

Abstract title: BISPECIFIC CEA/CD30-CAR T CELLS EXHIBIT SUPERIOR EFFICACY IN CEA+/CD30- GASTRIC CARCINOMA XENOGRAFT MODEL IN VIVO

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Abstract text:

Chimeric Antigen Receptor (CAR) T cells targeting solid tumors face significant challenges due to early exhaustion, often linked to immune checkpoint molecules. Previous research demonstrated that bispecific CAR T cells, targeting CD30—a TNFR superfamily member—exhibit superior in vitro effectiveness compared to CEA-specific CAR T cells. This study investigated whether inhibiting CD30 could enhance CAR T cell efficacy in vivo.

We transduced CEA- or CEA/CD30-specific second-generation CARs into primary human T lymphocytes using a retroviral method, achieving 50% to 70% transduction efficiency. Then, 30 NSG mice were xenotransplanted with 3 million CEA+/CD30-/ff.Luc+ N87 gastric tumor cells. On day 14, mice were treated with three different doses (250k, 500k, 1M) of either monospecific or bispecific CAR T cells. Tumor progression was monitored biweekly for 73 days using bioluminescence imaging. Non-transduced T cells served as a negative control.

We found that conventional CAR T cells did not achieve complete remission, whereas bispecific CAR Ts eradicated all tumors within a month, regardless of dose. To assess the impact of CD30 inhibition on effector cell persistence, 15 cured animals were retransplanted with CEA+ and CEA- colon carcinoma cells. After three weeks, the volume of the CEA+ tumors were significantly lower, indicating the persistence of CAR T cells.

In conclusion, bispecific CAR T cells outperformed their monospecific counterparts, effectively limiting CEA+ tumor progression upon reinoculation. These findings suggest CD30 plays a crucial role in modulating T cell functions, and suppressing CD30 could improve CAR T cell efficacy.