(idw)

idw - Informationsdienst Wissenschaft
Nachrichten, Termine, Experten

Pressemitteilung

Helmholtz-Zentrum für Infektionsforschung
Dr. Andreas Fischer

26.06.2024
http://idw-online.de/de/news836009
Forschungsergebnisse, Wissenschaftliche Publikationen
Biologie, Chemie, Medizin
überregional

Unlocking the world of bacteria

HIRI researchers introduce novel approach to DNA transformation and genetic mutation of bacteria

Bacteria possess unique traits with great potential for benefiting society. However, current genetic engineering methods to harness these advantages are limited to a small fraction of bacterial species. A team led by the Helmholtz Institute for RNA-based Infection Research (HIRI) in Würzburg has now introduced a novel approach that can make many more bacteria amenable to genetic engineering. Their method, called IMPRINT, uses cell-free systems to enhance DNA transformation across various bacterial strains. The findings were published today in the journal Molecular Cell.

Bacteria populate virtually every habitat on Earth, including within and on our own bodies. Understanding and engineering bacteria can lead to new methods for diagnosing, treating, and preventing infections. Additionally, it presents opportunities to protect crops from disease and create sustainable cell factories for chemical production, reducing environmental impact — just a few of the many benefits to society. To unlock these advantages, scientists need the ability to manipulate the genetic content of these bacteria. However, a longstanding bottleneck in genetically engineering bacteria has been the efficient transformation of DNA, the process of introducing foreign DNA into a cell. This has limited its application to only a small subset of microbes.

A major obstacle is the presence of restriction-modification systems. These protective systems mark the bacterial genome with a unique methylation pattern and destroy incoming foreign DNA lacking this pattern. Overcoming this barrier requires adding the bacterium's pattern to the DNA, a process that is strain-specific and involves multiple DNA methyltransferases. These enzymes attach methyl groups, small chemical groups containing one carbon atom bonded to three hydrogen atoms, to DNA bases. Current methods to replicate or circumvent these DNA methylation patterns are labor-intensive and not easily scalable, necessitating new approaches.

Addressing this challenge, a team led by the 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 (JMU), has introduced a novel approach to recreate such patterns and enhance DNA transformation. They called it IMPRINT, which stands for Imitating Methylation Patterns Rapidly IN TXTL. As part of this method, the researchers use a cell-free transcription-translation (TXTL) system—a liquid mixture that can produce ribonucleic acids (RNAs) and proteins from added DNA—to express a bacterium's specific set of DNA methyltransferases. The enzymes are then used to methylate DNA prior to its delivery into the target bacterium.

A wholly new application

"IMPRINT represents an entirely new use of TXTL. While TXTL is widely employed for various purposes, including producing hard-to-express proteins or as affordable diagnostic tools, it has not previously been utilized to overcome barriers to DNA transformation in bacteria," says Chase Beisel, head of the RNA Synthetic Biology department at the HIRI and professor at the JMU Medical Faculty. He spearheaded the study in collaboration with researchers from North Carolina State University (NC State) in Raleigh, USA. Their findings were published today in the journal Molecular Cell.

Compared to existing methods, IMPRINT offers speed and simplicity: “Current approaches require either laboriously purifying individual DNA methyltransferases or expressing them in E. coli, which often proves cytotoxic,” says Justin M. Vento, first author of the study who completed the work as a PhD student in the Department of Chemical and Biomolecular Engineering at NC State. “These methods can take days to weeks and only reconstitute a fraction of the bacterium's methylation pattern.”

The researchers demonstrated that IMPRINT could express a diverse array of DNA methyltransferases. Furthermore, these enzymes could be combined to recreate complex methylation patterns. This greatly enhanced DNA transformation in bacteria such as the pathogen Salmonella and the probiotic Bifidobacteria, including a challenging-to-transform strain of the latter, less-studied bacterium.

The basis for new antibiotics and cell-based therapies

The potential applications in modern medicine and research are extensive: IMPRINT can improve DNA transformation in clinical isolates of bacterial pathogens and in bacteria that combat infections, such as commensal bacteria or those producing antibacterial compounds. Genetic modification of these microbes could lead to new classes of antibiotics and cell-based therapies.

The research team aims to expand the use of IMPRINT: “We want to make a wide variety of bacterial pathogens genetically tractable for research,” Beisel says. He hopes that IMPRINT will be widely adopted by the research community: “Until now, certain bacteria have been favored as models simply because they are easier to genetically manipulate. We are hopeful that, by using IMPRINT, researchers will be able to focus on the most important bacterial strains, such as those with increased virulence or antibiotic resistance,” Beisel concludes.

Funding:
The study was supported through funding by the US National Science Foundation, the German Research Foundation, the Novo Nordisk Foundation, the Camille and Henry Dreyfus Foundation, and the Bavarian State Ministry for Science and the Arts through the research network bayresq.net.

