Transient Expression Of BCL-2 To Ameliorate Cytotoxicity Of Gene Modification Reagents In Stem Cells

Tech ID: 29651 / UC Case 2016-290-0

SUMMARY

Researchers at the UCLA Department of Microbiology, Immunology and Molecular Genetics have developed methods for efficient gene editing in stem cells by increasing the level of apoptosis regulator BCL-2.

BACKGROUND

Engineered nucleases, such as zinc finger nuclease (ZFN), transcription activator-like effector nuclease (TALEN), and CRISPR/Cas9, are popular tools to increase the frequency of gene repair events. These nucleases create sequence and site-specific double-stranded breaks in the DNA that induce cellular DNA damage repair pathways, resulting in DNA repair either through non-homologous end joining (NHEJ), or by homology-directed repair (HDR) when engineered nucleases are co-delivered with a donor template. HDR may be used to correct gene mutations or add new sequences to a specific chromosomal site. While efficient gene modification through HDR occurs at high frequencies in stem cells and progenitor cells, the rate of HDR in long-term reconstituting stem cells, such as hematopoietic stem cells (HSCs) remains low.

INNOVATION

Researchers at UCLA have observed increased sensitivity of HSCs to toxicity from the introduction of the gene modifying nucleases and donor template molecules by electroporation compared to progenitor cells, contributing to the reduced frequency of gene-modified HSC. Based on this observation, they have developed a novel method of transient delivery of BCL-2 mRNA along with the gene modifying reagents at the time of electroporation, which can promote the survival of gene-modified stem cells by blocking the apoptotic effects of the manipulation.

APPLICATIONS

Increase the number of gene-modified HSCs that may be used for transplantation or for regenerative medicine applications

ADVANTAGES

- Promote the survival of gene-modified stem cells
- Efficient targeted gene modification of stem cells

STATE OF DEVELOPMENT

The described method has been validated in human HSCs.

PATENT STATUS

Country	Type	Number	Dated	Case
Germany	Issued Patent	3417061	10/26/2022	2016-290
France	Issued Patent	3417061	10/26/2022	2016-290
United Kingdom	Issued Patent	3417061	10/26/2022	2016-290
United States Of America	Published Application	20190249172	08/15/2019	2016-290

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Augmentations to Lentiviral Vectors to Increase Expression
- Improvement To Retroviral Vectors Containing The Human Ubiquitin C Promoter

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OTHER INFORMATION

KEYWORDS

Gene editing, gene repair, gene modification, homology-directed repair, HDR, stem cell, hematopoietic stem cells, HSCs

CATEGORIZED AS

- **Biotechnology**
  - Genomics
- **Medical**
  - Gene Therapy
  - Research Tools
  - Stem Cell
  - Therapeutics

RELATED CASES

2016-290-0

- Generation Of Minimal Enhancer Elements Using Massively Parallel Reporter Assays
- Optimized Lentiviral Vector for Stem Cell Gene Therapy of Hemoglobinopathies
- Fusion Protein For Anti-Cd19 Chimeric Antigen Receptor Detection

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