Single-Chain Bispecific Chimeric Antigen Receptor Targeting BCMA And CS1 For The Treatment Of Multiple Myeloma

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SUMMARY

UCLA researchers in the Department of Chemical and Biomolecular Engineering have developed a single-chain bispecific chimeric antigen receptor targeting BCMA and CS1 for treating multiple myeloma.

BACKGROUND

Multiple myeloma (MM) is a cancer of the plasma cells that accounts for over 30,000 new diagnoses each year, according to the American Cancer Society. Despite the availability of therapeutics ranging from monoclonal antibodies to proteasome inhibitors, MM is incurable regardless of the patient's age and pre-diagnosis health status. Two surface antigens found on MM cells are B-cell maturation antigen (BCMA) and CS1. Several clinical trials have shown that chimeric antigen receptors (CARs) targeting BCMA can achieve complete remission in MM treatment. However, relapses caused by the outgrowth of tumor cells with downregulated BCMA expression have been reported. To address this challenge of antigen escape, a dual-CAR strategy, where T cells are engineered to co-express anti-BCMA and anti-CS1 CAR, has been demonstrated. However, this strategy poses manufacturing challenges due to the large genetic footprint that is necessary to encode for two CARs in one cell.

INNOVATION

UCLA researchers have developed single-chain bispecific CARs that simultaneously target BCMA and CS1 for MM treatment. BCMA/CS1 bispecific CARs with varying targeting efficiencies were developed for an ideal pairing selection that can achieve therapeutic efficacy while avoiding common pitfalls such as antigen escape and fratricide. The single-chain architecture minimizes the DNA footprint required to encode the CAR, thus generating bispecific CAR-T cells with significantly higher efficiency than the dual-CAR strategy. Both *in vitro* and *in vivo* data show that the bispecific BCMA/CS1 CAR-T cells can effectively target wildtype MM tumors as well as MM mutant cells that have lost either BCMA or CS1 expression.

APPLICATIONS

- CAR-T therapy for multiple myeloma
- Therapeutic for BCMA and CS expressing cancers

ADVANTAGES

- Achieves therapeutic efficacy while avoiding common pitfalls such as antigen escape and fratricide
- Single-chain architecture minimizes the DNA footprint required to encode the CAR
- Can effectively target wildtype MM tumors as well as MM mutant cells that have lost either BCMA or CS1 expression
- Can control MM xenografts *in vivo*

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	2021/023028	07/29/2021	2018-680
European Patent Office	Published Application	3806871	04/21/2021	2018-680
China	Published Application	112566643A	03/26/2021	2018-680

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OTHER INFORMATION

KEYWORDS

Multiple myeloma, leukemia, immunotherapy, chimeric antigen receptors, T-Cell therapy, B-cell maturation antigen, CS1, bispecific CARs

CATEGORIZED AS

- **Medical**
  - Disease: Blood and Lymphatic System
  - Therapeutics

RELATED CASES

2018-680-0

Additional Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Il-6 Receptor Alpha-Binding Protein And Its Use In Controlling Cytokine Release Syndrome In Immunotherapy

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