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THE CXCR3ALT-CXCL11 CHEMOKINE SYSTEM FOR THERAPEUTIC USE IN SOLID CANCER

Keywords: CAR, immunotherapy, solid tumor, CXCR3alt, CXCL11, biomarker, chemokine system, CONAN

INVENTION NOVELTY

The invention comprises a novel strategy for enhancing Chimeric Antigen Receptor (CAR) T cell migration and infiltration into solid tumors by incorporating the CXCR3 chemokine system into CAR T cells, thereby amplifying antitumor efficacy of therapeutic T cells and improving survival rates.

VALUE PROPOSITION

The technology aims to develop CAR T cell therapies for solid tumors, a promising approach in precision medicine. The challenge lies in the targeted delivery of CAR T cells into the tumor as solid tumors often lack appropriate chemokine signals, making infiltration and functional activation difficult for CAR T cells. This technology proposes the incorporation of the CXCR3 chemokine system into CAR T cells to control their activation and migration.

Key findings reveal a correlation between the abundance of CXCR3alt and CXCL11 in the tumor and high levels of tumor-infiltrating T cells, improved survival, and response to chemotherapy. The approach, termed "CONAN", holds promise for enabling the production of effective therapeutic products against a wide range of solid tumors and could be extended to other immune cells, thereby amplifying its therapeutic benefit (Fig. 1).

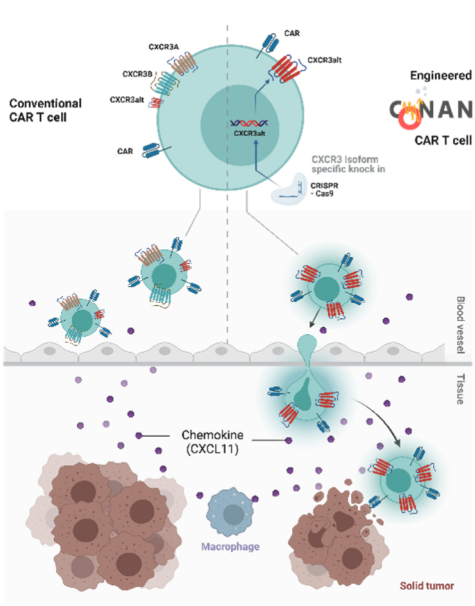

Fig. 1: Targeted adaptation of a homing chemokine system for chimeric antigen receptor (CAR) T-cell products: CONAN (Schmück-Henneresse Lab)

TECHNOLOGY DESCRIPTION

In a study of a cohort of 46 bladder cancer (BC) patients, researchers identified the intra-tumoral CXCR3-chemokine system as a critical component for chemotherapy-induced tumor eradication. Analysis of CD8+ T cell populations revealed the presence of stem cell memory (SCM) T cell subpopulations with high CXCR3alt expression that exhibit co-stimulatory activity specifically induced by the CXCL11 ligand. The technology involves the development of a protocol for autologous cell transfer and underscores the necessity of a complete CD4+ helper T cell pool for CD8+ TSCM expansion. Among all CXCR3 ligands, only CXCL11 was found to induce migration and activation of TSCMs, highlighting it as a potential therapeutic target.

DEVELOPMENT STATUS

The CONAN strategy and its derivative CAR T cell approaches are being developed for a broad range of applications and are currently under evaluation in preclinical models, including patient-derived lung cancer organoids.

COMMERCIAL OPPORTUNITY

In-licensing or collaboration for further development

PATENT SITUATION

Patents are pending in US, EP and CN with priority of January 2021.

FURTHER READING

Vollmer et al. (2021), Sci. Transl. Med. 13:eabb3735.

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