Dual-Antigen Targeting CAR-T Therapy for Acute Myeloid Leukemia (AML)

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TECHNOLOGY DESCRIPTION

We present a novel bicistronic chimeric antigen receptor (CAR)-T therapy designed to target two AML-specific antigens, CD70 and active integrin β2 (aITGB2). Utilizing an OR-gated logic, this therapy is engineered to recognize either antigen independently, significantly expanding tumor coverage while avoiding off-tumor toxicity against healthy hematopoietic stem and progenitor cells (HSPCs). The therapy incorporates a unique combination of costimulatory domains—CD28 and 4-1BB—on separate CARs, which synergistically enhance CAR-T expansion, persistence, and efficacy. Our innovative ex vivo co-culture system restores physiologic surface protein expression on frozen AML samples, enabling accurate preclinical profiling and validation of target antigens.

Competitive Advantages

High Efficacy Against AML Tumor Heterogeneity: The dual-targeting CAR-T approach targets >90% of AML blasts, addressing antigen-negative relapse risks often observed with single-target therapies.

Minimal Off-Tumor Toxicity: CD70 and aITGB2 are largely absent from healthy HSPCs and other normal tissues, avoiding the severe cytopenias and toxicities associated with other AML CAR-T therapies.

Enhanced CAR-T Performance: The bicistronic design combines CD28 and 4-1BB costimulatory domains for superior early proliferation and long-term persistence, with peak CAR-T expansion outperforming single-antigen CARs in vivo.

Clinically Translatable Workflow: The ex vivo co-culture system restores target antigen expression on frozen AML samples, enabling scalable testing and validation for future clinical applications.

Prevention of Antigen-Negative Relapse: OR-gated targeting ensures robust tumor control even in diverse AML antigen landscapes, as validated in murine and patient-derived xenograft (PDX) models.

Safety Validation: Rigorous preclinical testing shows no toxicity against healthy HSPCs, including colony-forming assays that confirm safety during hematopoietic differentiation.

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OTHER INFORMATION

KEYWORDS

Acute Myeloid Leukemia, CAR-T, CD70, active integrin beta2, aITGB2

CATEGORIZED AS

- Medical
  - Disease: Cancer
  - Therapeutics

RELATED CASES

2025-245-0, 2023-176-0

STAGE OF DEVELOPMENT

This dual-antigen CAR-T therapy is currently in advanced preclinical development. It has demonstrated:

- **In vitro efficacy:** Potent cytotoxicity against AML cell lines and primary patient samples.
- **In vivo validation:** Superior tumor clearance and extended survival in murine models of AML antigen heterogeneity and PDX models.
- **Safety testing:** No observed toxicity against healthy HSPCs in co-culture assays.

RELATED MATERIALS

- Bicistronic CAR T-cells Against CD70 & Active Integrin ß2 Overcome Antigen Heterogeneity and Preserve Safety in Acute Myeloid Leukemia - 09/21/2025

PATENT STATUS

Patent Pending

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