BCMA/CS1 Bispecific CAR-T Cell Therapy to Prevent Antigen Escape in Multiple Myeloma

Grant Award Details

BCMA/CS1 Bispecific CAR-T Cell Therapy to Prevent Antigen Escape in Multiple Myeloma

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-11555

Project Objective: To enable an FDA pre-IND meeting for a Bispecific CAR-T Cell Therapy targeting both BCMA and CS1 to Prevent Antigen Escape in Multiple Myeloma.

Investigator:

Name:	Yvonne Chen
Institution:	University of California, Los Angeles
Type:	PI

Disease Focus: Blood Cancer, Cancer, Multiple Myeloma

Human Stem Cell Use: Adult Stem Cell

Award Value: $3,176,805

Status: Active

Grant Application Details

Application Title: BCMA/CS1 Bispecific CAR-T Cell Therapy to Prevent Antigen Escape in Multiple Myeloma

Public Abstract:

Translational Candidate

A single-chain bispecific chimeric antigen receptor (CAR) targeting BCMA and CS1 will be used to in autologous T-cell therapy for multiple myeloma.

Area of Impact

Translational candidate will enable treatment of patients with heterogeneous or BCMA– multiple myeloma and prevent cancer relapse due to antigen loss.

Mechanism of Action

BCMA and CS1 are markers commonly found on multiple myeloma (MM) cells. Here, patient-derived naïve/memory T cells enriched in stem-cell memory phenotype are engineered to express a BCMA/CS1 bispecific chimeric antigen receptor (CAR), which triggers robust T-cell activation and anti-tumor effector function upon recognizing either BCMA or CS1 on the surface of target cells. The bispecific CAR-T cell can efficiently eliminate MM tumor cells even if they had lost expression of either BCMA or CS1.

Unmet Medical Need

Multiple myeloma (MM) is an incurable disease. CAR-T cell therapy targeting BCMA shows clinical promise against MM, but many patients have BCMA-negative tumors or develop BCMA-negative MM after treatment. BCMA/CS1 bispecific CAR-T cells can prevent tumor escape to increase clinical efficacy.

Project Objective

Pre-IND meeting; readiness for GMP manufacturing.

Major Proposed Activities

- Rodent studies to determine optimal T-cell dosing regimen and compare BCMA/CS1 bispecific CAR with bb2121 (a clinically tested single-input BCMA CAR)
- Cell-culture and rodent studies to identify any propensity for the Therapeutic Candidate to cause cytokine release syndrome and off-tumor toxicity
- Demonstration of GMP-compatible cell manufacturing and completion of clinical protocol and internal regulatory filings

Statement of Benefit to California:

Multiple myeloma afflicts >32,000 new patients in the US and leads to >1,200 deaths in California each year. A therapy with robust and durable efficacy against this otherwise incurable disease will not only improve the well-being of Californians, but also reduce the substantial medical costs associated with long-term and ultimately ineffective treatments. This will reduce burden on the state's medical system and enable redirection of resources to other areas of unmet needs.

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