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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).

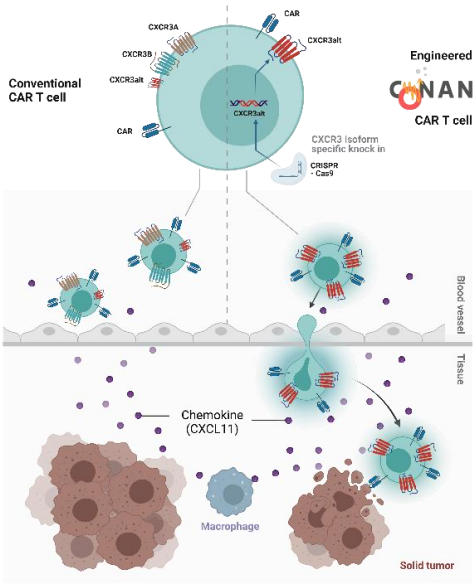

Fig. 1: Targeted adaptation of a homing chemokine system for chimeric antigen receptor (CAR) T-cell products: CONAN (Schmück-Henneresse Lab)

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

A PCT application was filed in 2022 (WO2022152767A3).

FURTHER READING

- Vollmer T, et al. The intratumoral CXCR3 chemokine system is predictive of chemotherapy response in human bladder cancer. Sci Transl Med. 2021 Jan 13;13(576): eabb3735.
- https://www.bihealth.org/en/research/research-group/schmueck-henneresse-lab-experimental-immunotherapy

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