# CRISPR-Cas9 can cut RNA, too

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Würzburg scientists discovered that the so-called Cas9 DNA scissors from Campylobacter can also readily target RNA. From the left: Prof. Dr. Cynthia Sharma, Sara Eisenbart, Thorsten Bischler, Belinda Aul from the Institute of Molecular Infection Biology (IMIB) and Prof. Dr. Chase Beisel from the Helmholtz-Institute of RNA-based Infection Research (HIRI) in Würzburg. Credit:Hilde Merkert, IMIB

The ability to edit genes at will, whether to reverse genetic diseases or improve food and energy crops, is undergoing a revolution. It is being driven by CRISPR-Cas9, a technology modeled on a cellular mechanism found in bacteria. CRISPR-Cas9 recognizes and cuts foreign genomic material from invading viruses and thus protects the bacteria from being infected.

The Cas9 protein acts as a pair of scissors, while other parts of the system guide Cas9 to the sections of DNA to be cut. Scientists have harnessed these molecular scissors in combination with artificial guides to specifically modify genes, not only in bacteria but also in plants and animals.

While the Cas9 scissors are known to cut DNA, researchers from the Julius-Maximilians-Universität Würzburg (JMU) and the Helmholtz Institute for RNA-based Infection Research (HIRI) in Germany have demonstrated that the Cas9 protein of the food-borne pathogen Campylobacter jejuni also cuts RNA.

"The protein is also capable of cutting ribonucleic acids—RNA, for short," says Prof. Cynthia Sharma from the JMU Institute for Molecular Infection Biology (IMIB). "Not only that, but we found that we could also program Cas9 to target and cut specific RNA molecules."

RNA plays a central role in all forms of life. A major role of RNAs is to serve as messenger of genomic material in the cell. Genes encoded in the DNA are extracted by transcribing them into RNA. The RNA then serves as template for the translation of this information into proteins. The ability to target RNA instead of DNA expands how Cas9 scissors can be used. Potential uses include controlling which genes are activated or deactivated, and combating human viruses, and rapidly detecting infectious agents.

The researchers discovered this function while looking at molecules that interact with the Cas9 in Campylobacter. These included numerous RNAs from the cell. Further analyses showed that Cas9 not only bound to RNA, but could also cut it as it does with DNA. The researchers determined that it could be easily instructed to cut specific RNAs.

"The finding was surprising, given that Cas9 is thought to naturally target DNA only," says Prof. Chase Beisel, who recently joined HIRI from NC State University (USA) and has been collaborating with Prof. Sharma on the project.

While the researchers made this finding with the Cas9 protein from Campylobacter, two other groups of researchers recently reported similar findings with Cas9s from two other bacteria. This raises the possibility that this fascinating new discovery could be a general trait of Cas9 proteins in nature. Another question raised by this study is whether the ability of Cas9 to target RNA has any physiological roles in Campylobacter. For instance, evidence is accumulating that CRISPR-Cas systems might not only serve to combat infections, but might rather be naturally involved in controlling which genes in Campylobacter are turned on and off. Prof. Sharma and Prof. Beisel agree: "We continue to be amazed by what Cas9 is capable of doing and what new applications and technologies these insights create."

**More information:** Gaurav Dugar et al, CRISPR RNA-Dependent Binding and Cleavage of Endogenous RNAs by the Campylobacter jejuni Cas9, *Molecular Cell* (2018). DOI: 10.1016/j.molcel.2018.01.032

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