Reactivation of CDKL5 Using Epigenetic Editors

Tech ID: 34759 / UC Case 2026-355-0

ABSTRACT

Researchers at the University of California, Davis have developed a targeted gene editing system that reactivates the silenced CDKL5 gene by precise epigenetic modulation to treat CDKL5 deficiency disorder (CDD).

FULL DESCRIPTION

This technology provides compositions and methods utilizing a split, catalytically inactive CRISPR-Cas9 (dCas9) fused to epigenetic effectors, including TET1 dioxygenase and transcriptional activators, to selectively demethylate and activate the CDKL5 gene on the inactive X chromosome. The system employs multiplexed guide RNAs and compact promoters optimized for efficient delivery and specific targeting within one kilobase of the CDKL5 transcriptional start site. It offers a modular platform for reversible epigenetic reprogramming to increase CDKL5 expression, with applications in treating disorders caused by CDKL5 gene silencing such as CDKL5 deficiency disorder.

APPLICATIONS

- Therapeutic treatment for CDKL5 deficiency disorder and related neurodevelopmental diseases.
- Gene therapy platforms targeting epigenetic dysregulation in X-linked genetic disorders.
- Research tools for epigenetic editing and study of X-chromosome inactivation dynamics.
- Personalized medicine approaches for allelic reactivation in female carriers of X-linked diseases.
- Development of viral vector-based delivery systems for in vivo gene modulation.
- Potential extension to other diseases driven by epigenetic gene silencing or DNA methylation abnormalities.

FEATURES/BENEFITS

- Precision targeting of CDKL5 promoter using CRISPR-dCas9 fused to TET1 catalytic domain for site-specific DNA demethylation.
- Multiplexed guide RNA array allows simultaneous multi-site targeting to enhance gene activation.
- Compact genetic elements tailored for efficient packaging in viral vectors like AAV.
- Split dCas9 design overcomes size constraints, enabling delivery of large fusion proteins.
- Potential for reversible and allele-specific reactivation of silenced X-linked genes.
- Versatile delivery options including lentiviral, adenoviral, and adeno-associated viral vectors.
- Applicable to cultured cells, primary cells, and in vivo treatment of mammalian subjects.

CONTACT

Prabakaran Soundararajan
psoundararajan@ucdavis.edu
tel: .

INVENTORS

- Fink, Kyle
- Halmai, Julian

OTHER INFORMATION

KEYWORDS

AAV vector, CDKL5 deficiency disorder, DNA demethylation, epigenetic editing, gene activation, gene therapy, multiplexed sgRNA, neurodevelopmental disorder, super core promoter, X-chromosome inactivation

CATEGORIZED AS

- **Biotechnology**
  - Genomics
- **Medical**
  - Disease: Genetic Diseases and

- Overcomes lack of targeted epigenetic editing methods specific for X-linked genes.
- Enables reactivation of silenced CDKL5 gene to address CDKL5 deficiency disorder.
- Reduces off-target and global side effects seen in non-specific DNA demethylating treatments.
- Addresses mosaic expression issues due to X-chromosome inactivation in females.
- Supports gene activation despite epigenetic barriers like promoter hypermethylation.
- Facilitates study and modulation of X-chromosome inactivation escape mechanisms.

PATENT STATUS

Patent Pending

Dysmorphic Syndromes
- Gene Therapy
- Research Tools
- Therapeutics

Research Tools
- Nucleic Acids/DNA/RNA
- Vectors

RELATED CASES

2026-355-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Epigenetic Prevention and Treatment of CDKL5 Deficiency Disorder
- Exon-skipping Therapy for ADNP Syndrome
- Multiplex Epigenetic Editing using a Split-dCas9 System

University of California, Davis
Technology Transfer Office
1 Shields Avenue, Mrak Hall 4th Floor,
Davis,CA 95616

Tel:
530.754.8649
techtransfer@ucdavis.edu
https://research.ucdavis.edu/technology-transfer/
Fax:
530.754.7620