Powerful new tool in the CRISPR genome editing toolbox
Recently discovered CRISPR enzyme from huge bacteriophages expands genome editing toolbox

20.07.2020 - A recently discovered hypercompact CRISPR enzyme found only in huge bacteriophages, and known as CRISPR-Cas\(\Phi\), is functional, a new study by Patrick Pausch, Jennifer Doudna and colleagues reports, and it provides a powerful new tool in the CRISPR genome editing toolbox, including because it can target a wider range of genetic sequences compared to Cas9 and Cas12.

The authors tested its target-expanding capabilities in human and plant cells. Given its small size, they also suggest Cas\(\Phi\) could offer novel advantages for cellular delivery relative to other CRISPR-Cas proteins. While commonly known as a tool for genetic engineering, in nature, CRISPR-Cas systems provide many single-celled organisms with an adaptive immunity against viruses and plasmids. CRISPR RNAs (crRNA) in the host recognize DNA in previously encountered viruses and direct CRISPR-associated or Cas enzymes to destroy the viruses. While CRISPR-Cas systems almost exclusively exist and operate in the genomes of bacteria and archaea, they've also recently been discovered in huge bacteriophages - the viruses of bacteria. However, these systems are different. They notably lack the Cas proteins commonly found in other CRISPR-Cas systems, yet exclusively harbor the genetically unique and unusually tiny Cas\(\Phi\) enzyme.

Here, Pausch, Doudna and colleagues describe the functionality of the phage-derived CRISPR-Cas\(\Phi\) system and demonstrate its potential for expanding the CRISPR genome editing toolbox. Despite being nearly half the size of Cas9 and Cas12 systems commonly used for genome editing, Pausch et al. show that the biochemically unique Cas\(\Phi\) is fully functional and capable of both producing mature crRNA and cleaving the foreign DNA using only a single active site, making it the most compact CRISPR-Cas system yet identified. What's more, the authors demonstrate Cas\(\Phi\)'s ability to be used successfully in both human and plant genome editing.

Original publication: