

Digital Molecular Medicine Approaches for Immunomonitoring Strategy Development and Improvement of Patient Care in Engineered Adoptive Cell Therapy

Dr. Ulrike Weirauch, Co-Head of Bioinformatics Unit | Fraunhofer IZI
SaxoCell Conference 03.06.2026

Conflict of interest



Nothing to declare

CAR T cell therapy leads to unprecedented response rates in hematological malignancies



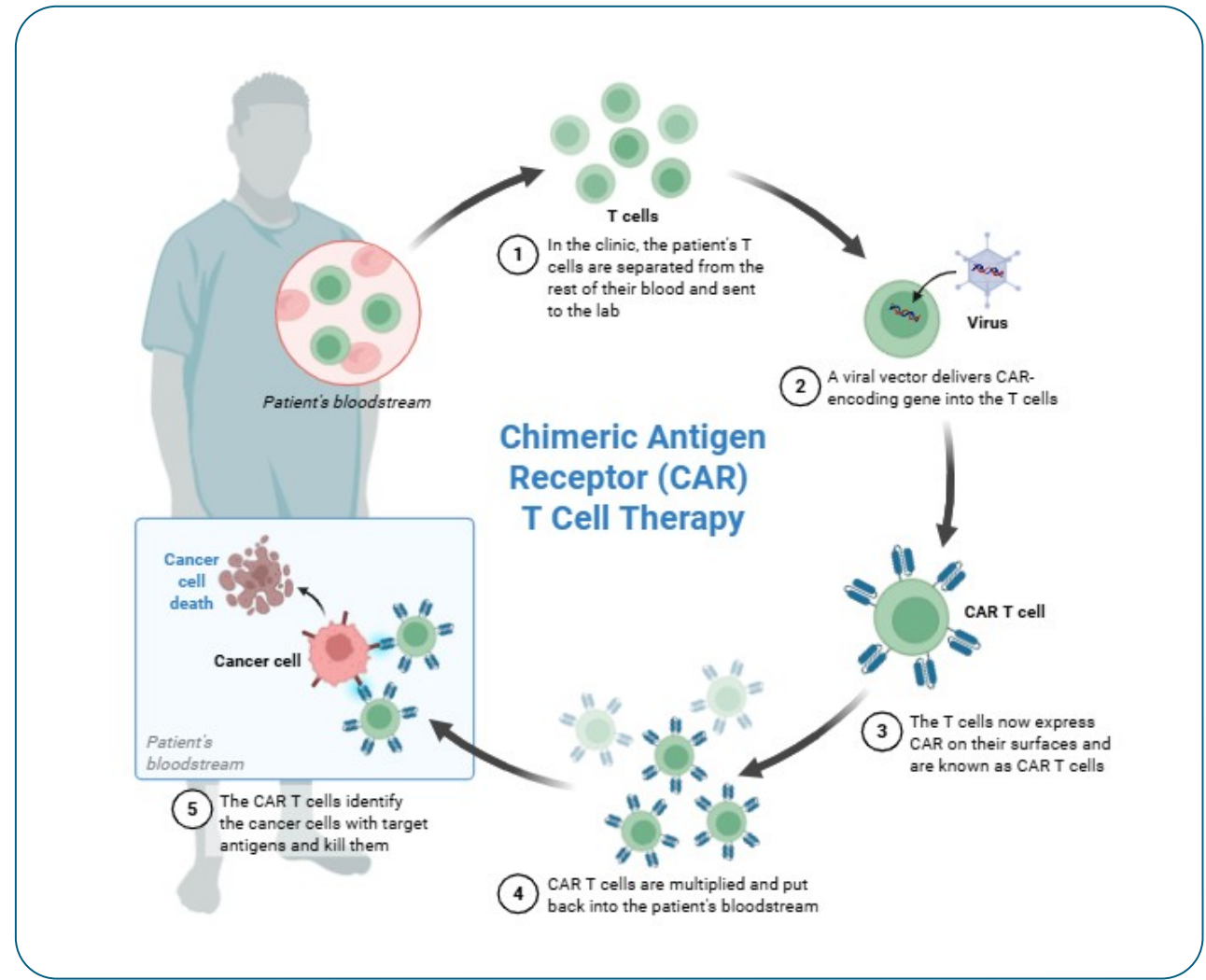
7 products on European market



Approved for hematological malignancies

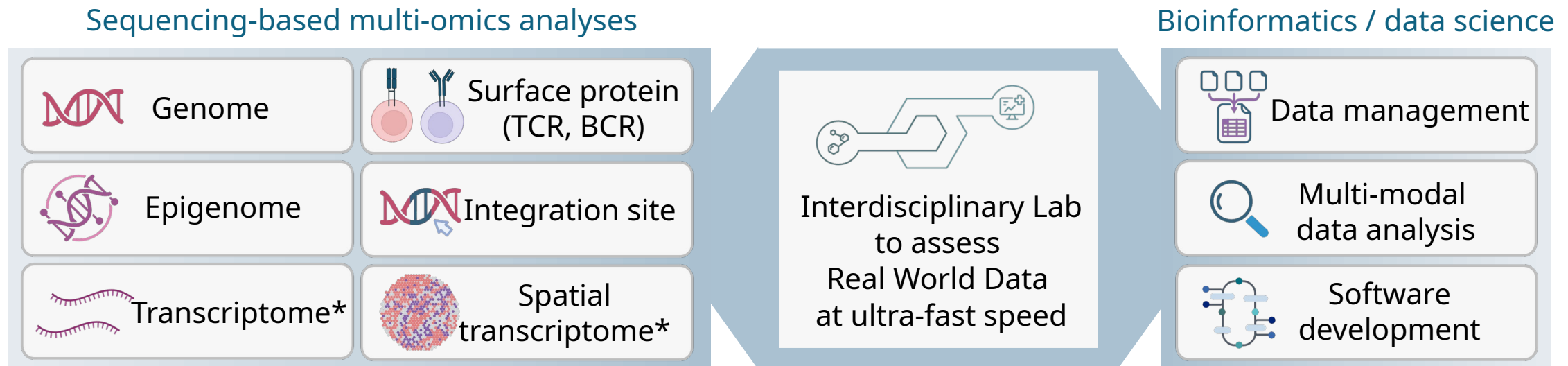


Products are autologous CAR T cells





Immunomonitoring using NGS-based multi-omics and biomedical AI



CERTOMICS: data processing pipeline tailored to single cell multi-omics and CAR-engineered cells

