Diarrhoeal pathogen measures human body temperature with RNA thermometer

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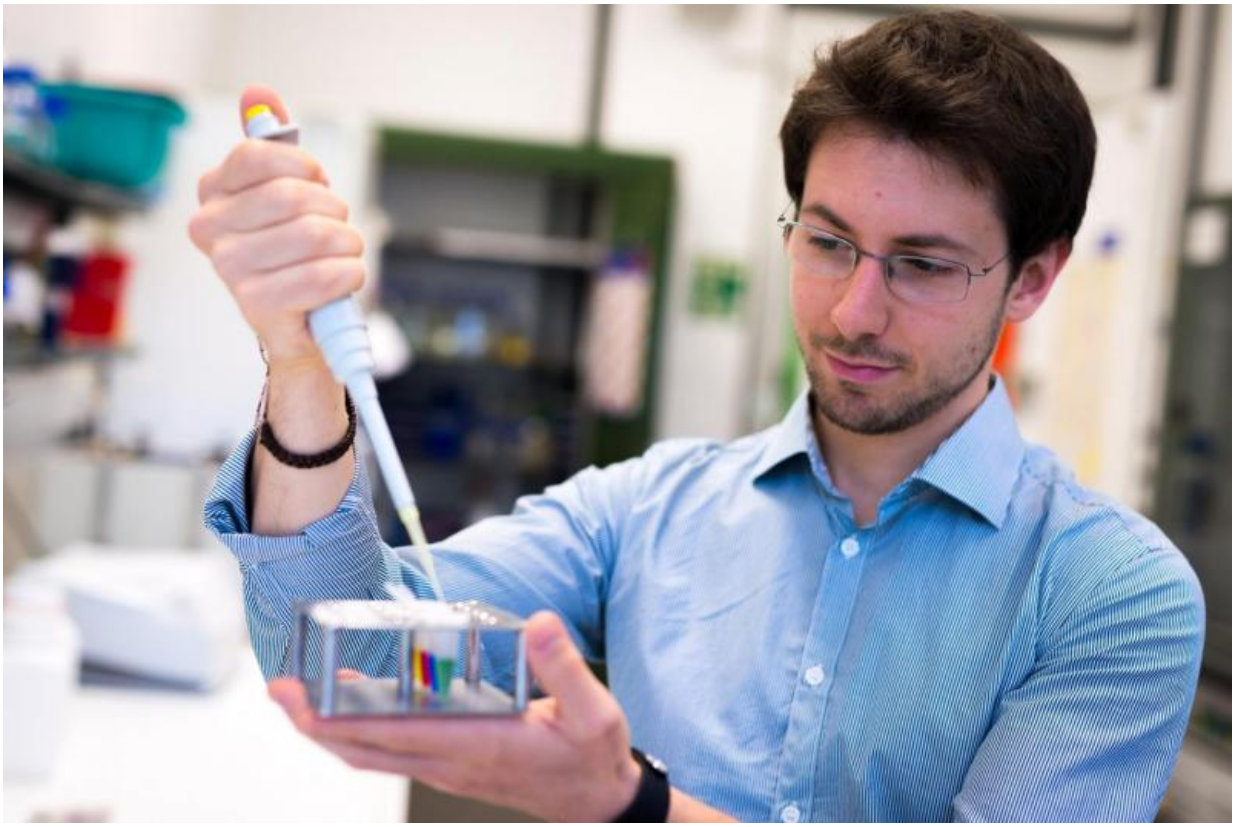

PhD student Francesco Righetti searches for the thermometers of bacteria. Credit: RUB, Kramer

Using cutting-edge high-throughput sequencing methods, researchers have mapped all RNA structures of a diarrhoeal pathogen at once. In the

process, they identified a number of temperature-responsive structures, so-called RNA thermometers. "To date, we only ever discovered individual RNA thermometers following a tedious search, and painstakingly analysed one after the other," says project manager Prof Dr Franz Narberhaus from Ruhr-Universität Bochum.

The results were reported by the team from Bochum and their colleagues at Helmholtz Center for Infection Research in Braunschweig and Leipzig University in the journal *Proceedings of the National Academy of Sciences*.

Folded RNA structures sense temperature

The fact that certain bacteria have the ability to identify their warm-blooded hosts by their body temperature has been known for several years; those include a close relative of the plague bacillus, namely Yersinia pseudotuberculosis, which was studied in the course of this project. In the process, bacteria use folded RNA structures that start to melt at a certain temperature, thus gene sequences are revealed that had been inaccessible. Those sequences can then be translated into proteins which control the progression of the disease.

New method established

In order to detect such cellular thermometers, the research team deployed a combination of biochemical RNA structure probing and high-throughput sequencing. Thus, the researchers mapped all 1,750 RNA structures contained in the bacterial cell at once. They performed the experiment at three different temperatures and generated a snapshot of RNA diversity in each instance.

"This is how we observed the dynamic modifications to RNA structures

when the temperature was rising, for example from 25 to 37 degrees centigrade," elaborates Francesco Righetti, the PhD student in charge of this project at the Chair of Microbial Biology in Bochum.

"The approach we used is very time-consuming and expensive," says Braunschweig-based researcher Dr Aaron Nuss. "However, it offers enormous potential for scientists interested in the biological function of RNA structures." The method is universally applicable, regardless if bacteria, plant, animal or human cells are being studied.

Many temperature-responsive genes

"Our results demonstrate that a surprising number of genes of the diarrhoeal pathogen Yersinia pseudotuberculosis respond directly to the host's body temperature," says Franz Narberhaus. The researchers selected 20 genes for follow-up experiments; 16 of them were indeed temperature-controlled. They belong to different functional groups. Some are, for example, involved in the bacterial response to oxidative stress.

"It makes a lot of sense to activate such processes immediately after infection of the host, in order to face the defence mechanisms in the human gastrointestinal system," explains Prof Dr Petra Dersch, infection biologist from Braunschweig.

Current studies are meant to reveal if the newly identified RNA structures play a decisive role during infection. Moreover, the researchers intend to find out if active substances do exist capable of preventing the melting of RNA thermometers. They might be able to interfere with the infection process.

More information: Francesco Righetti et al. Temperature-responsive in vitro RNA structurome of, *Proceedings of the National Academy of*

Sciences (2016). DOI: 10.1073/pnas.1523004113