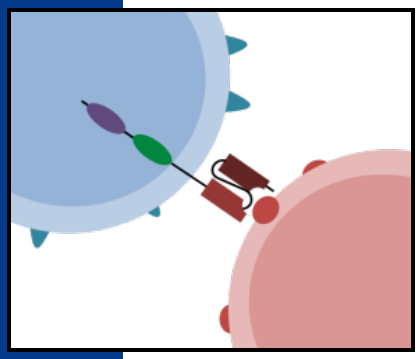
CD99 Targeting Chimeric Antigen Receptor Expressing T cell (CAR-T) for Acute Myeloid Leukemia Immunotherapy



A chimeric antigen receptor-expressing T cell that targets and kills CD99 expressing cancers such as acute myeloid leukemia (AML). The CAR construct works by using a novel anti-CD99 scFv region to enable T cell targeting of CD99 expressing cancer cells and T-cell activation by incorporating co-stimulator and intracellular signaling regions. CD99 is a tumor associated antigen over-expressed on AML blasts and leukemic stem cells. CD99's low or absent expression on normal hematopoietic stem cells makes it an attractive target for therapy as fewer adverse side effects are expected.

COMMERCIAL OPPORTUNITY

- AML is a type of blood cancer where the bone marrow makes abnormal myeloblasts. AML accounts for nearly one-third of all new leukemia cases each year. The American Cancer Society estimates that in 2017 there will be 21,380 patients who develop AML and 10,590 AML patients will die.
- The standard of care for AML treatment has changed little over the past four decades. Intensive chemotherapy followed by hematopoietic stem cell transplantation remains the most effective treatment. However, most newly diagnosed elderly patients are ineligible for intensive chemotherapy, and there are no effective second line treatments for patients with relapse/refractory disease. As a result, the 5-year overall survival rate is 27%, and is less than 10% for patients over age 60.
- CD99 is a promising target as it is aberrantly expressed in AML patients, where about 85% of leukemic stem cells express high levels of CD99 while expression is low or absent on normal hematopoietic stem cells. A recent pre-clinical study shows that a monoclonal antibody against CD99 has anti-leukemic activity in xenograft mouse models. Nanovalent Pharmaceuticals is planning Phase I trials in AML and other cancers to test their CD99-directed Antibody Drug Conjugates (ADCs): NV101 (doxorubicin-anti-CD99) and NV103 (irinotecan-anti-CD99).
- The marketplace is attractive for CAR-T development, as Novartis received approval in August 2017 for Kymriah, its anti-CD19 CAR-T therapy for pediatric B-cell ALL. The trial had an overall response rate of 82.5% (52/63). Although the list price for Kymriah is $475,000 for a one-time treatment, Novartis has said only those patients who respond by the end of the first month will need to pay. In October 2017, Gilead's Yescarta, an anti-CD19 CAR-T, was approved for large B-cell lymphoma and is listed at $375,000. In 2017, Gilead acquired Kite Pharma for $11.7B, and in 2018, Celgene has agreed to acquire Juno Therapeutics for $9B. Juno is also developing a CD-19 CAR-T therapy.

TECHNOLOGY

Anti-CD99 sequences were identified by a next generation sequencing screening coupled with a monoclonal antibody producing procedure. scFv VH domains and scFV VL domains were selected as polypeptide candidates. *In vitro* experiments showed that co-culturing CD99 positive cancer cells with Jurkat T cells transduced with synthetic anti-CD99 scFv regions elicited T-cell activation where the percentages of activated T-cells were measured by IFN-γ levels using flow cytometry.

PUBLICATION/PATENT

- Provisional Patent filed on January 8, 2018 for Dr. Davila.

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