OXFORD
ACADEMIC

Bioinformatics

JOURNAL ARTICLE

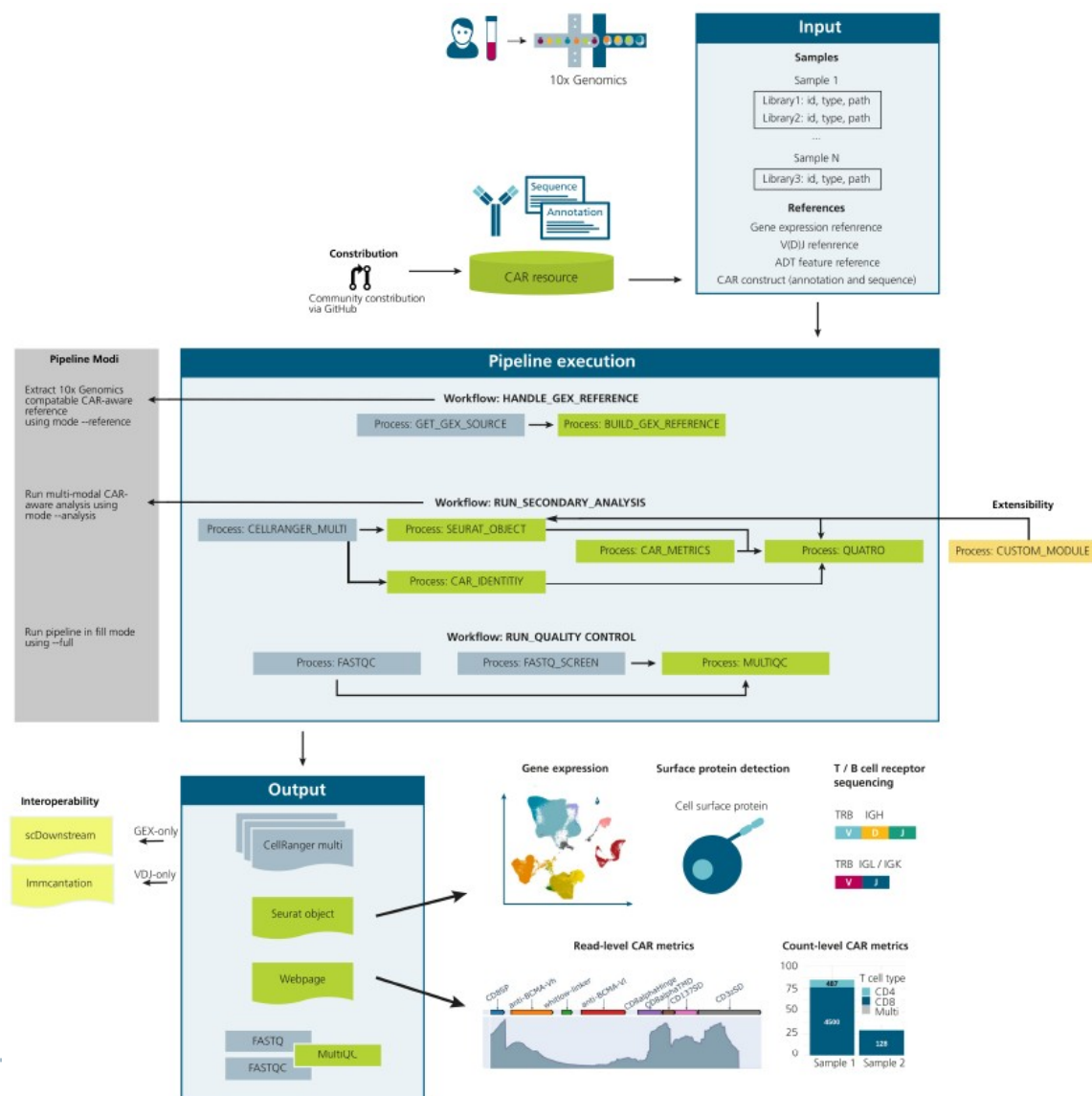
CERTOMICS: trusted single-cell multiomics pipeline for high-resolution profiling of adoptive cellular immunotherapies

Christina Katharina Kuhn ✉, David Schmidt, Michael Rade, Josephine Selke, U Sandy Tretbar, Maximilian Merz, Jan Grau, Kristin Reiche

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<https://doi.org/10.1093/bioinformatics/btag096>

Published: 25 February 2026 Article history ▾



Immunomonitoring gives in-depth insights and creates detailed knowledge



MoA CAR T cells – molecular and cellular signatures of efficacy and toxicities



Information on product and patient, changes over time



Regulatory-compliant software engineering to advance clinical biomarker discovery



Cohort-level information and ultra-personalized medicine



Fields of application: patient stratification, donor selection, preclinical studies, first-in-human / clinical studies

Immunomonitoring of a real-world cohort

Cohort of 61 patients, CAR T cell products: ide-cel or cilta-cel

Cancer Cell

Available online 4 December 2025

In Press, Corrected Proof ? What's this?

