PROGRAMMABLE TRANSCRIPTIONAL TUNING IN EUKARYOTIC CELLS WITH MECP2-DCAS9

Tech ID: 34063 / UC Case 2025-146-0

PATENT STATUS

Patent Pending

BRIEF DESCRIPTION

Achieving precise and tunable control over endogenous gene expression in eukaryotic cells remains a significant challenge, particularly for therapeutic applications or detailed biological studies where fine-tuning is required rather than complete on/off switching. This innovation, developed by UC Berkeley researchers, addresses this by providing a novel, programmable method for transcriptional tuning. The innovation is a two-domain fusion protein comprising the transcriptional repression domain (TRD) of the methyl-CpG-binding domain (MBD) protein MeCP2 linked to a dead Cas9 (dCas9) domain. When combined with a single guide RNA (sgRNA) that targets a specific endogenous gene, this fusion protein partially inhibits, or "tunes," the expression of that gene. Unlike traditional methods like RNAi or full CRISPR interference (CRISPRi), which often aim for complete knockdown, this system offers a highly specific and titratable way to dial down gene expression, providing a distinct advantage in studies requiring subtle modulation of gene dosage or for developing dose-dependent therapeutic strategies.

SUGGESTED USES

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Precision Research Tools: Utilize the system as a highly specific, dose-dependent tool to study the effects of subtle changes in endogenous gene expression on cellular phenotype and function.

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Drug Target Validation: Apply the system to tune down the expression of potential drug targets to better mimic the effect of a therapeutic agent (e.g., a partial inhibitor) and validate the target's role in disease.

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Therapeutic Development: Develop gene-tuning therapeutics for diseases driven by an over-expressed or dosage-sensitive gene, allowing for a safer, titratable intervention.

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Synthetic Biology: Incorporate the system into synthetic gene circuits for highly nuanced, programmable control of cellular pathways.

ADVANTAGES

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High Specificity and Programmability: The use of dCas9 guided by an sgRNA ensures specific targeting of the desired endogenous gene.

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Titratable/Tunable Control: The system allows for partial, or "tuned," inhibition of gene expression, offering an advantage over all-or-nothing knockdown systems.

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INVENTORS

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OTHER INFORMATION

CATEGORIZED AS

» **Biotechnology**
» Bioinformatics
» Genomics
» Health
» Other
» **Medical**
» Gene Therapy
» Other
» Research Tools
» Therapeutics
» **Research Tools**
» Bioinformatics
» Nucleic Acids/DNA/RNA
» Other
» Reagents
» Vectors

RELATED CASES

2025-146-0

Leverages Epigenetic Machinery: The use of the MeCP2 TRD provides a robust repression mechanism by harnessing a known component of the cell's natural epigenetic machinery.

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Applicable in Eukaryotic Cells: Effective for use in a wide range of eukaryotic cell types, making it broadly useful for research and therapeutic applications.

RELATED MATERIALS

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Delivery of CRISPR Epigenetic Editing Technologies

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