SMALL MOLECULE ENDOSOMAL DISRUPTOR FOR BIOTHERAPEUTIC DELIVERY

Tech ID: 29065 / UC Case 2018-074-0

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	12,059,407	08/13/2024	2018-074

BRIEF DESCRIPTION

The inventors have developed a new endosomolytic molecule, termed ED, for the intracellular delivery of macromolecule therapeutics. This is the first example of a small molecule that can perform endosomal disruption. The compound was designed with polyethylene glycol (PEG) moieties, which mask the hydrophobic membrane-disruptive portion of the molecule. Upon entering the endosomal compartment (pH~5) the acetal group hydrolyzes and triggers endosomal disruption, allowing cytosolic release of any co-delivered therapeutics. The membrane disruptive ability of ED was shown to be acid-dependent. Kinetic studies confirmed the pH-dependent hydrolysis with half-lives of >4h and 2.5 min at pH 7.4 and 5.0, respectively. This allows selective disruption of endosomal membrane compartments. Protein delivery was demonstrated using Saporin, a ribosome inactivation protein that has no mechanism of endosomal disruption3, and its toxic effect is therefore dependent on induced cytosolic delivery. Addition of 5 mg/mL endosomal disruptor to 10µg/mL Saporin in HEK293T cells caused complete cell death, compared to no cell death in cells treated with only Saporin or only ED.

SUGGESTED USES

Cas9 delivery

mRNA delivery

ADVANTAGES

This molecule can efficiently and safely disrupt endosomes.

Bio-macromolecules such as proteins and nucleic acids have the potential to revolutionize therapeutics through their superior specificity and activity compared to classic small molecule drugs. However, despite extensive research in the use of bio-therapeutics there are currently no commercially available macromolecule drugs that target the intracellular compartment, due to delivery problems. The greatest barrier in this delivery of macromolecular drugs is the uptake of large molecules into endosomes and the ensuing disintegration in lysosomes. Disruption of the endosomal compartment has been shown to increase the therapeutic ability of macromolecular drugs. The nanoparticle, protein, and peptide based strategies currently available for disrupting endosomes are challenging to assemble with macromolecular drugs, due to their large size and chemical complexity.

RELATED MATERIALS

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Cholesterol HMPA Block Copolymer Stabilize Lipid Nanoparticles (LNPs)
- Treatment Of Obesity With Lipid Nanoparticles That Induce Browning In White Fat

CONTACT

Terri Sale
terri.sale@berkeley.edu
tel: 510-643-4219.

INVENTORS

» Murthy, Niren

OTHER INFORMATION

KEYWORDS

endosomal disruption, endosomal, drug delivery, protein delivery, macromolecular drugs

CATEGORIZED AS

» **Medical**

» Delivery Systems

» Therapeutics

RELATED CASES

2018-074-0

University of California, Berkeley Office of Technology Licensing
2150 Shattuck Avenue, Suite 510, Berkeley,CA 94704
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