

## CAR Design Improvements for the Recognition of Low-Density Antigens

### Business Opportunity

Exclusive / Non-exclusive  
license  
Start-up

### Technology Type

Immuno-Oncology  
Cell Therapy

### State of Development

Preclinical in vivo

### Patent Information

US20220401537A1,  
EP4031583A4; patent  
pending

### Investigator

**Stanley Riddell, MD**  
Clinical Research Division,  
Burke O'Reilly Family  
Endowed Chair in  
Immunotherapy

### Tech ID

19-138

### Contact

[partnering@fredhutch.org](mailto:partnering@fredhutch.org)

### Brief Description

Methods and tools to increase CAR-T cell recognition of tumor cells expressing low density antigens

### Technology Overview

Adoptive transfer of CAR-expressing T cells is an effective cancer therapy for a proportion of individuals with B cell malignancies and multiple myeloma, but efficacy is limited by relapses that stem from antigen downregulation or loss. In addition, CAR T cell therapy is also not as effective for solid tumors, where tumor-associated antigens are expressed heterogeneously and at lower levels than hematological malignancies. Thus, enhancing CAR T cell recognition of low-density tumor antigens may both improve initial anti-tumor efficacy and reduce the risk of relapse. Although CARs were designed to mimic T cell receptor (TCR) signaling, natural TCRs have 100-fold greater sensitivity for recognition of peptide major histocompatibility antigen complexes. Members of the Riddell lab reasoned that comparing TCR and CAR signaling events might guide rationale adaptations to CAR design that improve antigen sensitivity. They studied the similarities and differences between TCR and CAR recognition-induced signaling and identified key TCR signaling intermediates not activated by CAR stimulation. They show that the addition of key domains into existing CAR structures improves CAR-T cell recognition of tumor cells expressing low amounts of surface antigen.

### Applications

- This platform technology can be incorporated into existing CAR structures to fine tune their activity against a range of tumor-associated antigens

### Advantages

- Increased efficacy of CAR-expressing T cell therapies, especially in disease states where efficacy is limited by downregulation or heterogeneous/low expression of tumor associated antigens.

### Market Overview

The global immuno-oncology market was valued at \$62.2 billion USD in 2020, and is projected to have a CAGR of about 15% from 2021 - 2028.