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Press release

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Achilles' heel of pathogenic bacteria discovered

Max Planck researchers find promising new target for antibiotics

Multidrug-resistant bacteria remain a major concern for hospitals and nursing homes worldwide. Propagation of bacterial resistance is alarming and makes the search for new antimicrobials increasingly urgent. Scientists at the Max Planck Institute for Biophysical Chemistry in Göttingen have now identified a potential new target to fight bacteria: the factor EF-P. EF-P plays a crucial role in the production of proteins that are essential for the virulence of EHEC or salmonellae. The researchers' findings suggest that drugs blocking EF-P would impair the fitness of pathogenic bacteria and might lead to a new generation of specific antibiotics that allow to combat infections caused by drug-resistant pathogens. (*Science, 13. December 2012*)

Bacteria in hospitals can pose a major risk to patients: According to estimates of the Robert Koch Institute in Berlin, up to 600,000 people in Germany alone contract a bacterial infection there every year; 15,000 of them die from the infection. A growing number of these cases are caused by multidrug-resistant pathogens – bacteria that have become resistant to most common antibiotics. Experts have long been warning that new antibiotics cannot be provided quickly enough to fight such pathogens.

Scientists working with Marina Rodnina, head of the Physical Biochemistry Department at the Max Planck Institute for Biophysical Chemistry, have now discovered a promising target for a new generation of antibiotics: a bacterial protein called elongation factor P (EF-P). Intestinal bacteria such as *Escherichia coli* (*E. coli*) or salmonellae lacking EF-P are less fit and not as virulent as usually. So far, however, the exact function of EF-P has remained unclear.

Structural studies by Nobel Prize laureate Tom Steitz from Yale University showed how EF-P binds to the cell's protein factories, the ribosomes. Ribosomes assemble proteins from the individual building blocks – the amino acids – according to the blueprints stored in the genes. "The results of the Yale group suggested that EF-P should influence protein production in bacteria. However, we knew that most proteins can be synthesized without EF-P," says Marina Rodnina. "Thus, the intriguing question for us was: Have we overlooked proteins that can only be produced with the help of EF-P? And if so: What are these proteins?"

With these ideas in mind, the young scientists Lili Dörfel and Ingo Wohlgemuth set out searching for the “needle in the haystack”. They systematically looked for amino acid sequences in proteins that could be formed only with EF-P – and found the pattern: Proteins containing more than two consecutive residues of the amino acid proline could only be manufactured efficiently in the presence of EF-P. “Proline-rich proteins are not only important for growth of bacteria, they also form dangerous weapons that salmonellae or the enterohaemorrhagic *E. coli* bacterium EHEC use to attack human cells,” explains Wohlgemuth. Approximately 270 of the total 4,000 *E. coli* proteins contain this type of amino acid pattern. “Our results show that EF-P is actually an important auxiliary factor in the production of such proteins. Furthermore, this factor has been found in all bacteria studied to date,” says the scientist.

The scientists involved in the EF-P project: Christina Kothe, Frank Peske, Lili Dörfel, Henning Urlaub, Marina Rodnina, and Ingo Wohlgemuth (from left)
(*Photo: Böttcher-Gajewski / MPI for Biophysical Chemistry*)

Protein production, besides cell wall synthesis and replication of the genetic material, is a major target for common antimicrobials. The growing number of multidrug-resistant bacterial strains makes the search for new therapeutics all the more urgent. “A factor similar to EF-P is indeed present in human cells as well, but it differs in a number of important features from its bacterial counterpart. Therefore, EF-P represents a promising new target for fighting multidrug-resistant pathogens without inhibiting the protein production in our own cells,” explains Rodnina. The Max Planck researchers in Göttingen hope that EF-P – and the proteins that regulate its activity in the bacterial cell – could be targets for a new generation of very specific, potent antibiotics.

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