Non-viral reprogramming of the endogenous TCRα locus to direct stem memory T cells against shared neoantigens in malignant gliomas

Grant Award Details

Non-viral reprogramming of the endogenous TCRα locus to direct stem memory T cells against shared neoantigens in malignant gliomas

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-11036

Project Objective: Modify the endogenous TCRα locus of stem memory T cells to direct against shared neoantigens in malignant pediatric gliomas.

Investigator:

Name:	Hideho Okada
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Brain Cancer, Cancer, Solid Tumors

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $900,000

Status: Active

Progress Reports

Reporting Period: Year 3/NCE

View Report

Grant Application Details

Application Title: Non-viral reprogramming of the endogenous TCRα locus to direct stem memory T cells against shared neoantigens in malignant gliomas

Public Abstract:

Research Objective

We will develop a non-viral gene editing technology to replace the endogenous TCRα locus of stem memory T cells with transgene TCRs that are specific to brain cancer neoantigens.

Impact

Gliomas are lethal tumors often affecting children and young adults. Therapy using Tscm directed to attack truncal neoantigens in these tumors may provide long-lasting protective immunity.

Major Proposed Activities

- Establish and optimize the TCR replacement in CD8+ or CD4+ Tscm with H3.3K27M-specific or IDH1(R132H)-specific TCRs, respectively.
- In vitro evaluation of TCR-replaced Tscm for their functional avidity in comparison to Tscm engineered with the conventional retroviral TCR vector and CRISPR-knock out of endogenous (e)TCR.
- In vivo evaluation of TCR-replaced Tscm cells for anti-glioma effects in comparison with Tscm engineered with the conventional retroviral TCR vector and CRISPR-knock out of eTCR.

Statement of Benefit to California:

In children, brain tumors are the leading cause of cancer-related mortality and morbidity. Furthermore, IDH1-mutant gliomas tend to occur in young adults. Our institution is one of the largest brain tumor centers in the world, developing a number of innovative clinical trials and treating patients primarily from CA. The proposed study will establish a strong basis to develop a novel, safe and effective stem memory T cell therapy for patients with malignant brain tumors, including ones in CA.
