RNA-TARGETING CAS9 SYSTEM FOR CONTROLLING VIRUSES

Sandia National Laboratories

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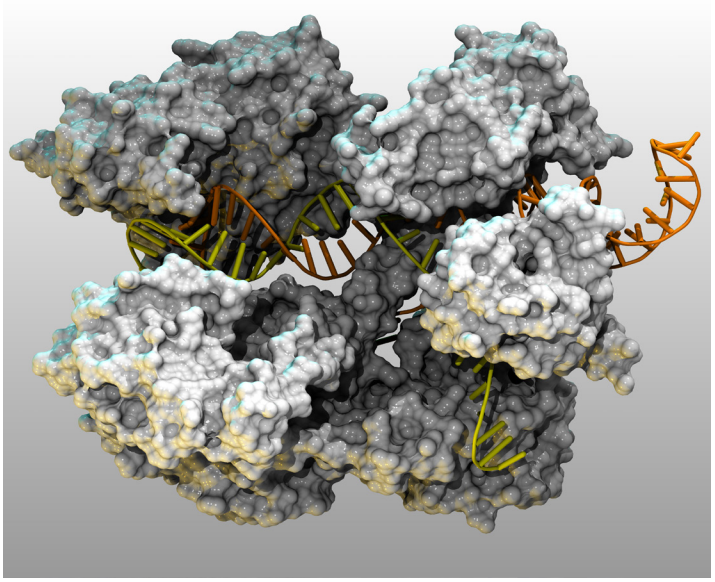
SD14537
Technology Readiness Level: 3
Concepts have been demonstrated experimentally and described in a publication

DEFENSE AGAINST DNA VIRUSES

CRISPR Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats associated protein 9) is a protein that plays an important role in immunological defense of bacteria against DNA viruses. A CRISPR-Cas based system can be used to target nucleic acid sequences. Cas9 is used frequently in genetic engineering. The protein functions by cutting DNA to alter a cell's genome. Cas9 can be used to perform site-directed double strand breaks in DNA. The breaks that occur can cause inactivation of some genes or introduction of others. Cas9 is typically guided by RNA and it identifies sections of DNA that are to be removed and removes them. Cas9 has focused on its function as a DNA endonuclease, however the cleaving of RNA has remained unexplored.



TRANSCRIPTIONAL AND TRANSLATIONAL REGULATION

Cas9 from Staphylococcus aureus (SauCas9) has been employed to target RNA. Similar to DNA cleavage, RNA cleavage activity depends on an RNA guide and an intact catalytic site. SauCas9 has been able to target single-stranded RNA in the absence of a protospacer adjacent motif (PAM). SauCas9 functions as a dual DNA/RNA targeting nuclease that can be employed in cells to regulate genes on both the transcriptional and translation level. Importantly, SauCas9 RNA-scission depends only on an sgRNA and does not need a PAMmer, thereby simplifying outstanding issues in delivery. With its small size, SauCas9 could easily be co-opted for RNA targeting applications. The RNA-targeting capability of SauCas9 offers the advantage of repressing viruses whose lifecycles consist of solely RNA molecules, thereby inaccessible to Cas9 DNA cleavage. SauCas9 holds promise for a range of RNA targeting applications. It has already been shown that SauCas9 could repress mRNA translation in E.Coli. The RNA-targeting capability of SauCas9 offers the advantage of repressing viruses whose lifecycles consist of solely RNA molecules, thereby inaccessible to DNA cleavage.

TECHNICAL BENEFITS

- Small size
- RNA targeting
- Expanded Functionality of CRISPR/Cas9

INDUSTRIES & APPLICATIONS

- Genetic Engineering
- Pharmaceuticals
- Antiviral Countermeasures RNA interference for Gene Regulation

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