ENGINEER OFF-THE-SHELF NKT CELLS FOR CANCER IMMUNOTHERAPY

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Background Cell-based immunotherapy has emerged as a promising approach in disease treatment, necessitating the development of readily available 'off-the-shelf' cell products that can be manufactured at scale. Invariant natural killer T (iNKT) cells have shown potential as ideal cell carriers for allogeneic cell therapy, as they possess potent anti-cancer/virus properties without the risk of graft-versus-host disease (GvHD).1–4 However, the scarcity of endogenous iNKT cells in healthy donor blood poses a challenge.

Methods Here we present a novel strategy combining hematopoietic stem cell (HSC) gene engineering and ex vivo differentiation to produce high-yield, high-purity allogeneic HSC-engineered iNKT (AlloHSC-NKT) cells that closely resemble endogenous iNKT cells.

Results Our investigation focuses on three key aspects of AlloHSC-NKT cells: 1) Evaluating their antitumor capacity and exploring their multiple tumor targeting mechanisms; 2) Assessing their antiviral activity, particularly against the SARS-CoV-2 virus; 3) Investigating their immunoregulatory potential, with a specific emphasis on their ability to ameliorate GvHD. Furthermore, we explore the potential for enhancing the tumor-targeting capabilities of AlloHSC-NKT cells through chimeric antigen receptor (CAR) engineering, as well as reducing their immunogenicity by gene editing to ablate surface human leukocyte antigen (HLA) molecules.

Conclusions Collectively, these preclinical studies provide compelling evidence for the feasibility and therapeutic potential of AlloHSC-iNKT cell products and support their translation into clinical and commercial development.1–4

REFERENCES

Ethics Approval Healthy donor human PBMCs were obtained from the UCLA/CFAR Virology Core Laboratory, without identification information under federal and state regulations. Patient bone marrow samples were collected following UCLA IRB approval (IRB#15–000062).

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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