
CAR-Tnm cell therapy for melanoma targeting TYRP-1

Grant Award Details

CAR-Tnm cell therapy for melanoma targeting TYRP-1

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-12258

Project Objective: The goal of the project is to develop Dr Saus' autologous anti TRYP-1 CAR-Tnm product candidate from research grade with early evidence of melanoma disease modifying activity to the pre-IND stage. The current target patient population is those melanoma patients who do not respond to immune checkpoint inhibitors.

This project will involve the following key activities: Technology transfer and scale up of lentiviral vector production

GMP vector production, CAR-T process development and scale up, in vitro safety, in vivo dose response, in vivo preliminary toxicity study and the conduct of three engineering runs, each using a unique donor.

Investigator:

Name:	Cristina Puig Saus
Institution:	University of California, Los Angeles
Type:	PI

Disease Focus: Cancer, Melanoma, Solid Tumors

Human Stem Cell Use: Adult Stem Cell

Award Value: \$5,904,462

Status: Active

Grant Application Details

Application Title: CAR-Tnm cell therapy for melanoma targeting TYRP-1

Public Abstract:**Translational Candidate**

Autologous naïve/memory progenitor T cells genetically modified to express a chimeric antigen receptor targeting the Tyrosinase-related protein 1

Area of Impact

Patient with melanoma, without response or with relapse after immune checkpoint blockade therapy and patients with rare melanoma subtypes.

Mechanism of Action

T cells genetically modified to express the 20D7SL CAR detect and kill melanoma cells with high expression of TYRP-1 (representing ~30% of all melanoma lesions). Our Therapeutic Candidate uses a subset of naïve/memory progenitor T cells (Tnm) with improved ability to engraft and reconstitute a functional memory response compared to fully differentiated T cells. We anticipate that using Tnm cells will lead to a potent and persistent antitumor response.

Unmet Medical Need

Immune Checkpoint Blockade (ICB)-resistant melanoma is an unmet medical need. Despite the success of ICB therapy, 40% of patients with melanoma do not respond, and some responders develop acquired resistance. ICB-resistant melanoma frequency is higher in patients with rare subtypes of melanoma.

Project Objective

Pre-IND meeting

Major Proposed Activities

- Optimize, implement, and validate the Therapeutic Candidate large-scale, GMP-compliant manufacturing and lot release criteria protocols
- Assess safety (selectivity, reactivity in normal tissues, toxicology) and antitumor efficacy (cytotoxicity, cytokine release, tumor growth control).
- Assess feasibility of enrolling patients with rare subtypes of melanoma in the clinical trial, draft clinical protocol and complete pre-IND meeting

Statement of Benefit to California:

In 2021, 11,450 Californians will be diagnosed with melanoma. Around 30% of all cases (3435) will present high levels of TYRP-1 and could potentially benefit from our Therapeutic Candidate. Acral and mucosal melanoma are subtypes of melanoma with higher expression of TYRP-1 and a much lower survival rate than cutaneous melanoma. Their incidence is higher in the Hispanic, Black, and Asian/Pacific Islander populations. This is especially relevant in California, given the diversity of our patients.

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