

# Multiplex Epigenetic Editing using a Split-dCas9 System

Tech ID: 32484 / UC Case 2021-640-0

## ABSTRACT

Researchers at the University of California, Davis have developed a new epigenetic editing system that overcomes packaging limitations of viral delivery systems and can be used for multiplexed epigenetic editing of a genome.

## FULL DESCRIPTION

Gene expression is widely recognized as a contributing factor in a variety of diseases. Epigenetic editing to correct the expression of disease-relevant genes within live cells has become an important therapeutic approach. Relatedly, CRISPR/Cas9 gene editing techniques and the use of fusion proteins targeted by catalytically inactive Cas9 (dCas9) for epigenetic editing offer promising therapeutic opportunities. However, these approaches can be hampered by packaging size limitations when using viruses such as adeno-associated virus (AAV) for delivery. As such, there is a need for improved epigenetic editing systems and methods of delivery to target cells.

Researchers at the University of California, Davis have developed a new epigenetic editing system that employs a "split" approach to overcome virus packaging size limitations and allow delivery of, for example, a large fusion protein (e.g., that comprises a catalytically inactive Cas9 protein and an epigenetic modifier domain) to target cells via an AAV delivery system. In particular, this technology utilizes an intein-mediated, trans-splicing, fusion protein, the coding sequences for which can be packaged into two separate AAV capsids for delivery. Polynucleotides that encode guide RNA (gRNA) can be included in the same two capsid(s), or can be delivered in parallel using additional capsid(s). Editing can be multiplexed through the use of gRNA-tRNA arrays. The system has been demonstrated in vitro to regulate gene expression and alter epigenetic states. This technology expands the use of viral delivery for epigenetic editing to clinical applications that were unavailable previously.

## APPLICATIONS

- ▶ Single- or multi-locus epigenetic editing
- ▶ Potential use in gene editing and other therapeutic applications

## FEATURES/BENEFITS

- ▶ Improved, more effective gene therapy
- ▶ Overcomes prior limitations of packaging sizes that are associated with viral delivery systems such as AAV

## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	<a href="#">20240123088</a>	04/18/2024	2021-640

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## OTHER INFORMATION

### KEYWORDS

AAV, CRISPR, split-dCas9, DNA methylation, epigenetic editing, gene therapy, inteins, therapeutics

### CATEGORIZED AS

- ▶ **Biotechnology**
  - ▶ Genomics
  - ▶ Health
- ▶ **Medical**
  - ▶ Delivery Systems
  - ▶ Gene Therapy
  - ▶ Therapeutics

### RELATED CASES

2021-640-0

Additional Patent Pending

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [Modular CRISPRa System for Tunable Transcription of FOXG1](#)
- ▶ [Exon-skipping Therapy for ADNP Syndrome](#)

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