Defining the Optimal Gene Therapy Approach of Human Hematopoietic Stem Cells for the Treatment of Dedicator of Cytokinesis 8 (DOCK8) Deficiency

Grant Award Details

Defining the Optimal Gene Therapy Approach of Human Hematopoietic Stem Cells for the Treatment of Dedicator of Cytokinesis 8 (DOCK8) Deficiency

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-13415

Project Objective: To develop an autologous, gene modified HSC therapy for treating DOCK (Dedicator of Cytokinesis 8) deficiency

Investigator:

Name:	Caroline Kuo
Institution:	University of California, Los Angeles
Type:	PI

Disease Focus: Blood Disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,386,232

Status: Active

Grant Application Details

Application Title: Defining the Optimal Gene Therapy Approach of Human Hematopoietic Stem Cells for the Treatment of Dedicator of Cytokinesis 8 (DOCK8) Deficiency

Public Abstract:

Research Objective

A new therapeutic option for DOCK8 deficiency using autologous human hematopoietic stem cells modified through either lentiviral gene addition or CRISPR/Cas9 based gene editing.

Impact

Allogeneic HSCT is complicated by comorbidities that can be addressed by autologous stem cell gene therapy. This is relevant for DOCK8 deficiency and can be applied broadly to other genetic diseases.

Major Proposed Activities

- Develop an optimized lentiviral vector gene therapy approach of autologous hematopoietic stem cells for the treatment of DOCK8 deficiency.
- Design a site-specific CRISPR/Cas9-mediated gene editing approach for DOCK8 deficiency.
- Compare the effects of the DOCK8 lentiviral vector gene addition and CRISPR/Cas9 gene editing on hematopoietic stem and progenitor cell survival.
- Assess the repopulating capacity of gene-modified hematopoietic stem and progenitor cells through transplantation into immunodeficient mice.
- Finalize the therapeutic candidate to advance to the next stage of development and initiate assays to characterize the Drug Product.
- Assemble an INTERACT Meeting Package for submission to the FDA to request a consultation to discuss the therapeutic candidate.

Statement of Benefit to California:

Safe, definitive therapies for DOCK8 deficiency represent an unmet medical need. Allogeneic stem cell transplant is frequently complicated by graft-versus-host disease and worsening of pre-existing infections. Demonstration that autologous stem cell gene therapy can safely and effectively cure DOCK8 deficiency will shift the paradigm by which patients will be treated, led by California's position as a leader in the field of gene therapy.