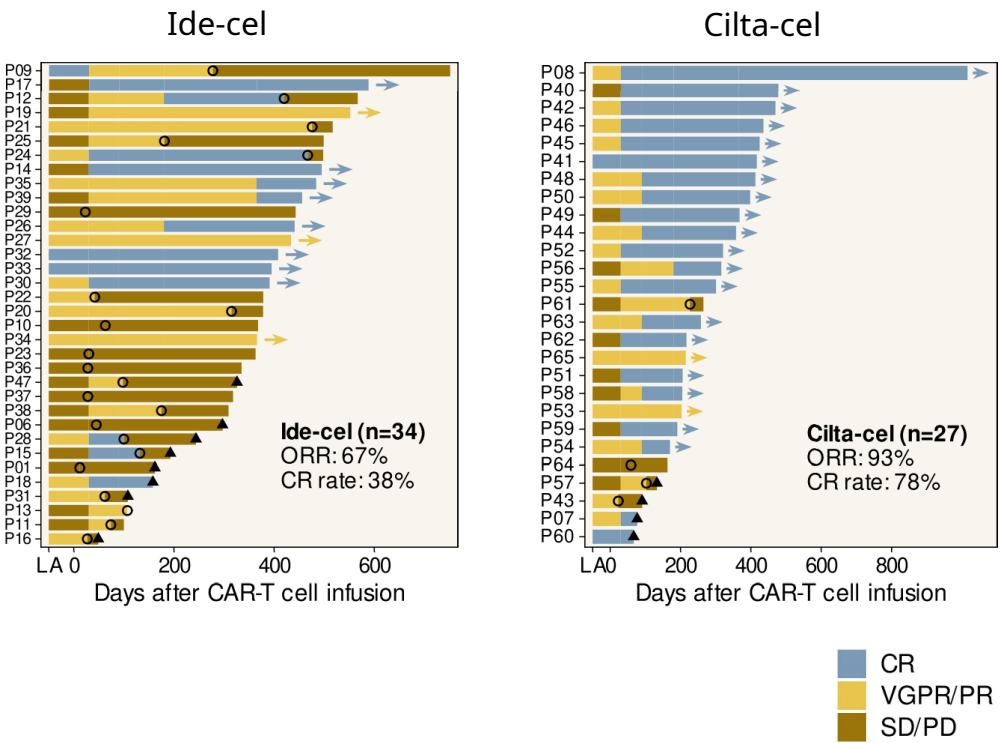
Article

A longitudinal single-cell atlas to predict outcome and toxicity after BCMA-directed CAR T cell therapy in multiple myeloma

Michael Rade ^{1 17}, David Fandrei ^{1 2 13 17}, Markus Kreuz ^{1 17}, Sabine Seiffert ³, Anja Grahner ³, Maik Friedrich ³, Thomas Wiemers ^{2 13}, Patrick Born ^{2 13}, Luise Fischer ^{2 13}, Heike Weidner ⁴, Lorenz C. Hofbauer ⁴, Ronny Baber ^{5 6}, Song Yau Wang ^{2 13}, Enrica Bach ^{2 13}, Sandra Hoffmann ^{2 13}, Jonathan Scolnick ⁷, Mirco Friedrich ⁸, Farid Keramati ⁹, Peter Brazda ^{9 10}, Zsolt Sebestyen ^{10 11}... Maximilian Merz ^{1 2 13 16 18 19 * ✉}



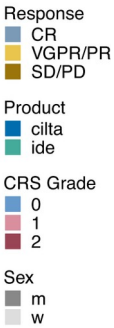
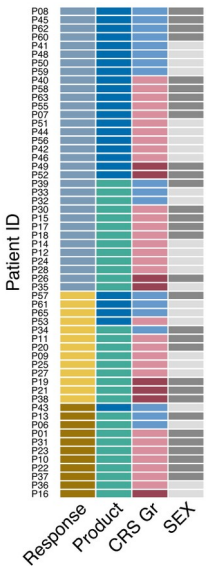
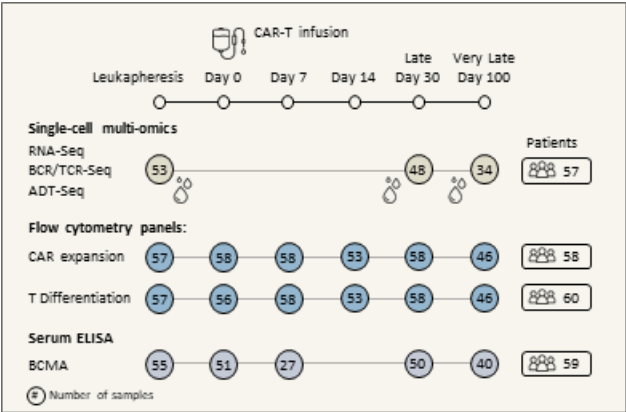
Cilta-cel compared to ide-cel led to **higher complete response rates (78% vs 38%)**



