Dr. med. Julia Unglaub & Dr. rer. nat. Dominic Alexej Depke

Engineering and optimization of CD96-specific CAR T cells: Advancing a novel immunotherapeutic strategy for patients with acute myeloid leukemia without HSPC toxicity

© UKHD

Junior Clinician Scientist
nTTP-GCT-Cohort 2026

Sauer Group
Department of Hematology, Oncology and Rheumatology
HEIDELBERG UNIVERSITY HOSPITAL

Fields of Research:

- Immunotherapy and cellular therapies in acute leukemia
- Engineering and optimization of CAR modified immune effector cells
- Early phase clinical trials and translational trial development in AML

Contact:

julia.unglaub@med.uni-heidelberg.de

© UKHD

Translational Scientist
nTTP-GCT-Cohort 2026

Sauer Group
Department of Hematology, Oncology and Rheumatology
HEIDELBERG UNIVERSITY HOSPITAL

Fields of Research:

- Technology & process development
- Cell therapies
- Genome editing
- Acute myeloid leukemia
- Hereditary disorders

Contact:

dominic.depke@uni-heidelberg.de

Project Description:

Acute myeloid leukemia (AML) is a severe malignancy of the hematopoietic system with an overall poor prognosis. Despite multiple therapeutic innovations, 5-year overall survival remains at only around 30–35%, and more than half of patients relapse after an initial response to therapy. Outcomes are particularly poor in patients who experience relapse after allogeneic hematopoietic stem cell transplantation.

Chimeric antigen receptor (CAR) T-cell therapy has revolutionized the treatment of CD19-positive malignancies, achieving impressive response rates in patients with B-cell acute lymphoblastic leukemia (B-ALL) and selected B-cell non-Hodgkin lymphomas (NHLs).

In contrast, AML is a highly heterogeneous disease, and it has proven challenging to identify a shared AML-specific surface antigen that is robustly expressed on AML cells but absent, or only minimally expressed, on normal hematopoietic stem and progenitor cells (HSPCs) and other healthy tissues.

The type I transmembrane receptor CD96 is expressed on leukemic blasts and, in particular, on leukemic stem cells (LSCs) in a substantial proportion of AML cases (40%), while being largely absent from normal HSPCs. Its dual role as an immune checkpoint receptor and its restricted expression pattern make CD96 an attractive target for CAR T-cell therapy, which is the focus of this project.

Using our CAR warehouse platform, we will generate in parallel a broad panel of structurally diverse CD96-directed CAR T-cell variants and functionally screen them *in vitro* to identify potent CAR T-cell constructs. Lead candidates will subsequently undergo *in vivo* validation, and we will establish a GMP-compliant manufacturing process at the GMP facility of Heidelberg University Hospital.

The results of this project are intended to be translated into a clinical trial evaluating CD96-specific CAR T-cell therapy in patients with AML.

GCT
National Strategy
Gene- and Cell-Based Therapies
Promotion of Translational Talents

Dr. med. Julia Unglaub & Dr. rer. nat. Dominic Alexej Depke

Engineering and optimization of CD96-specific CAR T cells: Advancing a novel immunotherapeutic strategy for patients with acute myeloid leukemia without HSPC toxicity