NUCLEAR DELIVERY AND TRANSCRIPTIONAL REPRESSION WITH A CELL-PENETRANT MECP2

Tech ID: 32833 / UC Case 2022-131-0

PATENT STATUS

Patent Pending

BRIEF DESCRIPTION

Methyl-CpG-binding-protein 2 (MeCP2) is a nuclear protein expressed in all cell types, especially neurons. Mutations in the MECP2 gene cause Rett syndrome (RTT), an incurable neurological disorder that disproportionately affects young girls. Strategies to restore MeCP2 expression phenotypically reverse RTT-like symptoms in male and female MeCP2-deficient mice, suggesting that direct nuclear delivery of functional MeCP2 could restore MeCP2 activity.

The inventors have discovered that ZF-tMeCP2, a conjugate of MeCP2(aa13-71, 313-484) and the cell-permeant mini-protein ZF5.3, binds DNA in a methylation-dependent manner and reaches the nucleus of model cell lines intact at concentrations above 700 nM. When delivered to live cells, ZF-tMeCP2 engages the NCoR/SMRT co-repressor complex and selectively represses transcription from methylated promoters. Efficient nuclear delivery of ZF-tMeCP2 relies on a unique endosomal escape portal provided by HOPS-dependent endosomal fusion.

In a comparative evaluation, the inventors observed the Tat conjugate of MeCP2 (Tat-tMeCP2) (1) degrades within the nucleus, (2) is not selective for methylated promoters, and (3) traffics in a HOPS-independent manner.

These results support the feasibility of a HOPS-dependent portal for delivering functional macromolecules to the cell interior using the cell-penetrant mini-protein ZF5.3. Such a strategy could broaden the impact of multiple families of protein-derived therapeutics.

SUGGESTED USES

This technology describes a potential treatment for Rett Syndrome. It further demonstrates the utility of ZF5.3 for protein delivery.

ADVANTAGES

RELATED MATERIALS

CONTACT

Laleh Shayesteh
lalehs@berkeley.edu
tel: 510-642-4537.

INVENTORS

» Schepartz, Alanna S.

OTHER INFORMATION

KEYWORDS

Rett syndrome, Protein delivery

CATEGORIZED AS

» **Biotechnology**
» Health
» Proteomics
» **Imaging**
» Medical
» Molecular
» **Medical**
» Research Tools
» Therapeutics
» **Research Tools**
» Other

RELATED CASES

2022-131-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Methods To Generate Novel Acyl-Trna Species

University of California, Berkeley Office of Technology Licensing
2150 Shattuck Avenue, Suite 510, Berkeley,CA 94704
Tel: 510.643.7201 | Fax: 510.642.4566
ipira.berkeley.edu/ | otl-feedback@lists.berkeley.edu