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.
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 www.helmholtz-hiri.de.

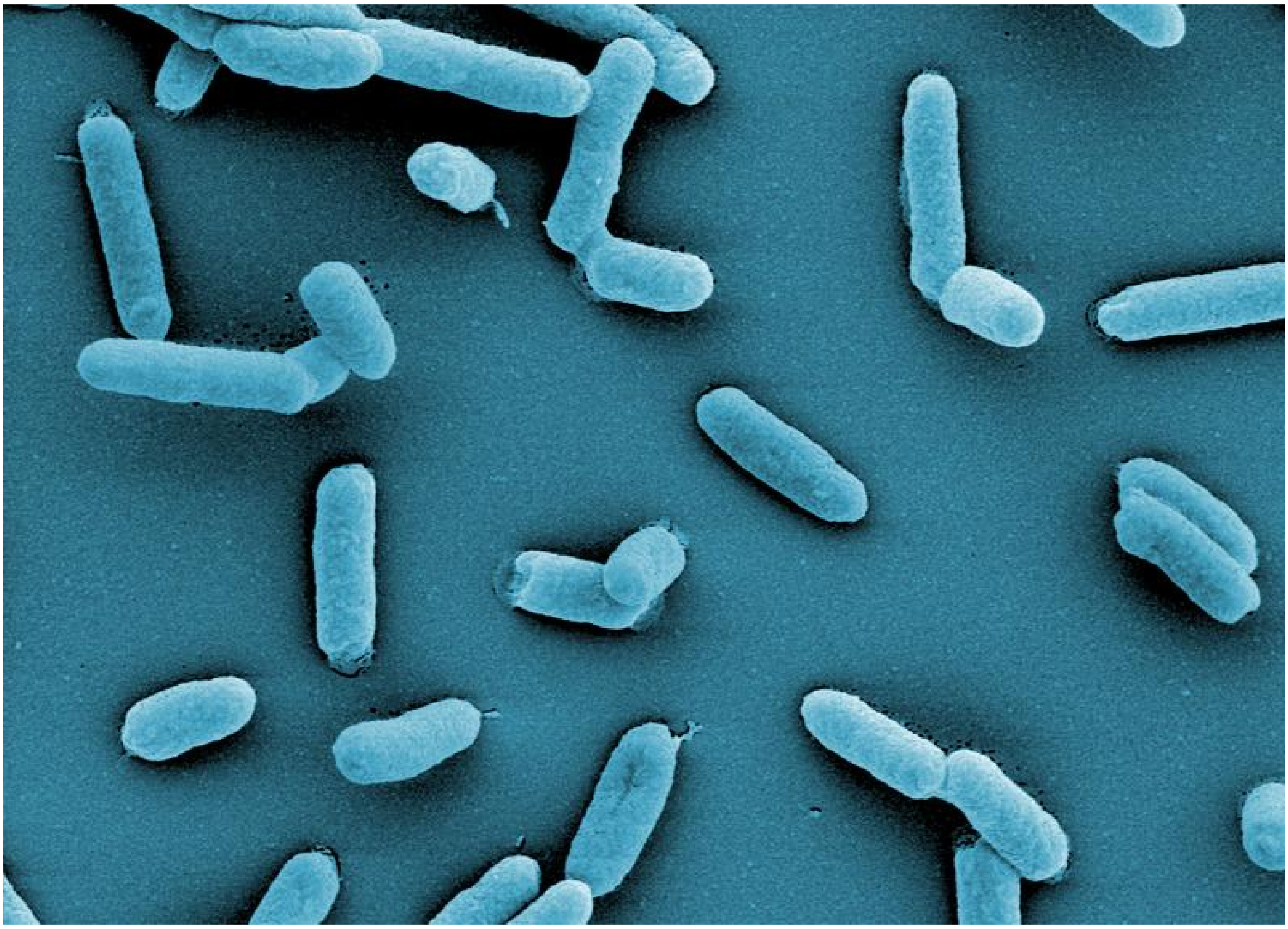
Media Contact:
Luisa Macharowsky
Manager Communications
Helmholtz Institute for RNA-based Infection Research (HIRI)

luisa.macharowsky@helmholtz-hiri.de
+49 (0)931 31 86688

Originalpublikation:

Vento JM, Durmusoglu D, Li T, Patinios C, Sullivan S, Ttofali F, van Schaik J, Yu Y, Wang Y, Barquist L, Crook N, Beisel CL. A cell-free transcription-translation pipeline for recreating methylation patterns boosts DNA transformation in bacteria. Molecular Cell (2024), DOI: 10.1016/j.molcel.2024.06.003

URL zur Pressemitteilung:
https://www.helmholtz-hzi.de/en/media-center/newsroom/news-detail/unlocking-the-world-of-bacteria



Employing IMPRINT, the researchers could significantly boost DNA transformation in Salmonella.
Manfred Rohde
HZI/Manfred Rohde