

# TYPE III CRISPR-CAS SYSTEM FOR ROBUST RNA KNOCKDOWN AND IMAGING IN EUKARYOTES

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## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	20240026323	01/25/2024	2022-128

## BRIEF DESCRIPTION

Type III CRISPR-Cas systems recognize and degrade RNA molecules using an RNA-guided mechanism that occurs widely in microbes for adaptive immunity against viruses. The inventors have demonstrated that this multi-protein system can be leveraged for programmable RNA knockdown of both nuclear and cytoplasmic transcripts in mammalian cells.

Using single-vector delivery of the *S. thermophilus* Csm complex, RNA knockdown was achieved with high efficiency (90-99%) and minimal off-targets, outperforming existing technologies of shRNA- and Cas13-mediated knockdown. Furthermore, unlike Cas13, Csm is devoid of trans-cleavage activity and thus does not induce non-specific transcriptome-wide degradation and cytotoxicity. Catalytically inactivated Csm can also be used for programmable RNA-binding, which the inventors exploit for live-cell RNA imaging. This work demonstrates the feasibility and efficacy of multi-subunit CRISPR-Cas effector complexes as RNA-targeting tools in eukaryotes.

## SUGGESTED USES

This invention has the potential to completely supplant RNAi and Cas13-based RNA knockdown technologies.

Suggested uses include:

- » research purposes requiring gene perturbation at the transcript (RNA) but not genome (DNA) level.
- » efficiently knocking down both cytoplasmic and nuclear RNAs.
- » RNA imaging in live cells.
- » RNA detection for diagnostic purposes.
- » utilizing the enzyme's ssDNase and/or cyclic oligoadenylate synthesis activities.

## ADVANTAGES

The advantages include:

- » yields robust, highly efficient RNA knockdown with minimal off-targets and no cell toxicity
- » cheap, easy to use, and easy to deliver as an all-in-one vector
- » allows for gene perturbation at the transcript (RNA) level
- » efficiently knocks down both cytoplasmic and nuclear RNAs

## RELATED MATERIALS

## CONTACT

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## INVENTORS

- » Doudna, Jennifer A.

## OTHER INFORMATION

### KEYWORDS

siRNA, shRNA, knockdown, ncRNA, RNA, Type III, CRISPR, Cas, Csm, Cas13, RNAi

### CATEGORIZED AS

- » **Biotechnology**
  - » Genomics
  - » Health
- » **Engineering**
  - » Engineering
- » **Imaging**
  - » Molecular
- » **Medical**
  - » Diagnostics
  - » Gene Therapy
  - » Imaging
  - » Research Tools
- » **Research Tools**
  - » Nucleic Acids/DNA/RNA

### RELATED CASES

2022-128-0

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ COMPOSITIONS AND METHODS FOR IDENTIFYING HOST CELL TARGET PROTEINS FOR TREATING RNA VIRUS INFECTIONS
- ▶ Genome Editing via LNP-Based Delivery of Efficient and Stable CRISPR-Cas Editors
- ▶ Tissue-Specific Genome Engineering Using CRISPR-Cas9
- ▶ Cas9 Variants With Altered DNA Cleaving Activity
- ▶ Cas12-mediated DNA Detection Reporter Molecules
- ▶ Improved guide RNA and Protein Design for CasX-based Gene Editing Platform
- ▶ Cas13a/C2c2 - A Dual Function Programmable RNA Endoribonuclease
- ▶ Miniature Type VI CRISPR-Cas Systems and Methods of Use
- ▶ RNA-directed Cleavage and Modification of DNA using CasY (CRISPR-CasY)
- ▶ Generation of Chimeric RNA with Type III CRISPR-Cas
- ▶ CasX Nickase Designs, Tans Cleavage Designs & Structure
- ▶ In Vivo Gene Editing Of Tau Locus Via Liponanoparticle Delivery
- ▶ Methods and Compositions for Modifying a single stranded Target Nucleic Acid
- ▶ A Dual-RNA Guided CasZ Gene Editing Technology
- ▶ A Protein Inhibitor Of Cas9
- ▶ RNA-directed Cleavage and Modification of DNA using CasX (CRISPR-CasX)
- ▶ Compositions and Methods for Genome Editing
- ▶ IS110 and IS1111 Family RNA-Guided Transposons
- ▶ Variant Cas12a Protein Compositions and Methods of Use
- ▶ In Vitro and In Vivo Genome Editing by LNP Delivery of CRISPR Ribonucleoprotein
- ▶ CRISPR CASY COMPOSITIONS AND METHODS OF USE
- ▶ Single Conjugative Vector for Genome Editing by RNA-guided Transposition
- ▶ Improved Cas12a Proteins for Accurate and Efficient Genome Editing
- ▶ CRISPR-CAS EFFECTOR POLYPEPTIDES AND METHODS OF USE THEREOF
- ▶ Methods Of Use Of Cas12L/CasLambda In Plants
- ▶ Type V CRISPR/CAS Effector Proteins for Cleaving ssDNA and Detecting Target DNA
- ▶ THERMOSTABLE RNA-GUIDED ENDONUCLEASES AND METHODS OF USE THEREOF (GeoCas9)
- ▶ Variant TnpB and wRNA Proteins
- ▶ Efficient Site-Specific Integration Of New Genetic Information Into Human Cells
- ▶ Class 2 CRISPR/Cas COMPOSITIONS AND METHODS OF USE
- ▶ Compositions and Methods of Use for Variant Csy4 Endoribonucleases
- ▶ Immune Cell-Mediated Intercellular Delivery Of Biomolecules
- ▶ Methods and Compositions for Controlling Gene Expression by RNA Processing



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