Technology Offer

Ref.-No. M05/24

Exploring the CXCL16/CXCR6 as a potential biomarker and therapeutic target in CAR T cell-associated neurotoxicity

Introduction

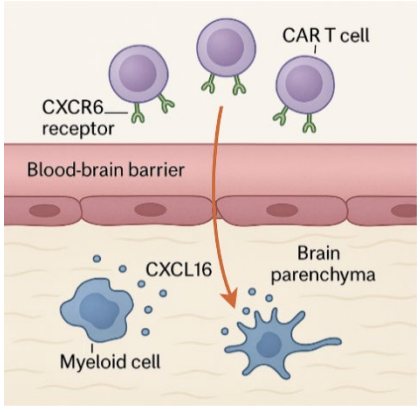
Several chimeric antigen receptor T cells (CAR T cell) and bispecific antibody therapies are approved for cancer treatment. Although the treatments are highly effective, they can induce severe adverse effects including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), which can potentially be lethal. Diagnosing ICANS is challenging and predicting which patients are at risk to develop ICANS is still impossible. This limits the applicability of CAR T cells and bi-specific antibodies and options for de-risking.

Invention

The study of the inventors identifies the CXCL16/CXCR6 axis as a contributory factor in ICANS pathophysiology, pointing to the recruitment and activation of cytotoxic CXCR6+CD4 CAR T cells by CXCL16-expressing myeloid cells in the CNS as a potential pathway driving neuroinflammation. This insight provides a foundation for potentially using this axis as a biomarker for disease severity and a therapeutic target.
The present invention possibly enables the diagnosis, prognosis, stratification and/or monitoring of progression of neurotoxicity in a subject, by determining an increased level of at least one biomarker selected from the group consisting of CXCR6 and CXCL16 in the biological sample compared to a control sample in the subject. Further, the present invention also relates to a diagnostic kit for conducting the method of the present invention. Moreover, the present invention is directed to a therapeutic agent for use in a method of treating or preventing neurotoxicity in a subject. The present invention is also directed to a method for evaluating the treatment response of a subject who received a therapy for treating neurotoxicity.

Advantages of the invention

The inventors showed that the activation and recruitment of CAR T cells to the brain during ICANS may be driven by CXCL16/CXCR6 interaction, providing CXCR6 as a potential diagnostic marker and new therapeutic target for ICANS.



CXCL16/CXCR6-mediated recruitment of CAR T cells across the blood-brain barrier (BBB) during ICANS.
CAR T cells expressing the chemokine receptor CXCR6 are attracted toward the brain parenchyma by CXCL16 secreted by CNS myeloid cells. This interaction may facilitate the transmigration of CAR T cells across the blood-brain barrier (BBB), contributing to neuroinflammation observed in ICANS.

Areas of application
Diagnostics, Biomarker, Therapeutic Target

Keywords
CAR T cell therapy, ICANS

Development Status
Proof of concept

Commercial Opportunity
The technology is offered for in-licensing and co-development

Patent Status
Application filed in Europe

Publication
Lu et al., Genome Med 17, 71 (2025), „The CXCL16/CXCR6 axis is linked to immune effector cell-associated neurotoxicity in chimeric antigen receptor (CAR) T cell therapy", doi.org/10.1186/s13073-025-01498-6

Contact

Clinic Invent
Medical Faculty
University of Münster
Albert-Schweitzer-Campus 1,
Building D3
48149 Münster, Germany

Dr. Elke Benkhart
clinic-invent@uni-muenster.de
www.clinic-invent.de