TOOLBOX

With new part, CRISPR can cut RNA in living cells

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A new version of the gene-editing tool CRISPR can target and cut RNA, the messenger molecule for DNA, according to a new study[1]. The tool could offer a versatile way to tinker with the expression of autism genes and observe the effects.

The CRISPR-CAS9 system uses RNA guides to direct an enzyme called CAS9 to make cuts at targeted spots on the genome, creating mutations. The system can also simply attach to the target and turn gene activity **up** or **down**. CRISPR systems can include enzymes other than CAS9.

The new research, which appeared 2 June in *Science,* harnesses a native CRISPR system from the bacterial species *Leptotrichia shahii*. In this system, RNA guides direct a bacterial enzyme called C2C2 to cut viral RNA.

The researchers found they could insert the code for these RNA guides into bacterial cells and program the CRISPR-C2C2 system to cut RNA sequences of their choosing.

Earlier this year, another research team modified CRISPR-CAS9 to adhere to RNA in living cells[2]. The new work describes the first natural CRISPR system for targeting only RNA.

So far, the researchers have coaxed the CRISPR-C2C2 system to cut RNA molecules in the bacterium *Escherichia coli*. They plan to adapt the system for mammalian cells.

Cuts to RNA can temporarily lower RNA and protein levels without altering the DNA blueprint. This capability could help researchers learn how mutations in DNA lead to changes in cell function.

It should be possible to further tweak C2C2 to insert sequences into RNA — for example, to reproduce mutations linked to autism or other conditions, says lead researcher **Feng Zhang**, a bioengineer at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts.

CRISPR-C2C2 could, for instance, help reveal how changes to **CHD8**, the top autism candidate gene, lead to features of the condition, Zhang says. Researchers could adjust levels of CHD8 RNA within short time intervals during development to study how those changes contribute to autism.

C2C2 could also be modified to bind to RNA and serve as an RNA-tracking device. **Problems with RNA transport** may play a role in autism.

REFERENCES:

1. Abudayyeh O.O. *et al. Science* Epub ahead of print (2016) **PubMed**
2. Nelles D.A. *et al. Cell* **165**, 488-496 (2016) **PubMed**