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# Novel Cell Therapy for CTLA4 Haploinsufficiency

Tech ID: 33012 / UC Case 2021-282-0

## INVENTION NOVELTY

Scientists have developed a CRISPR-Cas9 based genome editing method for universal correction of disease-causing mutations in the CTLA4 gene, which most commonly manifest as a Primary Immunodeficiency. Current treatment involves monthly IV injections or weekly subcutaneous injections of a recombinant CTLA4-Ig fusion protein abatacept. This invention includes one-time infusion of a CTLA4-corrected autologous T cell therapy. The corrected patient cells are generated by ex vivo electroporation of a specific gRNA:Cas9 ribonucleoprotein (RNP) complex and cognate homology-directed-repair template (HDRT) targeting a functional copy of the CTLA4 gene within an intronic region of the endogenous CTLA4 gene. This combination allows for (1) highly efficient knockin (up to 70% in patient cells), (2) cell-type and context specific regulation of CTLA4 expression under natural promoter and regulatory elements, and (3) preservation of endogenous CTLA4 expression in uncorrected cells.

## VALUE PROPOSITION

- ▶ Universal open reading frame replacement strategy can be applied to the vast majority of known CTLA4 mutations.
- ▶ Intronic targeting approach prevents loss of CTLA4 in targeted cells to enhance product safety and activity.
- ▶ Fully non-viral engineering methods reduce manufacturing cost and complexity.
- ▶ Strategies can be applied to a wide variety of alternative inherited immune disorders.

## RELATED MATERIALS

- ▶ [High-yield genome engineering in primary cells using a hybrid ssDNA repair template and small-molecule cocktails](#) - 08/25/2022

## PATENT STATUS

Patent Pending

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### OTHER INFORMATION

#### KEYWORDS

CTLA4 haploinsufficiency,  
  
Primary Immunodeficiency,  
  
Non-viral gene editing,  
  
CRISPR-Cas9, CTLA4,  
  
Autologous T cell therapy

#### CATEGORIZED AS

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

#### RELATED CASES

2021-282-0

