GENE EDITING FOR FOXP3 IN HUMAN HSC

Grant Award Details

GENE EDITING FOR FOXP3 IN HUMAN HSC

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-09526

Project Objective: To develop an autologous, gene-modified, HSC cell therapy candidate for treating IPEX Syndrome using CRISPR/Cas9 technology

Investigator:

Name:	Rosa Bacchetta
Institution:	Stanford University
Type:	PI

Disease Focus: Blood Disorders, Immune Disease, IPEX Syndrome

Human Stem Cell Use: Adult Stem Cell

Award Value: $984,228

Status: Active

Progress Reports

Reporting Period: Year 3/NCE

View Report

Grant Application Details

Application Title: GENE EDITING FOR FOXP3 IN HUMAN HSC

Public Abstract:

Research Objective

CRISPR/Cas9 mediated FOXP3 gene editing in patient-derived hematopoietic stem cells as a cure for IPEX syndrome

Impact

FOXP3 mutation in IPEX syndrome leads to immune system dysregulation. Allogeneic HSCT, the only available treatment, has very poor outcomes including GvHD and low immune reconstitution.

Major Proposed Activities

- Demonstrate specificity of targeted insertion of FOXP3 cDNA – ΔNGFR cassette in HD HSCs as assessed by deltaNGFr expression and correct genome integration of the expression cassette.
- Demonstrate that edited HD HSCs maintain their proliferative and differentiation potential in vitro using liquid culture, colony forming cell (CFC) and T cell differentiation assay.
- Reconstitution of immunodeficient (NSG) mice using gene edited human healthy donor HSCs and demonstration of Teff and Treg in vivo development.
- Obtain successful gene editing in IPEX patient HSCs and hu-mouse reconstitution with FOXP3 gene edited HSCs.
- Demonstrate in vivo efficacy by amelioration of IPEX-like phenotypes in hu-mice engrafted with gene edited IPEX HSCs, as compared to those injected with not edited.
- not included

Statement of Benefit to California:

FOXP3 mutation causes dysregulation of Treg and Teff cells leading to immune dysregulation and IPEX syndrome. Using CRISPR/Cas9 gene editing, we will insert a wild type copy of the FOXP3 gene into patient-derived HSCs, enabling pre-clinical proof of concept data for clinical trials that could reduce IPEX patient pathologies. This work will the first-in-man demonstration of the curative potential of edited HSCs and will help maintain California's lead position in Stem Cell research and cure.

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