Docket #: S23-403

Trivalent CAR-T Cells for Targeting of Cancerous Hematopoietic Cells

Stanford scientists have developed a trivalent CAR T cell that targets three proteins that are essential for self-renewal and differentiation of leukemic stem cells. These CAR T cells can also effectively traffic to the bone marrow by overexpressing a relevant chemokine receptor. The use of these CAR T cells to treat acute myeloid leukemia could enable full disease eradication.

Leukemia is one of the most common types of cancers in children and teens, but disease outcomes are generally poor with a survival rate of ~50% and disease relapse being a common issue. A reason for high relapse rates with current therapies is the persistence of residual cell with tumor-initiating capacity, often referred to as leukemic stem cells. These cells have been shown to perpetuate and maintain leukemia and standard chemotherapies that target leukemia tend to minimally effect leukemic stem cells. Hence, new therapies that can target leukemic stem cells are necessary to improve leukemia outcomes and enable full disease eradication.

A trivalent CAR T cell that overexpresses a chemokine receptor to enhance targeting to the bone marrow was developed that showcased broad cytotoxicity to leukemia cell lines. Importantly, the trivalent CAR T cells could also kill hematopoietic stem cells and progenitors, leukemic stem cells, and leukemic blasts in vitro. Consequently, this establishes proof-of-concept that a trivalent CAR T cell can be utilized to eradicate leukemia in cancer patients.

Stage of Development:
Pre-clinical

Applications

- Treatment of leukemia and other blood cancers

- Development of more efficacious CAR T-cell therapies

Advantages

- Enhanced killing of leukemic cells by using a trivalent CAR
- Overexpression of a chemokine receptor enhances targeting to the bone marrow

Publications

- Quenton Rashawn Bubb, Mohammad Balood, Gabe Eduardo Seir, Leah Swartzrock, Ethan Haslett, Katie Ho, Peng Xu, Saida G. Wiltz, Elena Sotillo, Tanja A. Gruber, Rebecca M. Richards, Crystal L. Mackall, Agnieszka Czechowicz. Development of multivalent CAR T cells as dual immunotherapy and conditioning agents. *Molecular Therapy Oncology*, Volume 33, Issue 1, 2025, 200944, ISSN 2950-3299.

Patents

- Published Application: WO2025213182

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