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Press release

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New findings on Bacteroides thetaiotaomicron physiology under bile stress

A small RNA modulates the growth of the microbes

Researchers from the Würzburg Helmholtz Institute for RNA-based Infection Research (HIRI) deployed CRISPR interference for the first time for the functional characterization of the gut mutualist Bacteroides thetaiotaomicron. They identified a small ribonucleic acid (sRNA) that modulates the microorganisms' growth in the presence of bile. The findings should contribute to a better understanding of the bacterium's lifestyle in its native environment, the human intestine, and to the development of clinical applications. The study was published in the journal PNAS.

Bacteroides thetaiotaomicron is an abundant member of the human intestinal microbiota. The bacterium supports the digestion of polysaccharides and is of paramount importance for human health, but it can also cause or promote infections. As a model organism, B. thetaiotaomicron is increasingly being researched, however, its gene functions are still poorly understood. The latter is particularly true for the noncoding genes which are transcribed into small, noncoding ribonucleic acids (sRNAs for short) without being translated into proteins.

"Our gut mutualists are affecting our health as well as diseases, but there is barely any knowledge as to the function of noncoding genes," says Alexander Westermann, explaining the background to the study, which was published in the journal PNAS (Proceedings of the National Academy of Sciences). Given the important functions that the noncoding DNA regions have in infection by pathogens, it can be assumed that they play a similar key role in beneficial bacteria such as Bacteroides, says Westermann. The professor who initiated the study is a research group leader at the Würzburg Helmholtz Institute for RNA-based Infection Research (HIRI), a site of the Braunschweig Helmholtz Centre for Infection Research (HZI) in cooperation with the Julius-Maximilians-Universität Würzburg.

A lack of specific therapies

"Microbiota-centric interventions are limited by our incomplete understanding of the gene functions of many of its constituent species. While the importance of sRNA genes in bacteria has been recognized, tools for their global functional characterization have been lacking," says Westermann.

In collaboration with Chase Beisel's department at HIRI, the scientists from the Westermann lab have now deployed a molecular biochemical tool known as CRISPR interference (CRISPRi for short) to tackle this problem. Using specifically engineered guide RNAs, CRISPRi blocks the expression of selected genes, virtually knocking them out.

"Despite ongoing attempts, to our knowledge CRISPRi has not previously been used for a systematic functional screening of Bacteroides thetaiotaomicron genes," says Gianluca Prezza, first author of the study and PhD student in Alexander Westermann's lab.

A previously uncharacterized ribonucleic acid

The researchers employed CRISPRi to generate a targeted knockdown library of the intergenic sRNA repertoire of these important gut bacteria. In the subsequent screening, they identified a previously uncharacterized sRNA, which regulates genes involved in Bacteroides cell surface assembly and confers enhanced susceptibility to bile salts. Gianluca Prezza: “Suppressing the identified sRNA, called BatR, increases Bacteroides resilience to bile stress.”

Overall, the guide RNA library presented bears potential to systematically uncover the gene functions of Bacteroides under a variety of experimental conditions. ”Our work illuminates the benefits of CRISPRi for the functional characterization of sRNAs and lays the ground for a targeted gene knockdown in these abundant human microbiota members,” Alexander Westermann sums up. At the same time, the study provides the foundation for the replication of this approach in other bacterial species, says the lead author of the study.

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This press release is also available on our homepage: https://www.helmholtz-hzi.de/en/news-events/news/view/article/complete/neue-erkenntnisse-zum-mikrobiota-keim-bacteroides-thetaiotaomicron-unter-gallenstress/

Helmholtz Centre for Infection Research:
Scientists at the Helmholtz Centre for Infection Research (HZI) in Braunschweig and its other sites in Germany are engaged in the study of bacterial and viral infections and the body’s defence mechanisms. They have a profound expertise in natural compound research and its exploitation as a valuable source for novel anti-infectives. As member of the Helmholtz Association and the German Center for Infection Research (DZIF) the HZI performs translational research laying the ground for the development of new treatments and vaccines against infectious diseases.
http://www.helmholtz-hzi.de/en

