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INNOVATION VENTURES AVAILABLE TECHNOLOGIES

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Cas12a System For Combinatorial Transcriptional Repression In Eukaryotic Cells

Tech ID: 33430 / UC Case 2022-223-0



OTHER INFORMATION

KEYWORDS

transcriptional silencing,

Cas12a, gRNA, high-

throughput sequencing,

functional genomics, single-

cell, RNA-seq, cellular

therapies

CATEGORIZED AS

- Medical
 - ► Therapeutics
- Research Tools
 - ► Nucleic
 - Acids/DNA/RNA
 - Screening Assays

RELATED CASES 2022-223-0

TECHNOLOGY DESCRIPTION

The invention is a novel system for delivering combinatorial transcriptional silencing.

Conventional approaches using Cas12a for transcriptional silencing rely on transient transfection experiments where both protein and guide RNA (gRNA) components are highly overexpressed. This system can function under low ribonucleoprotein expression to enable combinatorial targeting of multiple genomic sites per cell in high-throughput sequencing based pooled screens and therapeutic delivery in vivo.

ADVANTAGES

· Transcriptionally silence up to 6 targeted genomic sites per cell

- · Functional under low ribunucleoprotein expression
- o Enables combinatorial targeting of multiple genomic sites per cell in high-throughput sequencing based pooled screens

and therapeutic delivery in vivo.

 Approach enables Cas12 based CRISPRi functional genomics in pooled screens for the first time (cannot be done in transient experiments)

· Enables delivery under limiting amounts of gRNA

o For therapeutic applications low concentrations of gRNA can be delivered to enable epigenetic editing

· Novel gRNA expression vector design to enable single-cell RNA-seq readout

o Simultaneous single-cell RNA-seq and gRNA identity readouts within the same single cells

APPLICATION

- · Potential for system use as a therapeutic or research tool
- o Can be used to discover the combinatorial function(s) of genes and genomic regulatory elements
- o Can be part of therapeutic delivery in vivo or ex vivo programming in cell-based therapy
- System enables targeting of up to 10 genomic sites per cell for transcriptional silencing under limiting ribunucleoprotein concentrations, including for:
- o high-throughput functional genomics screens
- o cellular therapies ex vivo (e.g. iPSC or CAR-T)
- o therapeutic delivery in vivo

o single-cell sequencing readouts

LOOKING FOR PARTNERS

To develop and commercialize the technology

STAGE OF DEVELOPMENT

Proof of concept

RELATED MATERIALS

DATA AVAILABILITY

Data available under CDA

PATENT STATUS

Patent Pending

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