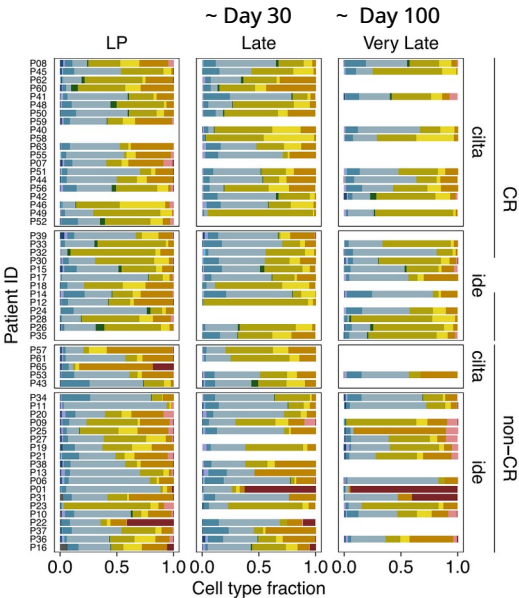
Immunomonitoring of a real-world cohort

137 peripheral blood samples across 57 patients and 3 time points

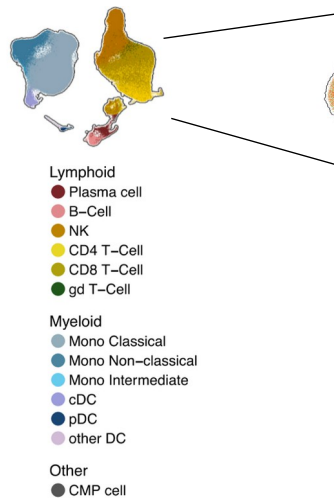
Sample setup



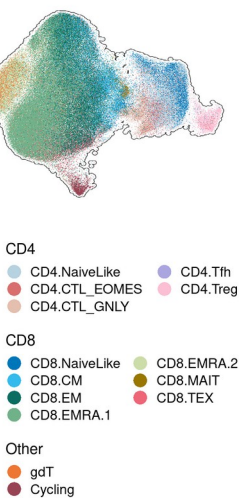
Cell type composition for each sample



Coarse level cell type annotation



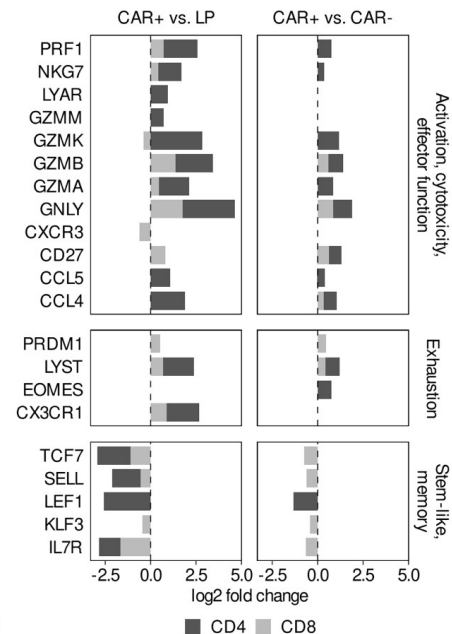
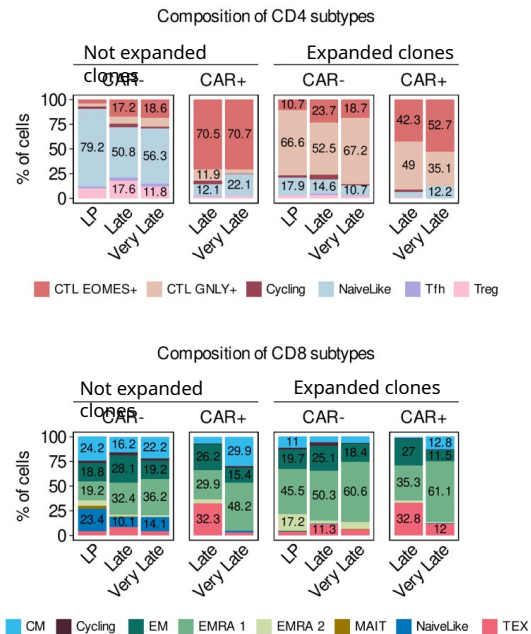
T cell subtypes



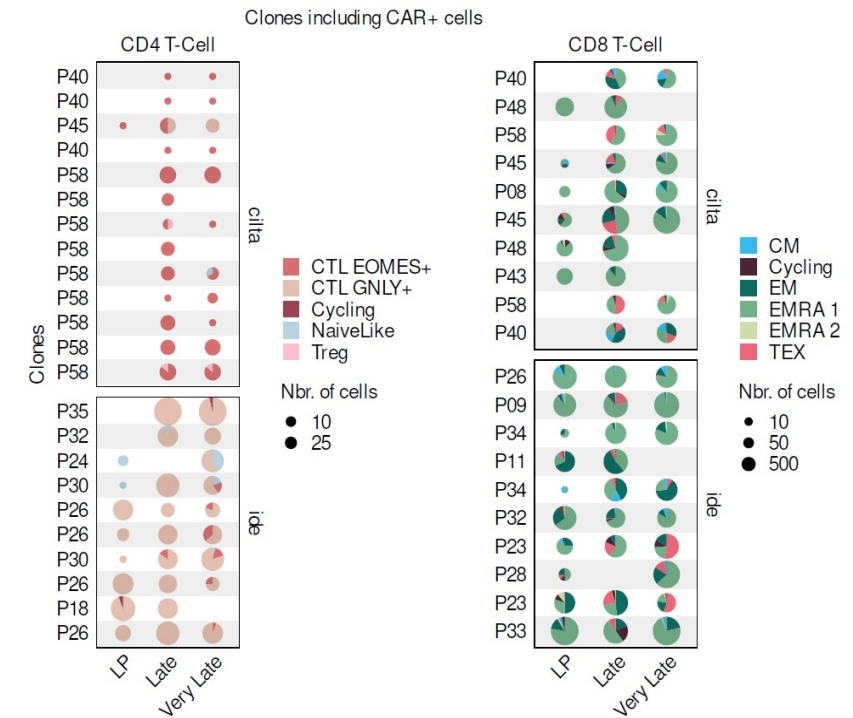
Characterization of cell composition and transcriptional programs

