



Anti-CLL1 binding agents for AML therapy

Technology Offer

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Category

Therapy

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Preclinical

Seeking

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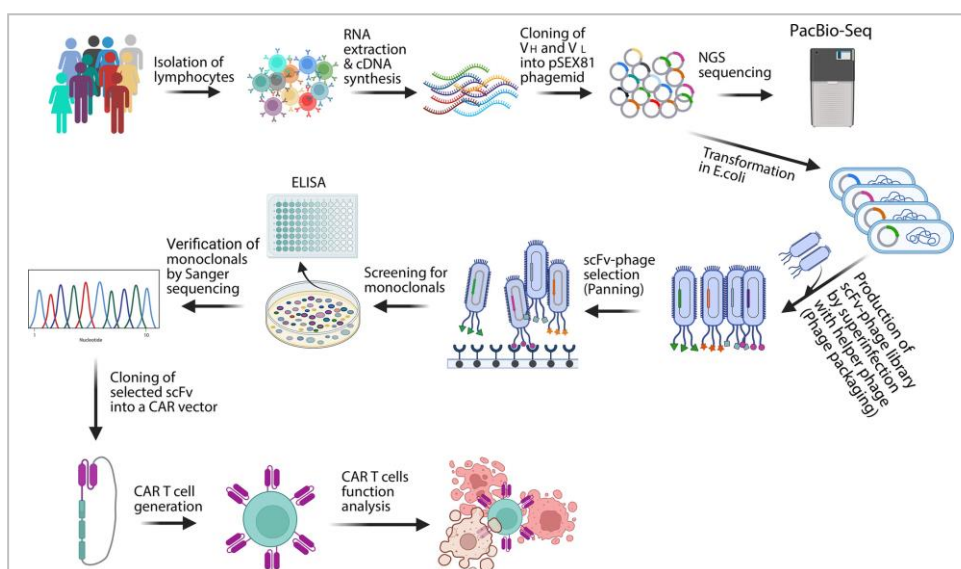


Fig. 1: A rapid, one-stop platform - encompassing scFv library generation with samples of cured AML patients, scFv identification, and CAR T cell generation - was used to generate anti-CCL1 binding agents.

Background

Acute myeloid leukemia (AML) is one of the most common types of adult acute leukemia characterized by the rapid growth of immature blood cells (“blasts”) in the bone marrow and blood. Typically, AML is initially treated with chemotherapy, sometimes along with a targeted therapy drug. Targets for therapeutic intervention in AML include antigens such as C-type lectin like molecule 1 (CLL1), which is an antigen frequently overexpressed on most acute myeloid leukemia stem cells compared to normal hematopoietic stem cells or other cell types.

Antibodies and antibody fragment-mediated targeted immunotherapy offers a promising alternative to traditional chemotherapy. While the FDA has approved seven CAR T cell therapies incorporating scFvs for hematologic malignancies, none exists yet for myeloid leukemia.

Contact

ScienceValue Heidelberg GmbH
Berliner Straße 47 | 69120 Heidelberg | Germany
+49 (0)6221 - 567435 | www.sciencevalue-heidelberg.de/en
ScienceValue-Heidelberg@med.uni-heidelberg.de



Technology

Based on samples of cured AML patients

A single chain variable fragment (scFv) library containing over 45 million unique clones was generated from samples of cured AML patients, followed by a process integrating scFv identification and subsequent CAR T cell generation (see Fig. 1).

Novel anti-CLL1 binding agents

Using this new approach, scFvs specific for CLL1 were identified and employed to engineer CAR T cells that demonstrated potent in vitro and in vivo toxicity against CLL1-positive tumor cells.

In vitro cytotoxicity: CLL1-target specificity

A short-term 2-day coculture experiment showed that these CAR T cells effectively eradicated CLL1-positive tumor cells MV4-11, but had no impact on CLL1-negative K562 cells. Notably, K562 cells, which are CD33-positive, could be targeted and destroyed by CD33-directed CAR T cells.

In vivo cytotoxicity: Reduced tumor burden and improved survival rates

NSG mice engrafted with zsGreen MV4-11 were treated with non-transduced T cells (non Td) and anti-CLL1 CART cells. Tumor cells were monitored weekly using bioluminescent imaging (BLI). Fourteen days after injection, three mice from the non-transduced T cell group had died already, while all six mice in the anti-CLL1 CAR T cell-treated group had survived and displayed rather low tumor cell levels.

Summary

These results collectively demonstrate that the scFv platform was successfully used to generate anti-CLL1 CAR T cells incorporating an anti-CLL1 binding domain, which effectively target CLL1-expressing tumor cells both in vitro and in vivo.

Benefits

- Patient-derived anti-CLL1 binding agents
- High target specificity and confirmed in vivo efficacy

Applications

- Cancer treatment
- Acute myeloid leukemia (AML) therapy
- Personalized immunotherapy

Publications

- Liu Y, Lauk A, Sedloev D, Brysting J, Cetin E, Liu C, Mönning M, Luft T, Yun H, Schmitt M, Sauer T, Zhou F, Rohde C, Müller-Tidow C. Integrated scFv identification and CAR T cell generation for AML targeting in vivo. *Int J Cancer*. 2025 Oct 2. doi: [10.1002/ijc.70146](https://doi.org/10.1002/ijc.70146).

Contact

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