SELECTIVE CONTROL AND TUNING of CHIMERIC AGONIST RECEPTORS (CARs) ACTIVITY for CELL-BASED IMMUNOTHERAPY

Tech ID: 24753 / UC Case 2013-025-0

INVENTION NOVELTY

An On-switch engineering method to increase safety and efficacy of cell-based therapies by allowing ongoing *in vivo* control of CARs activity in patients

VALUE PROPOSITION

A major class of targeted cell-based immunotherapy for cancer and autoimmune diseases involves the use of genetically modified human T cells expressing Chimeric Antigen Receptors (CARs). CAR-modified immune cells can have toxic effects, either through reaction with normal cells that also express the target antigen or though systemic hyperimmune stimulation. Thus there is a major need to pharmacologically control the response of CAR-modified cells after administration to the patient.

The current invention provides the additional advantages:

- Specific tuning of the CARs activity by varying dose of the small-molecule drug
- Specific temporal control of CAR activity by varying time course of drug administration
- Specific targeting of CAR activity by varying distribution of drug
- Reduce on-target toxicities and hyperimmune response toxicities; improve treatment efficacy
- Compatible with a wide range of CARs and activation agents
- Improved safety, tunability and efficiency compared to apoptosis-based safety switches for eliminating CAR T cells (adoptive cell transfer therapy can be tuned instead of aborted; mutation of switch will not lead to constitutively active T cells)

TECHNOLOGY DESCRIPTION

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OTHER INFORMATION

KEYWORDS

Chimeric antigen receptors, CARs, Cell-based therapy, Cancer, Modulation, T-cells

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Therapeutics

RELATED CASES

2013-025-0

Scientists at the University of California San Francisco developed a method to design split Chimeric Antigen Receptors (CARs) including an extracellular antigen recognition, a transmembrane, and an intracellular signaling domain for pharmacologically conditional switch-on via a small-molecule drug. In other words, the on-switch CAR expressing immune cells as delivered to patients are rendered inactive until the small-molecule is present. Then, the customized antibody portion of CARs binds to an antigen of interest on a target tumor cell surface. Upon antigen engagement, the intracellular signaling domain will activate the immune cell resulting in the release of cytolytic molecules to induce tumor cell death.

APPLICATION

Development of therapeutics requiring conditional activation of synthetic receptors

LOOKING FOR PARTNERS

To develop and commercialize this technology for a tunable cell-based immunotherapy

STAGE OF DEVELOPMENT

Preclinical

RELATED MATERIALS

- Manuscript available under CDA/NDA

DATA AVAILABILITY

In vitro data

PATENT STATUS

Country	Type	Number	Dated	Case
Australia	Issued Patent	2023204612	08/07/2025	2013-025
United States Of America	Issued Patent	12,371,466	07/29/2025	2013-025
Rep Of Korea	Issued Patent	10-2813881	05/23/2025	2013-025
Japan	Issued Patent	7676476	05/02/2025	2013-025
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United States Of America	Issued Patent	9,587,020	03/07/2017	2013-025
European Patent Office	Published Application	4303232	01/10/2024	2013-025

Canada	Published Application	2013-025

Additional Patents Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- A Chimeric Receptor Platform for Combinatorially Modulating Control of Cell Activities
- A Novel Method to Functionally Screen Pooled Libraries of Synthetic, Genetically-encoded Signaling Molecules and Systems

ADDRESS

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