Real-world cohort – CAR T cell phenotypes

CAR-T cells exhibit an **effector-like phenotype** with upregulation of cytotoxicity genes



Top CAR containing clones revealed differences in phenotypes of expanded CD4+ clones (TCR-Seq)



Real-world cohort – major clinical take-aways

- Time-dependent impact of immune cell type abundance on PFS.
- TCR repertoire and its dynamics are important to predict outcomes and side effects
- Cilta-cel induces expansion of CD4⁺ cytotoxic CAR T cells driving tumor killing
- Clonal cytotoxic CD4⁺ T cells link also to severe CRS and prolonged cytopenia
- sBCMA is a great marker to predict and monitor response

Multiomic profiling of T cell lymphoma after therapy with anti-BCMA CAR T ultra-personalized molecular diagnostics

Patient received cilta-cel and talquetamab for RRMM; developed leukemic peripheral T cell lymphoma with cutaneous / intestinal involvement 9 months after CAR T

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Article | Published: 21 February 2025

Multiomic profiling of T cell lymphoma after therapy with anti-BCMA CAR T cells and GPRC5D-directed bispecific antibody

[Till Braun](#), [Michael Rade](#), [Maximilian Merz](#) , [Hanna Klepzig](#), [Florian Große](#), [David Fandrei](#), [Nhu-Nguyen Pham](#), [Markus Kreuz](#), [Christina Katharina Kuhn](#), [Florian Kuschel](#), [Dennis Löffler](#), [Jörn Meinel](#), [Eva Heger](#), [Viola Schweinsberg](#), [Natali Pflug](#), [Uwe Platzbecker](#), [Michael Hallek](#), [Udo Holtick](#), [Ulrike Köhl](#), [Christof Scheid](#), [Kristin Reiche](#), [Marco Herling](#) & [Tim Richardson](#)

[Nature Medicine](#) **31**, 1145–1153 (2025) | [Cite this article](#)

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Manuscript under review

Multimodal Profiling Reveals Actionable Vulnerabilities in CAR T-Derived T-Cell Lymphoma

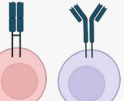
Till Braun^{1,*}, Christina Katharina Kuhn^{2,3,*}, Julia Bischoff⁴, Markus Kreuz^{2,3}, Hanna Klepzig¹, Verena Konetzki⁵, David Fandrei^{2,3,4,6}, Markus Glaß⁷, Jörn Meinel⁶, Anja Grahner⁹, Amel Chebel¹⁰, David Armisen¹⁰, Christian Becker¹¹, Kerstin Becker¹¹, David Stahl¹, Dennis Jungherz⁴, Theresa Schönrade¹, Christoph Kämpf^{2,3}, Dennis Löffler^{2,3}, Nhu-Nguyen Pham^{2,3}, Roland Ullrich¹, Ulrike Köhl^{2,3,6,9,12}, Natali Pflug¹, Tim Richardson¹, Udo Holtick¹, Christof Scheid¹, Michael Hallek¹, Maik Friedrich⁹, Stefan Hüttelmaier⁷, Laurent Genestier¹⁰, Alexandra Schrader¹⁰, Michael Hudecek^{2,5}, Sabrina Friedel⁵, Kristin Reiche^{2,3,6,9,12,13**}, Marco Herling^{4,5,**}, Maximilian Merz^{2,4,6,14,**}

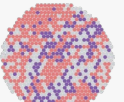
In-depth characterization of T cell lymphoma

