anna Burrichter and Karin Denker. This picture does not show the collaboration partners from Harvard University Emily Balskus, Spencer Peck and Stephania Irwin.

Photo: University of Konstanz

[https://cms.uni-](https://cms.uni-konstanz.de/fileadmin/pi/fileserver/2019/Bilder/Neuartiges_Enzym_in_Darmbakterien_entdeckt_Schleheck.jpg)

[konstanz.de/fileadmin/pi/fileserver/2019/Bilder/Neuartiges_Enzym_in_Darmbakterien_entdeckt_Schleheck.jpg](https://cms.uni-konstanz.de/fileadmin/pi/fileserver/2019/Bilder/Neuartiges_Enzym_in_Darmbakterien_entdeckt_Schleheck.jpg)

Caption:

Schematical illustration of the taurine degradation pathway in anaerobic Bilophila bacteria. The newly discovered glycy radical enzyme (IslAB) is able to cleave the sulfur-containing group of taurine from its degradation intermediate, isethionate. The sulfite released is then utilized as electron acceptor for anaerobic energy conservation (sulfite respiration), while the toxic hydrogen sulfide (H₂S) is produced.

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