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Press Release

How a germ catches a virus

Scientists from Tübingen investigate the recognition mechanism between phage Phi11 and certain bacteria, the staphylococci

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Bacteriophages – short phages – represent a group of small viruses that infect bacteria and are able to alter or destroy them. That is why their name can be translated as bacteria-eater. In order to infect a bacterium, a phage has to first recognize structures on the bacterial cell wall and adhere to it. Under the leadership of Professor Thilo Stehle, Cengiz Koç and other coworkers of the Collaborative Research Center 766 (The Bacterial Cell Envelope) at the University of Tübingen have investigated this mechanism of recognition. They focused their studies on the pathogenic bacterium *Staphylococcus aureus* and the phage Phi11, which infects staphylococci. The scientists identified a phage protein that mediates the recognition of the receptor on the bacterium. Details on the three-dimensional structure of this protein and its mode of recognition of the bacterial receptor were elucidated with the help of X-ray structure analysis. The scientists published their work in two recent articles of the journal *Scientific Reports*. The results could contribute to the development of a novel therapy against bacterial infections.

Phages insert into the genes of bacteria and “hide” there until they reactivate under certain conditions to initiate the destruction of the cell. Bacteria are by far the most abundant life form on earth, and yet there still exist about ten times more phages than bacteria. Phages exert a selection pressure and contribute substantially to the evolution of bacteria. „Among other things, they are complicit in the generation of novel, sometimes even highly infectious bacterial species,“ says Thilo Stehle. On the other hand, bacteria are also capable to exploit phage components by using their protein structures for other purposes. In daily life, phages are especially useful in the food industry, in the health care system, and for analytical diagnostics.

In order to find out by what mechanism bacteriophage phi11 adheres to the cell wall of staphylococci, the scientists used a combination of bioinformatical, microbiological and structure analytical methods. The

characterization of the receptor-binding protein (Rbp) was initially probed through immunogold-labeled specific antibodies. The interactions on the phages were then analyzed by electron microscopy and through infection studies. These data demonstrated that an essential chemically altered building unit in the cell wall scaffold is crucial for the interaction with the receptor-binding protein.

The X-ray structure analysis of the receptor-binding protein, which was carried out in Tübingen, revealed the Rbp to be a complex, elongated molecule consisting of three subunits. “In addition to the actual receptor-binding component, the protein also possesses an unusual hinge region which could work as a tilting mechanism,“ explains Stehle. “This mechanism could allow the phage to bind to bacterial cell wall receptors coming from different orientations.“ Furthermore the Rbp contains an enzymatically active element, which apparently is able to digest sugar structures on the host organism’s surface in order to obtain access to the actual receptors. The scientists expect that the underlying mechanism of receptor recognition is similar for many sugar-binding phages. “Our studies also contribute to a better understanding of evolutionary processes involving phages,“ the scientist concludes.

Publications:

Xuehua Li, Cengiz Koç, Petra Kühner, York-Dieter Stierhof, Bernhard Krismer, Mark C. Enright, José R. Penadés, Christiane Wolz, Thilo Stehle, Christian Cambillau, Andreas Peschel & Guoqing Xia: An essential role for the baseplate protein Gp45 in phage adsorption to *Staphylococcus aureus. Scientific Reports,* DOI 10.1038/srep26455

Cengiz Koç, Guoqing Xia, Petra Kühner, Silvia Spinelli, Alain Roussel, Christian Cambillau & Thilo Stehle: Structure of the host-recognition device of *Staphylococcus aureus* phage φ11. *Scientific Reports*, DOI 10.1038/srep27581

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