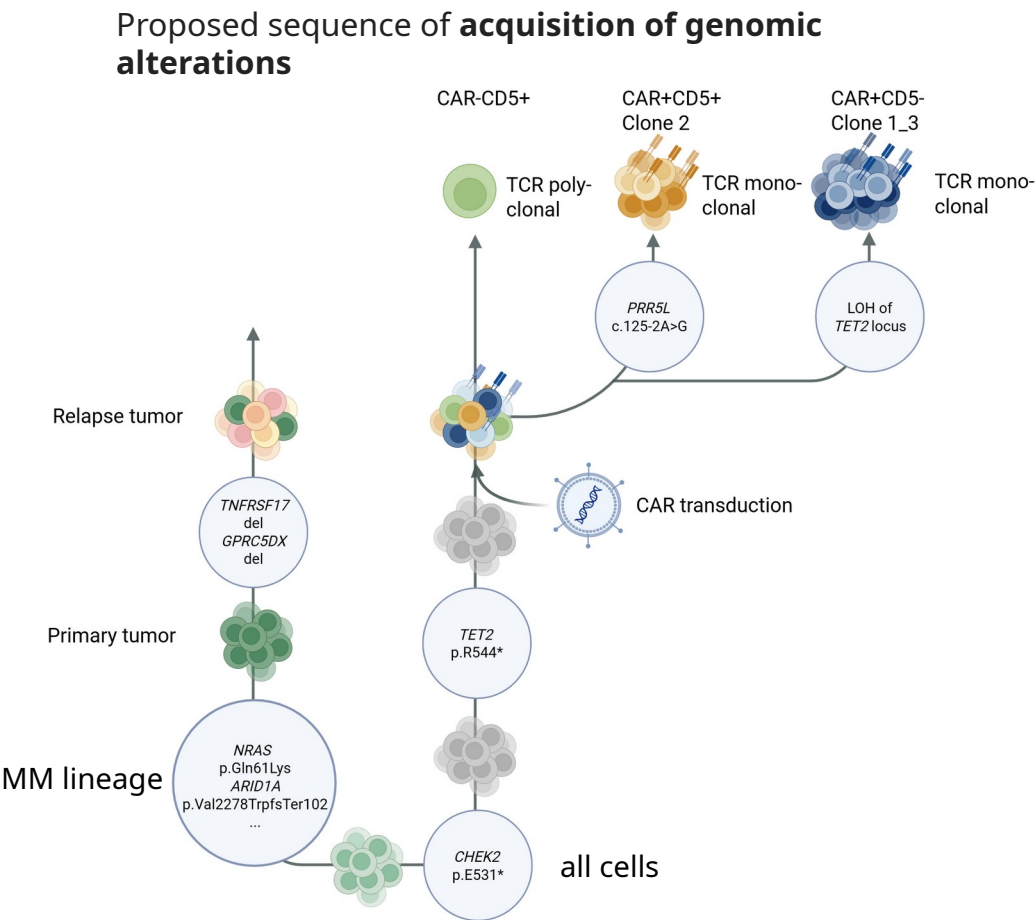
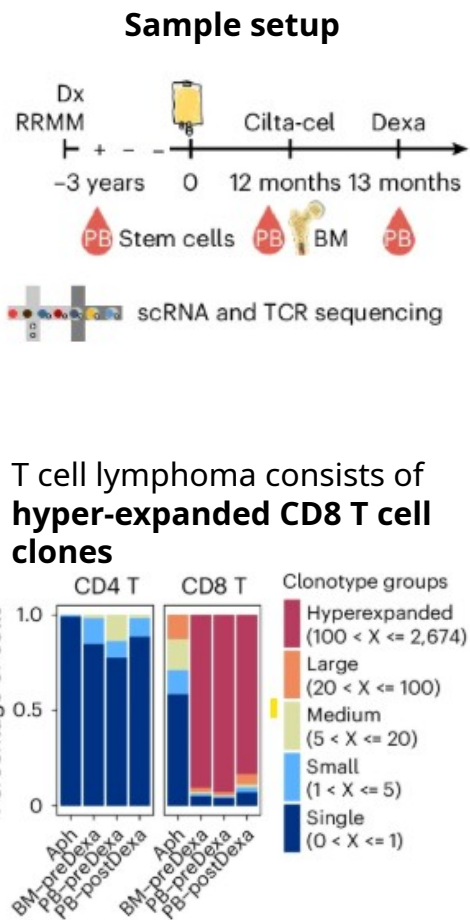
 **Genome**

