Robust Genome Engineering in Primary Human T Cells using CRISPR/Cas9 Ribonucleoproteins

Tech ID: 24858 / UC Case 2015-118-0

INVENTION NOVELTY

This invention enables highly effective experimental and therapeutic genomic engineering of primary human T cells and other hematopoietic cells with CRISPR/Cas9 ribonucleoprotein (RNP) technology.

VALUE PROPOSITION

CRISPR/Cas9-mediated genome editing provides an exceptional opportunity to engineer human T cells for research and therapeutic purposes, including cell-based therapies for cancer, viral infections and autoimmune diseases. However, therapeutic applications of CRISPR/Cas9 have been limited until now by inefficient DNA editing and inability to perform targeted DNA sequence replacement in human T cells. This invention augments the efficiency of CRISPR/Cas9-mediated genome editing in human T cells and raises the prospect of the therapeutic application of gene correction in T cells for treatment of myriad human diseases.

Additional advantages of this invention include:

- First CRISPR-mediated homology directed repair (HDR) in human immune cells could allow therapeutic editing of disease mutations in patient cells and introduction of specific sequences into TCR and CAR-transduced T cells.
- Strict temporal control over genome editing with Cas9 RNPs could increase the CRISPR safety profile for therapeutic applications.

TECHNOLOGY DESCRIPTION

UCSF researchers have developed a powerful Cas9 RNP-based technology that uses purified Cas9 ribonucleoproteins (RNP) for successful and efficient genome editing in primary human $CD4^+$ T cells. Cas9 protein pre-complexed with a single guide RNA (sgRNA) is introduced as an RNP into human T cells by transient electroporation. The active complexes enabled the first successful Cas9-mediated homology directed repair (HDR) in primary human T cells. Cas9 RNPs have allowed generation of ‘knock-in’ primary human T cells with targeted genetic replacement of specific nucleotides, which was previously unattainable.

APPLICATION

1) Unprecedented flexibility to ‘knock-out’ and ‘knock-in’ specific genetic elements in engineered T cells for cancer immunotherapy

CONTACT

Todd M. Pazdera
todd.pazdera@ucsf.edu
tel: 415-502-1636.

INVENTORS

- Bluestone, Jeffrey A.
- Doudna, Jennifer A.
- Lin, Steven
- Marson, Alexander
- Schumann, Kathrin

OTHER INFORMATION

KEYWORDS

CRISPR/Cas9, Primary human T cells, Genome engineering, Cas9 ribonucleoprotein (RNP), Gene correction/replacement, Homology-directed repair (HDR)

CATEGORIZED AS

- **Medical**
  - Gene Therapy
  - Research Tools

2) New opportunity for therapeutic gene correction for primary immune deficiencies, treatment of infections and autoimmune diseases

3) Diverse research applications examining the function of coding and non-coding genetic variation in human immune regulation

▶ Therapeutics

RELATED CASES

2015-118-0

STAGE OF DEVELOPMENT

Proof of principle

RELATED MATERIALS

▶ Not available at this time

DATA AVAILABILITY

In vitro human data

PATENT STATUS

Country	Type	Number	Dated	Case
New Zealand	Issued Patent	733807	09/03/2024	2015-118
Rep Of Korea	Issued Patent	10-2605464	11/20/2023	2015-118
Japan	Issued Patent	7356750	09/27/2023	2015-118
Singapore	Issued Patent	11201706059S	12/20/2022	2015-118
Japan	Issued Patent	7114117	07/29/2022	2015-118
Australia	Issued Patent	2016211161	07/14/2022	2015-118
Hong Kong	Issued Patent	HK1248755	01/28/2022	2015-118
China	Issued Patent	ZL201680016762.8	10/15/2021	2015-118
Germany	Issued Patent	602016058406.9	05/26/2021	2015-118
Spain	Issued Patent	3250693	05/26/2021	2015-118
France	Issued Patent	3250693	05/26/2021	2015-118
United Kingdom	Issued Patent	3250693	05/26/2021	2015-118
Italy	Issued Patent	502021000066404	05/26/2021	2015-118
Japan	Issued Patent	6886404	05/18/2021	2015-118
Israel	Issued Patent	253498	12/01/2020	2015-118
European Patent Office	Published Application	3929296	12/29/2021	2015-118
United States Of America	Published Application	20190388469	12/26/2019	2015-118
Canada	Published Application			2015-118

Additional Patents Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ XYZeq – Spatially-Resolved Single Cell Sequencing

▶ Anti-Dpp6 Car For Targeted Regulatory T Cell Therapy For Inflammation In Pancreatic Islets And Central Nervous System

ADDRESS
UCSF
Innovation Ventures

CONTACT
Tel:
innovation@ucsf.edu

CONNECT
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600 16th St, Genentech Hall, S-272,
San Francisco,CA 94158

https://innovation.ucsf.edu
Fax: