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

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INVENTORS

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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
- Cas12-mediated DNA Detection Reporter Molecules
- Highly Multiplexed Tagging Methods for RNA Imaging and Other Applications
- 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)
- 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
- Single-Stranded Nucleic Acid Detection And Imaging System Using Cas9
- CRISPR-CAS EFFECTOR POLYPEPTIDES AND METHODS OF USE THEREOF (“Cas-VariPhi”)
- A Protein Inhibitor Of Cas9
- RNA-directed Cleavage and Modification of DNA using CasX (CRISPR-CasX)
- Compositions and Methods for Genome Editing
- Split-Cas9 For Regulatable Genome Engineering
- Methods to Interfere with Prokaryotic and Phage Translation and Noncoding RNA
- Minimal RNA Targeting CRISPR Cas Systems
- Variant Cas12a Protein Compositions and Methods of Use
- 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
- Engineered/Variant Hyperactive CRISPR CasPhi Enzymes 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)
- Structure-Guided Methods Of Cas9-Mediated Genome Engineering
- Efficient Site-Specific Integration Of New Genetic Information Into Human Cells
- CRISPR-Cas Effector Polypeptides and Methods of Use Thereof
- Virus-encoded DNA-binding Proteins
- Class 2 CRISPR/Cas COMPOSITIONS AND METHODS OF USE
- Compositions and Methods of Use for Variant Csy4 Endoribonucleases
- Methods and Compositions for Controlling Gene Expression by RNA Processing

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