Helmholtz Institute for RNA-based Infection Research:
The Helmholtz Institute for RNA-based Infection Research (HIRI) is the first institution of its kind worldwide to combine ribonucleic acid (RNA) research with infection biology. Based on novel findings from its strong basic research program, the institute’s long-term goal is to develop innovative therapeutic approaches to better diagnose and treat human infections. HIRI is a site of the Braunschweig Helmholtz Centre for Infection Research (HZI) in cooperation with the Julius-Maximilians-Universität Würzburg (JMU) and is located on the Würzburg Medical Campus. More information at http://www.helmholtz-hiri.de.

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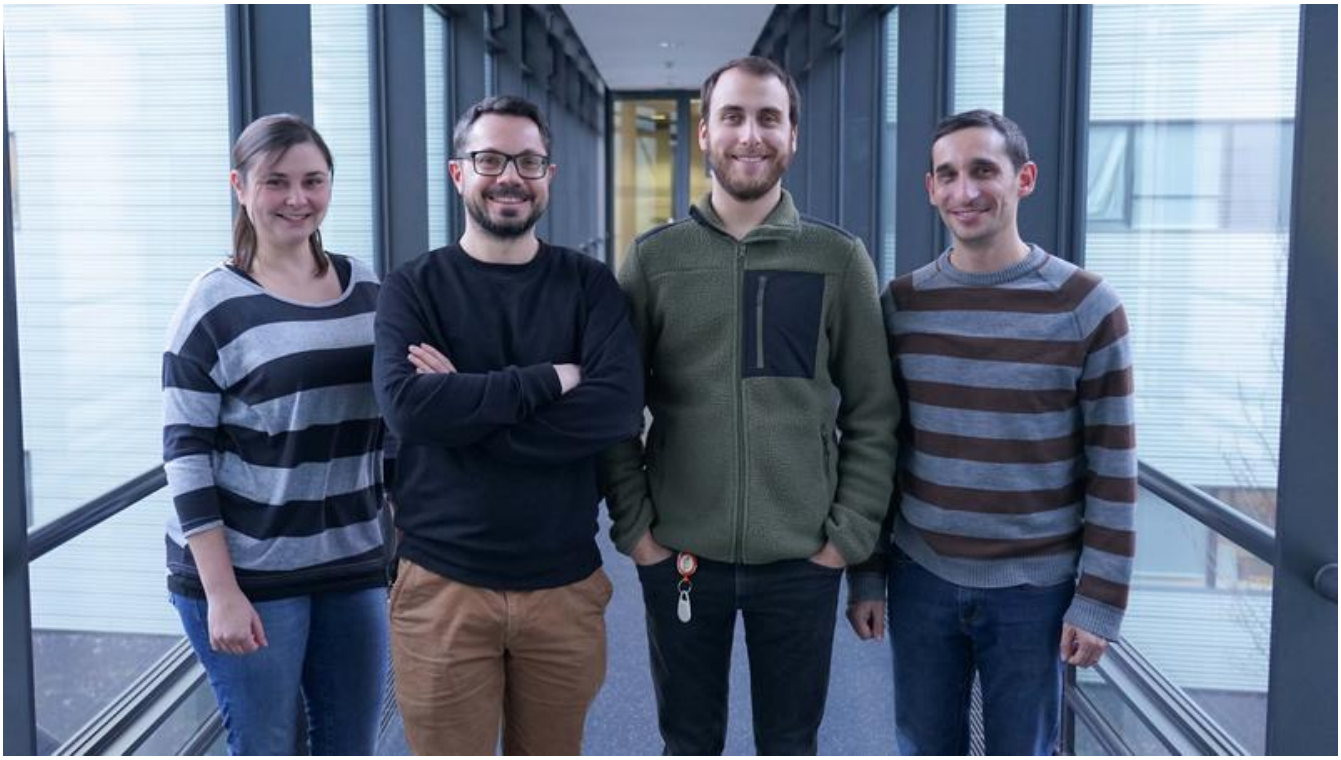

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