# Intracellular-Ligand-Responsive Cytotoxic Molecules For Selective T-Cell Mediated Cell Killing

Tech ID: 27500 / UC Case 2015-382-0

## SUMMARY

UCLA researchers in the Department of Chemical and Biomolecular Engineering have developed a novel immunotherapeutic strategy that uses a selectively-activated cytotoxic molecule to enable tumor-specific T cell-mediated killing.

## BACKGROUND

A promising area of clinical investigation in a variety of cancer types involves the adoptive transfer of T cells that have been engineered to express tumor-targeting chimeric antigen receptors (CARs). CAR-T cells target and kill cells expressing surface markers that are recognized by the expressed CAR. Despite widespread enthusiasm for the potential of CAR-T cell therapy, significant safety concerns remain. In particular, off-target and on-target/off-tumor toxicities have led to multiple patient deaths in clinical trials. Most cell surface markers are not exclusively tumor-specific, leading to collateral damage on healthy cells. Therefore, there exist an unmet need for CAR-T cell treatment methods that minimize on-target/off-tumor as well as off-target side effects through increased precision in distinguishing tumor cells from healthy tissues.

## INNOVATION

Dr. Chen and colleagues at UCLA have developed a novel system to enable T cells to interrogate the intracellular environment of a potential target cell prior to triggering target-cell apoptosis. Specifically, the researchers have engineered a synthetic cytotoxic molecule that remains inactive until it encounters a tumor-associated antigen inside a cancerous cell. Following initial recognition of the cancerous cell based on surface-marker expression, T cells deliver the functionalized cytotoxic molecule into the target cell, where the molecule remains dormant until it encounters an intracellular tumor antigen. Recognition of the cancerous antigen activates the cytotoxic molecule and induces target cell death. When used in conjunction with CAR-T cell therapy, this system provides a two-step verification of cancerous cells. This technology has the potential to significantly improve the safety profile of CAR-T cell therapy by reducing on-target/off-tumor, as well as off-target, toxicities.

## APPLICATIONS

- Broad therapeutic potential in oncology (leukemia, lymphoma, and solid tumors)
- Potential use in conjunction with CAR-T cell therapy
- Combinatorial use with less-specific surface antigens (e.g., HER2 and carcinoembryonic antigen (CEA)) that could otherwise cause significant toxicity in adoptive T cell therapy

## ADVANTAGES

Reduced off-tumor T cell-mediated toxicity (leading to reduced side effects) by providing a two-step verification process for targeted cells

## STATE OF DEVELOPMENT

*In vitro* work has demonstrated selective, antigen-specific activity of the cytotoxic molecule when functionalized.

## PATENT STATUS

| Country | Type | Number | Dated | Case |
|---|---|---|---|---|
| United States Of America | Issued Patent | 12570968 | 03/10/2026 | 2015-382 |
| European Patent Office | Issued Patent | 3234120 | 09/03/2025 | 2015-382 |
| Unitary Patent | Issued Patent | 3234120 | 09/03/2025 | 2015-382 |
| Canada | Issued Patent | 2,971,186 | 08/12/2025 | 2015-382 |

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## INVENTORS

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## OTHER INFORMATION

### KEYWORDS

Cancer immunotherapy, genetic engineering, cytotoxic, intracellular, chimeric antigen receptor T-cells (CAR-T cells), T-cell therapy, protein engineering, cytotoxic proteins

### CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Gene Therapy
  - Stem Cell
  - Therapeutics

### RELATED CASES

2015-382-0

Additional Patents Pending

## ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Single-Chain Bispecific Chimeric Antigen Receptor Targeting BCMA And CS1 For The Treatment Of Multiple Myeloma
- Transforming Growth Factor-Beta (TGF-β)-Responsive Single-Chain Variable Fragments And Chimeric Antigen Receptors
- Il-6 Receptor Alpha-Binding Protein And Its Use In Controlling Cytokine Release Syndrome In Immunotherapy



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