

Novel compositions and methods for targeted replacement of endogenous T-cell receptor with a chimeric antigen receptor

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TECHNOLOGY DESCRIPTION

This invention is a method for targeted and high-efficiency replacement of the endogenous T-cell receptor (TCR) with a chimeric antigen receptor (CAR) by introducing a Cas9 and guide RNA (gRNA) ribonucleoprotein (RNP) that targets a genomic break to the endogenous T-cell receptor alpha constant chain (TRAC) locus. The depletion of TCR-positive cells by magnetic beads enriches the cells which have both the CAR knockin and TCR knockout. Also cells, which are modified successfully by homology-directed-repair (HDR) through minimizing non-homologous-end-joining (NHEJ)-mediated TCR knockout by the selection of gRNA targets that do not disrupt protein-coding regions, are enriched. A set of HDR templates, which use recombinant adeno-associated virus (rAAV) or ssDNA/dsDNA Cas9 “shuttle” hybrid templates, is adapted along with selected gRNA targets that stimulate high-efficiency HDR with reduced disruption of endogenous TCR expression in the absence of HDR.

PATENT STATUS

| Country | Type | Number | Dated | Case |
|------------------------|-----------------------|----------------|------------|----------|
| Japan | Issued Patent | 7834651 | 03/13/2026 | 2020-206 |
| Australia | Published Application | WO 2021/183884 | 09/16/2021 | 2020-206 |
| Canada | Published Application | WO 2021/183884 | 09/16/2021 | 2020-206 |
| China | Published Application | WO 2021/183884 | 09/16/2021 | 2020-206 |
| Israel | Published Application | WO 2021/183884 | 09/16/2021 | 2020-206 |
| Mexico | Published Application | WO 2021/183884 | 09/16/2021 | 2020-206 |
| Brazil | Published Application | | | 2020-206 |
| European Patent Office | Published Application | | | 2020-206 |

Additional Patents Pending

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OTHER INFORMATION

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Disease: Autoimmune and Inflammation
 - ▶ Disease: Cancer
 - ▶ Gene Therapy
 - ▶ Therapeutics

RELATED CASES

2020-206-0

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