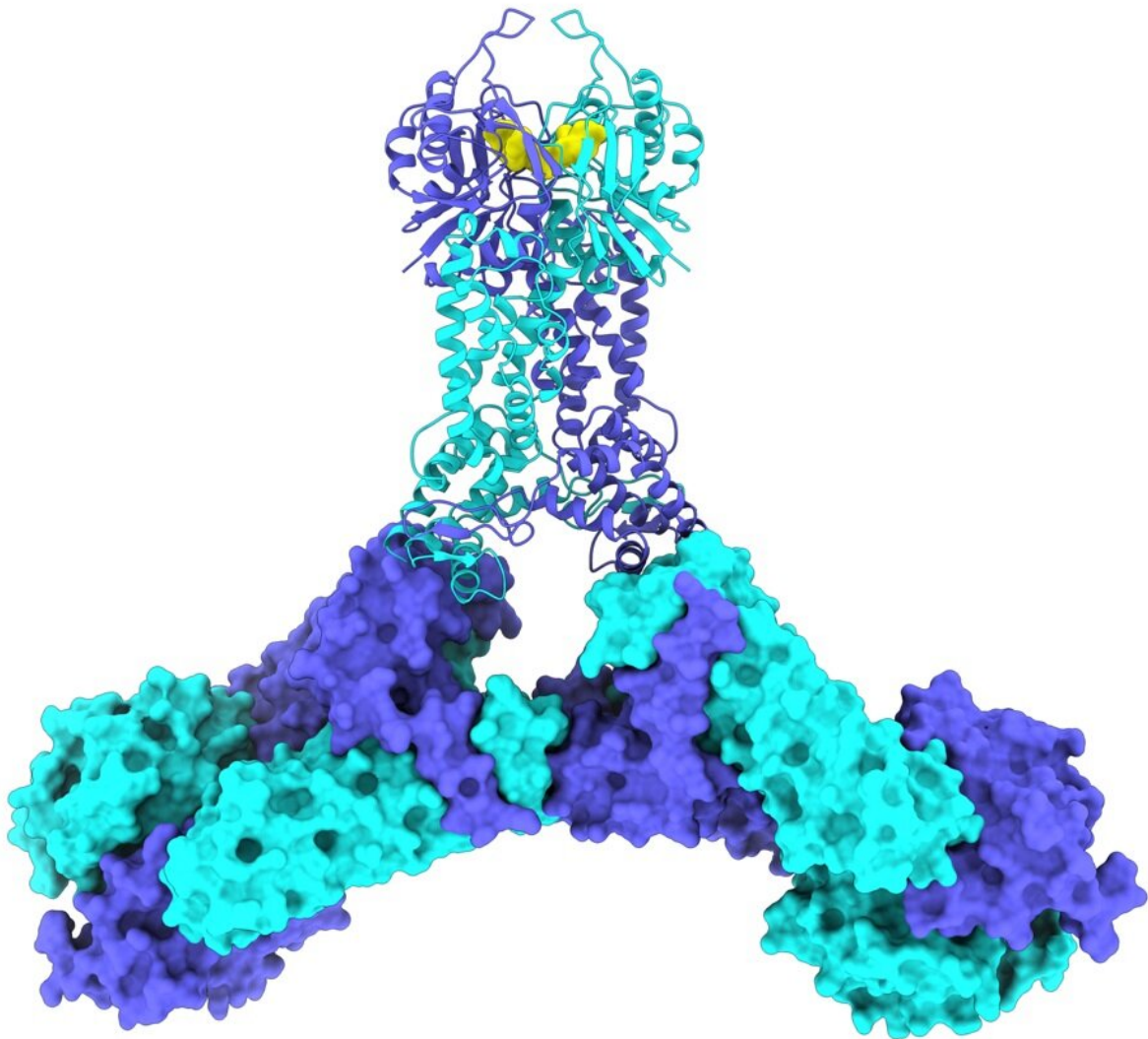


New discoveries map out CRISPR-Cas defense systems in bacteria

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Model of CSX1 protein complex. Credit: Novo Nordisk Foundation Center for Protein Research

For the first time ever, researchers at the University of Copenhagen have mapped how bacterial cells trigger their defense against outside attacks. This could affect how diseases are fought in the future.

With the aid of highly advanced microscopes and synchrotron sources, researchers from the University of Copenhagen have gained seminal insight into how bacteria function as defense mechanisms against attacks from other bacteria and viruses.

The study, which has just been published in the renowned journal, *Nature Communications*, also describes how the defense systems can be activated on cue. This discovery can turn out to be an important cornerstone in fighting diseases in the future.

The researchers have shown how a cell attacked by a virus activates a molecule called COA (Cyclic Oligoadenylate), which in turn activates a so-called protein complex called CSX1 to eradicate the attacker.

"Expressed in popular terms, the CSX1 starts cutting up the intruder. We can see how CSX1 is activated, rotates and starts defending the cell, once COA is activated," says Professor Guillermo Montoya from Novo Nordisk Foundation Center for Protein Research at the Faculty of Health and Medical Science.

Can help fight disease

The researchers at the University of Copenhagen have also managed to successfully activate the process themselves. They sent a COA molecule after the [protein complex](#), so to say, and thus started the defense mechanism.

"In short, we have found a switch that turns on the cell's defense system when we want it to, and so we can diffuse possible attacks," Montoya says.

It is the first time ever that researchers have managed to map and activate a bacterial immune system.

"A few years ago, science wasn't even aware that bacteria had some sort of immune defense system. With this discovery, we have come a great deal further in terms of understanding these mechanisms," Montoya says.

Furthermore, the discovery is interesting because the defense system in bacteria resemble in many ways the human innate immune system.

"Therefore, it is also a step along the way of understanding the human immune system better as well as knowing how to fight bacteria and defend oneself against viruses and in the long run even multiple resistance," Montoya says.

Minimal molecules and a huge magnifying glass

The discovery of a [bacteria](#) defense system was made possible by using so-called X-ray crystallography at an establishment in Switzerland and one of the world's most powerful microscopes—the so-called synchrotron MAX IV—in Lund, Sweden.

The image of the CSX1 protein complex was made possible by the advanced cryogenic electron microscope at the University of Copenhagen's high tech CryoEM facility—in popular terms a strong magnifying glass.

"CSX1 is approximately 0.00005 mm long. This equates cutting one

millimeter into 10,000 slices and then placing five pieces on top of each other. We have taken the pictures one by one and made a short film that reveals the activity inside CSX1," says Montoya.

More information: Rafael Molina et al, Structure of Csx1-cOA4 complex reveals the basis of RNA decay in Type III-B CRISPR-Cas, *Nature Communications* (2019). [DOI: 10.1038/s41467-019-12244-z](https://doi.org/10.1038/s41467-019-12244-z)

Provided by University of Copenhagen

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