 **Integration site**

 **Transcriptome**

 **Surface protein
(TCR, BCR)**

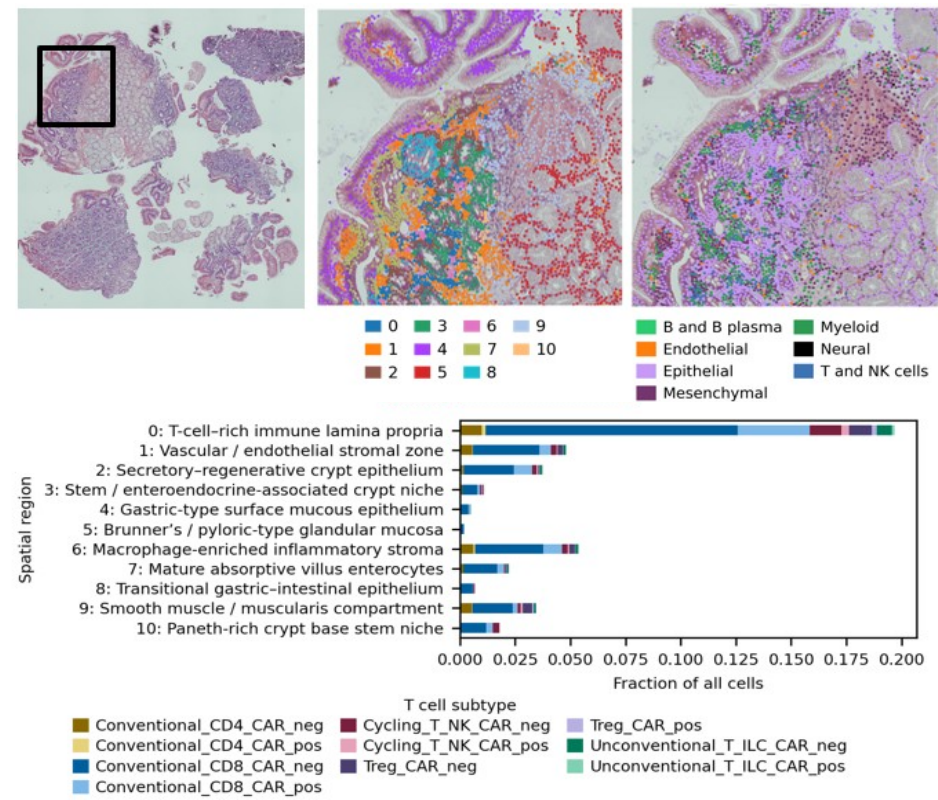
 **Spatial
transcriptome**



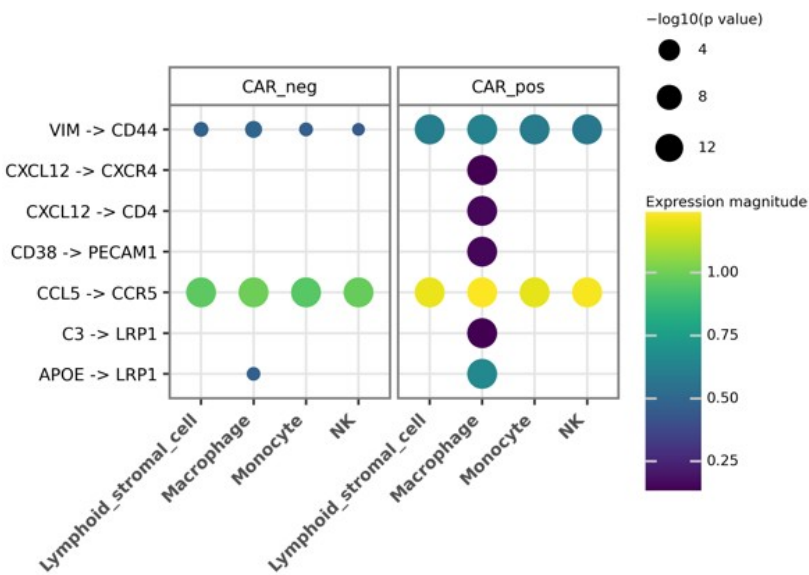
Spatial analysis of T cell lymphoma sites

