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703.CELLULAR IMMUNOTHERAPIES: BASIC AND TRANSLATIONAL

Evaluation of CD70 Chimeric Antigen Receptor T (CAR-T) Cells As a Potential Treatment for Non-Hodgkin's Lymphoma: A Preclinical Study

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Background :CD70 is a member of the tumor necrosis factor (TNF) superfamily. While its expression is limited in healthy tissues, CD70 highly constitutive expressed on cell surface of various malignancies. This expression profile make CD70 a promising target for cancer immunotherapy. We described a CD70 CAR-T based on a potent VHH nanobody named 11C9 in treatment of renal cell carcinoma (RCC). Recently, we received approval to initiate a phase I clinical study by Center for Drug Evaluation, National Medical Products Administration (NMPA) in China. Motivated by promising evidence that CD70 aberrantly expressed on Non-Hodgkin's lymphoma (NHL), including diffuse large B-cell lymphomas, follicular lymphomas, Burkitt and mantle cell lymphomas, we conducted a preclinical evaluation of CD70 CAR-T cells as a potential treatment by preclinical model.
Method: We successfully generated CD70 CAR-T cells based on a VHH nanobody (11C9) and CD19 CAR-T cells based on murine scFv (FMC63) following the exact manufacturing protocols used for phase I and phase II clinical trial products respectively. Then, we evaluated CAR-T cell cytotoxicity, phenotype, proliferation, and cytokine production *in vitro*. Furthermore, we established NHL tumor cell-xenograft NOG mice models to compare their anti-tumor activity *in vivo*.
Result: *In vitro* test demonstrated two types of CAR-T cells have comparable proliferation, and cytokine production. We observed more potency for CD70 CAR-T to kill CD70 and CD19 double positive Raji cells than CD19 CAR-T cells. *In vivo* test showed that both CD70 CAR-T cells and CD19 CAR-T cells eradiated Raji cells xenografted NOG mice models at high dose. However, after treated at lower dose CD19 CAR-T, tumor relapsed in one week when the same lower dose CD70 CAR-T treated mice keeping tumor free statue.
Conclusion: Our results indicate that CD70 CAR-T cell is potential treatment for NHL. We will conduct an investigation of single and dual CD70 CAR-T on treatment of lymphoma especially for CD19 negative NHL.

Disclosures Jiang: *Shanghai HRAIN:* Current Employment. **Xiong:** *Shanghai HRAIN:* Current Employment. **Yuan:** *Shanghai HRAIN:* Current Employment. **Zhang:** *Shanghai HRAIN:* Current Employment. **Shen:** *Shanghai HRAIN:* Current Employment. **Wang:** *Shanghai HRAIN:* Current Employment. **Gong:** *Shanghai HRAIN:* Current Employment.

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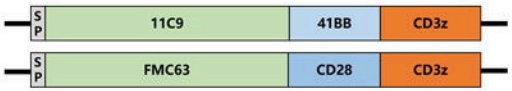

Figure 1: Scheme of CD19 and CD70 CAR-T.

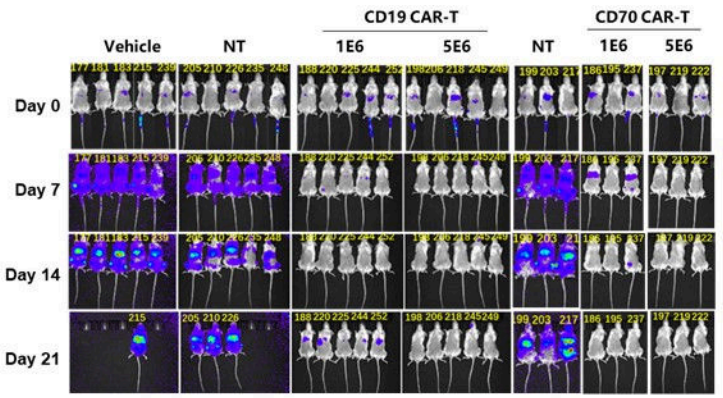

Figure 2: Evaluation of CAR-T cell *in vivo* functionality in a Raji Xenograft model.

Figure 1