Novel Cell Therapy for CTLA4 Haploinsufficiency

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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 ribonucleoprotien (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

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