Manifestation in skin and duodenum

T cell lymphoma homing to duodenum

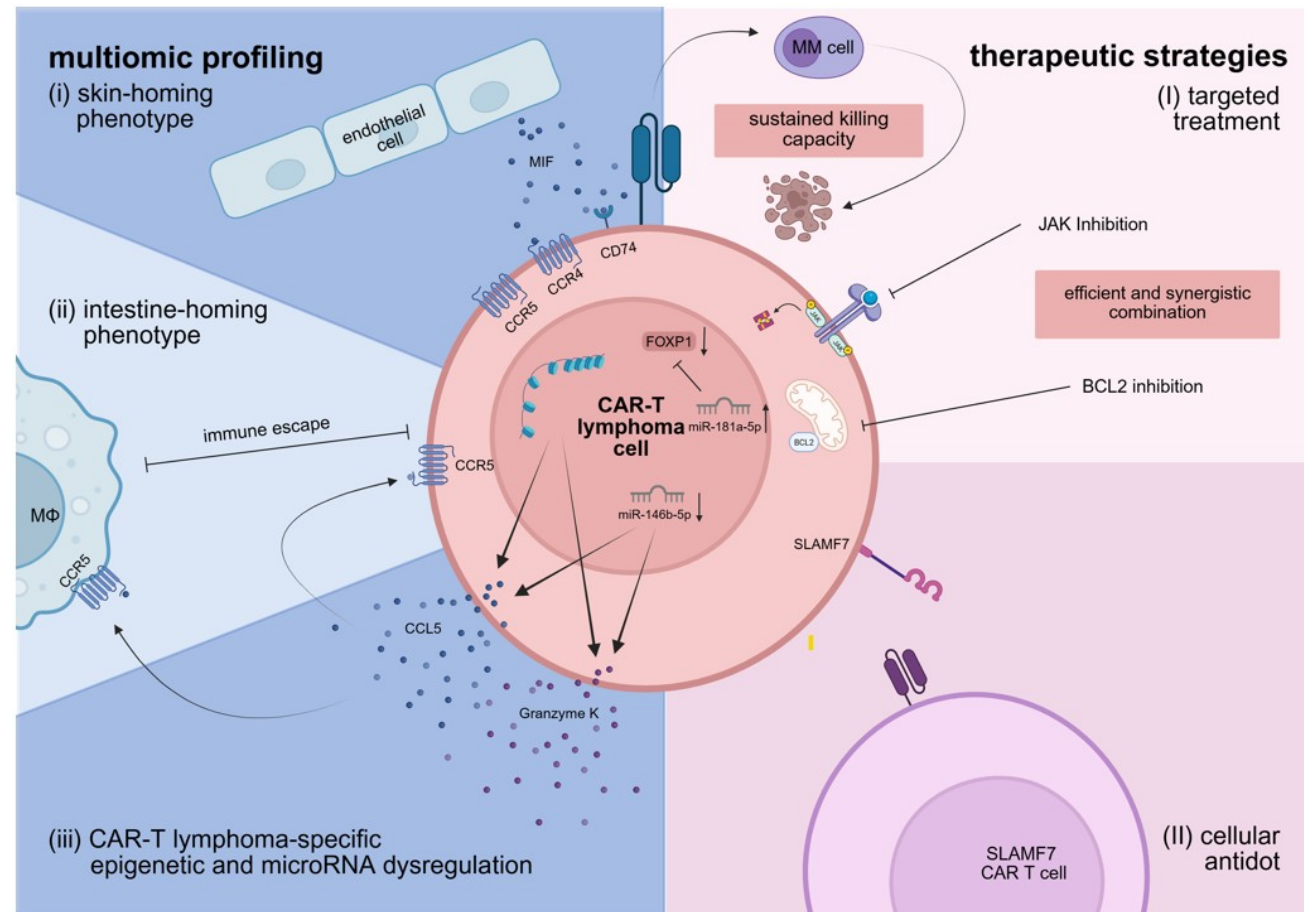


Receptor-ligand interactions



Deduction of therapeutic strategies from multi-omics profiling

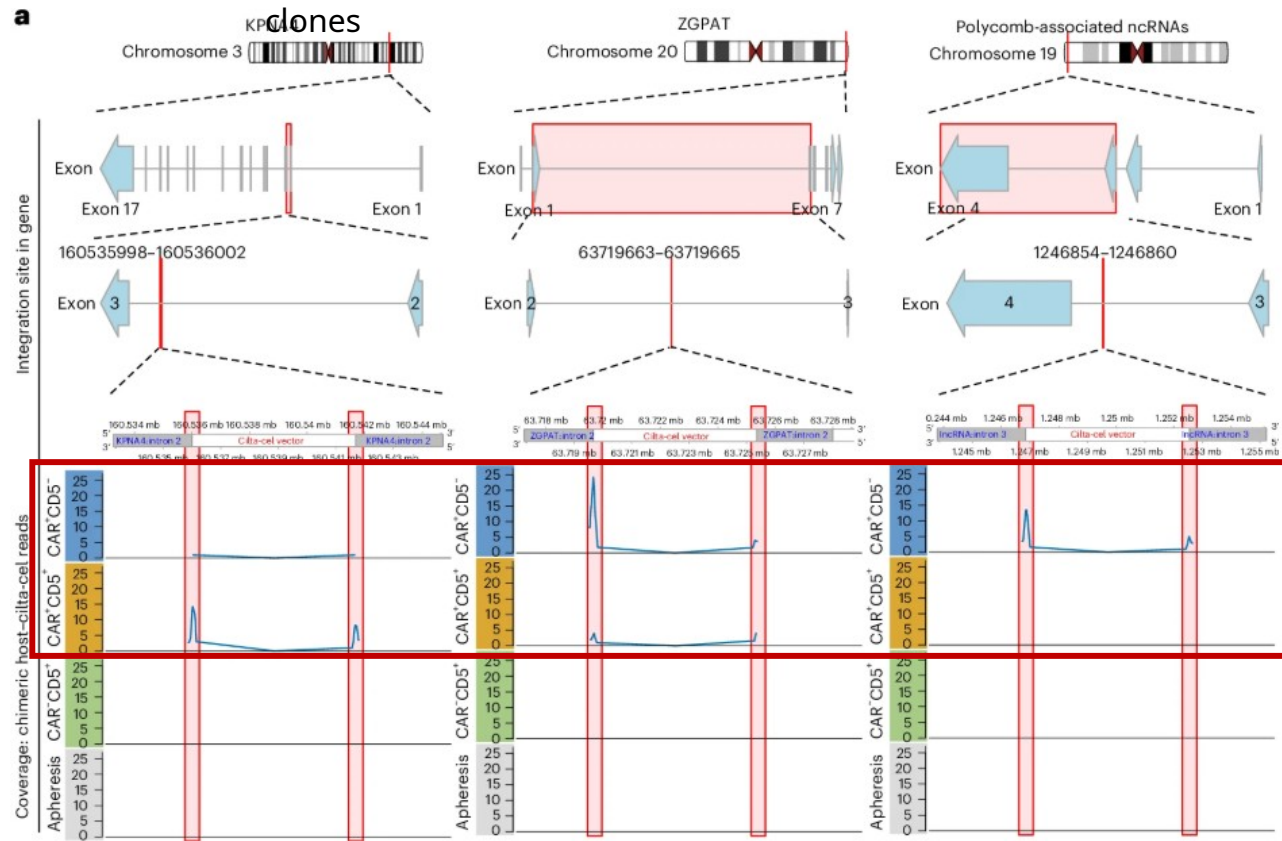
+ epigenome
+ miRNA
compartment



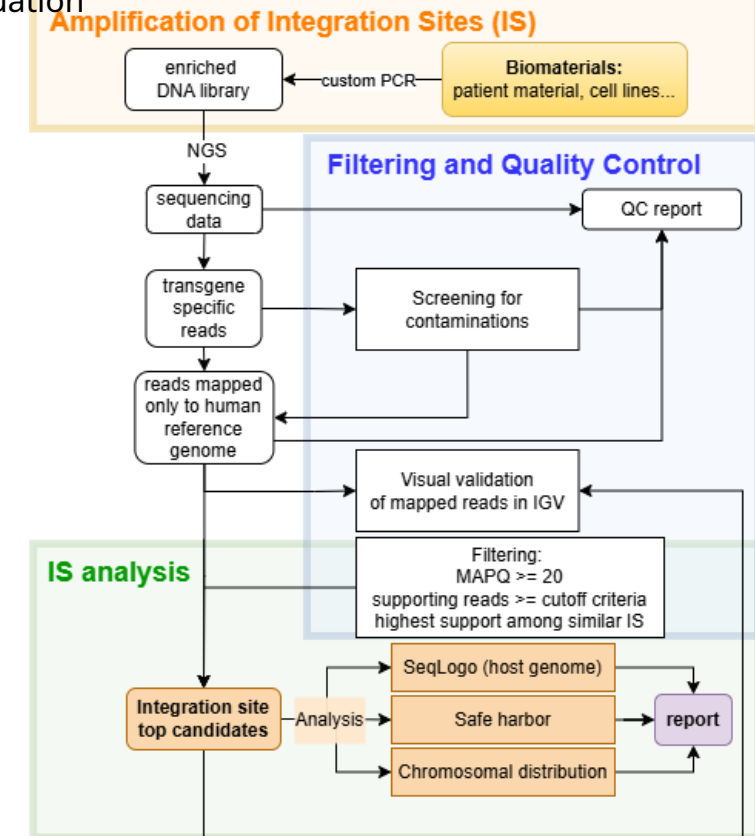
Integration site analysis and bioinformatics pipeline development

Risk of secondary malignancies due to insertion site mutagenesis

Integration sites of expanded CAR T cell lymphoma



Bioinformatics pipeline for integration site analysis and evaluation



Summary - digital molecular medicine approach for immunomonitoring

Combining NGS-based data generation and bioinformatics analysis is feasible (biobanking, sample and data logistics, data protection,...) and can support:



Obtaining novel insights into CAR T cell MoA regarding efficacy and safety,



Creating clinically relevant cohort-level and single patient information,



Informing clinical decision making

Aknowledgements

Subline, Frutiger LT Com Lt, 20 pt

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Patients and their
families



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the European Union



CERTainty
A cellular immunotherapy virtual twin
for personalised cancer treatment

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