Researchers clarify bacterial resistance

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Just like plants and animals, bacteria have a range of defence mechanisms against viruses and other threats. Dutch researchers at the Wageningen Laboratory for Microbiology and their American and Russian colleagues have largely clarified the workings of one of these, they reported in the scientific journal *PNAS* at the beginning of June. This is important not only for fundamental research on bacteria but also for manufacturers working with bacteria, in the dairy industry for example.

The immune system that the Wageningen researchers have got to the bottom of is called the CRISPR/Cas complex and is a feature of half of all bacteria. It consists of a protein-RNA complex that blocks viruses by binding itself to the DNA of these unwelcome guests and subsequently prevented them from reproducing. 'We discovered last year how the protein complex recognizes the viruses and then gets rid of them', says John van der Oost, professor of Microbiology at Wageningen University and one of the authors.

As soon as a virus has infected the cell, the CRISPR/Cas complex scans the genetic material of the invader. It pays attention to two specific parts of the virus, the research revealed. These are the protospacer, a small piece of the virus's DNA that can specifically bind itself to the RNA of the CRISPR/Cas complex, and the PAM motif, an even smaller piece of DNA next to it. If both these parts are present and match, the immune system launches the counterattack, breaking down the viral DNA so that it cannot be expressed and the virus cannot reproduce. Both the protospacer and the PAM are essential for the recognition of the virus.

'When we provided laboratory viruses in which the PAM had been removed through a point mutation, the resistance process did not get going', explains Van der Oost.

Bacteria are constantly updating their immune systems. As soon as a new virus turns up, the CRISPR/Cas complex makes a genetic copy in the form of RNA. This spacer is added to the protein complex and goes into action when the virus attacks again. The next generation benefits too, as the entire CRISPR/Cas complex is passed on.

The clarification of the bacterial immune system is important not just for fundamental research but also for practical purposes, says Van der Oost. 'Producers can use our knowledge to make their bacteria more resistant.' In 2008, his research group introduced a CRISPR/Cas complex into a bacteria which did not have a comparable immune system at its disposal. The bacteria therefore became ten million times more resistant to a certain virus. The dairy industry makes constant use of this knowledge, and is already protecting its yoghurt cultures against new viruses by expanding their CRISPR/Cas complexes through natural recombination. 'I am convinced that more producers will benefit from our discovery', says the microbiologist.

His publication in PNAS is the third in a row about the CRISPR/Cas complex, and will not be the last for the time being. It is likely that an article will soon appear in *Nature*. "I am afraid I am not allowed to tell you anything about the content."

Provided by Wageningen University