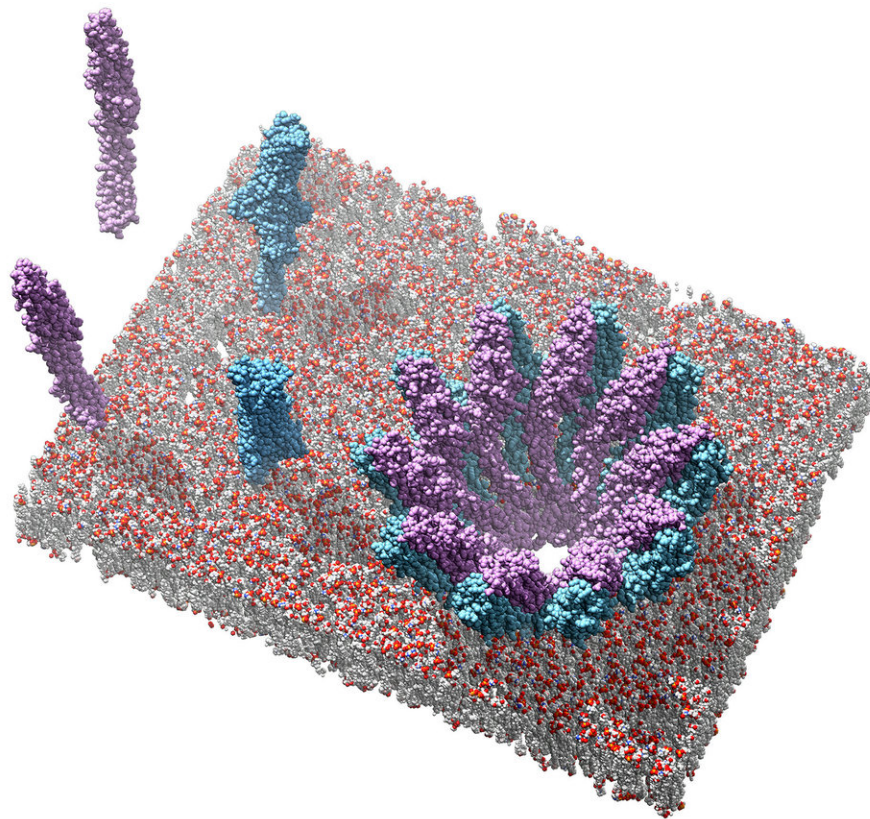


Research team uncovers mechanism of action for a class of bacterial toxins

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Pore-forming toxins are common bacterial poisons. They attack organisms by introducing holes in cell membranes. A team of scientists at the Technical University of Munich (TUM) has now unraveled the mechanism of action for one of these toxins. The picture shows the two components YaxA (blue) and YaxB (purple) and a pore built up from these subunits. Credit: Bastian Braeuning / TUM

Pore-forming toxins are common bacterial poisons. They attack organisms by introducing holes in cell membranes. A team of scientists at the Technical University of Munich (TUM) has now unraveled the mechanism of action for one of these toxins. The findings could help combat associated diseases and advance crop protection.

Many bacterial pathogens produce such toxins, including, for example, some strains of the intestinal bacterium *Escherichia coli* as well as *Yersinia enterocolitica*, a pathogen related to the plague. They attack all kinds of organisms, including plants, insects and humans. Scientists all over the world are trying to understand how these toxins produce the fatal openings in cell membranes.

After several years of research, an interdisciplinary team from the Technical University of Munich managed to elucidate the mode of action of a toxin subspecies in which two components interact to develop the deadly effect.

Two partners with lethal impact

Combining crystallographic and cryo-electron microscopy methods, Bastian Bräuning and Professor Michael Groll from the Department of Biochemistry, in collaboration with Eva Bertosin and Professor Hendrik Dietz from the Department of Experimental Biophysics, managed to shed light upon the precise molecular structures of the soluble individual components, as well as the pore complex.

"We determined that only one of the two components is able to bind to the membrane. In a second step it recruits the other component and the base domains of two proteins together form the basic pore unit," explains Bastian Bräuning. "This is a new kind of mechanism from

which we can obtain much useful insight."

The structure of the resulting hole in the [cell membrane](#) resembles a crown, whose teeth comprise 40 subunits of the two interacting partners.

One mechanism—a myriad of potential applications

The team of researchers led by Bräuning and Groll investigated the interaction of the two partner proteins in form of toxins from *Yersinia enterocolitica* and *Photobacterium luminescens*. The latter is a symbiotic bacterium in nematodes that attack insects and might prove useful for the development of novel insecticides.

These new insights put the development of substances that inhibit the interaction of two toxin components, and therefore prevent the formation of pores into the realm of the conceivable.

"Our combination of crystallography and [cryo-electron microscopy](#) was key to understanding the necessity of the two-component construction of the [toxin](#) from a biochemical perspective," explains Professor Michael Groll. "This insight will also help us understand more complex variants in the future, for example those in which three components work together."

More information: Bastian Bräuning et al, Structure and mechanism of the two-component α -helical pore-forming toxin YaxAB, *Nature Communications* (2018). [DOI: 10.1038/s41467-018-04139-2](https://doi.org/10.1038/s41467-018-04139-2)

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