Chimeric Antigen Receptor-Engineered Stem/Memory T Cells for the Treatment of Recurrent Ovarian Cancer

Grant Award Details

Chimeric Antigen Receptor-Engineered Stem/Memory T Cells for the Treatment of Recurrent Ovarian Cancer

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-11107

Project Objective: To identify and validate a lead therapeutic candidate for treating recurrent ovarian cancer, comprising CAR T memory/stem cells that target TAG72 surface antigen with “built-in” cytokine production for enhanced anti-tumor activity.

Investigator:

Name:	Saul Priceman
Institution:	City of Hope, Beckman Research Institute
Type:	PI

Disease Focus: Cancer, Ovarian Cancer, Solid Tumors

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,381,104

Status: Active

Grant Application Details

Application Title: Chimeric Antigen Receptor-Engineered Stem/Memory T Cells for the Treatment of Recurrent Ovarian Cancer

Public Abstract:

Research Objective

We are developing a tumor-associated glycan-targeting CAR T cell with inducible cytokine production that drives T cell stem/memory phenotype and persistence for effective treatment of ovarian cancer.

Impact

25% of ovarian cancer patients recur within 6 months. Targeting cancer stem cells with a persistent progenitor CAR T cell product offers a potent strategy to address this recurrence.

Major Proposed Activities

- Evaluate tumor associated glycan-specific CAR constructs using in vitro studies by varying extracellular and intracellular signaling domains to optimize for potency and selectivity
- Evaluate multiple antigen-binding domains (i.e., scFv) within optimized CAR construct using in vitro studies.
- Assess anti-tumor efficacy of lead CAR candidates in preclinical human xenograft models of serous ovarian cancer.
- Generate a T cell activation-inducible cytokine production, comparing IL-12 and IL-15, for improved T cell functionality, stem/memory phenotype, and persistence using in vitro studies.
- Optimize CAR T cells with 'built-in' inducible cytokine production and identify lead CAR stem/memory T cell therapeutic product using in vitro studies.
- Assess therapeutic efficacy of optimized CAR T cells with 'built-in' inducible cytokine production in preclinical human xenograft models of serous ovarian cancer.

Statement of Benefit to California:

Ovarian cancer is the 5th most common cause of cancer mortality among women with ~10% of the annual diagnoses and ovarian cancer-related deaths in the US occurring in California alone. Fewer than 20% of advanced ovarian cancer patients survive past 5 years. This proposal aims to develop a targeted therapy for patients with recurrent ovarian cancer, which, if successful, would be a major advancement in the fight against this devastating disease and other aggressive cancers.
