

Research profile for applicants

Name of DKFZ research division/group:	CCU Neuroimmunology and Brain Tumor Immunology (D170)
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Group homepage: <i>Visit this website for further information on current research and recent publications.</i>	https://www.dkfz.de/en/neuroimmunology-and-brain-tumor-immunology

RESEARCH PROFILE AND PROJECT TOPICS

The central nervous system (CNS) is considered an immune-privileged organ, and intrinsic CNS tumors such as gliomas are characterized by profound immunosuppression. Experimental and clinical evidence demonstrates that the immune system can recognize and eliminate tumors, but endogenous anti-tumor responses are often insufficient. These responses can be enhanced through vaccination, immune checkpoint inhibition, or the in vitro expansion of tumor-reactive immune cells.

As a translational research group, we develop innovative immunotherapeutic approaches for brain tumors in preclinical models and clinical trials while establishing bioinformatic and experimental pipelines for the identification, cloning, and therapeutic delivery of patient-specific T cell receptors (TCRs). Recently, we demonstrated that vaccine-induced TCRs targeting a glioblastoma stemness antigen can be successfully applied for TCR therapy, providing proof-of-concept for a novel immunotherapeutic strategy against glioblastoma (13).

From a well-characterized glioma patient cohort, we have established a comprehensive repository of TCRs targeting IDH1, a recurrent clonal neoepitope in this poorly immunogenic tumor type (1). Several hundred IDH1-reactive TCRs have been identified using functional immune assays, TCR repertoire profiling, and single-cell sequencing of blood and tumor samples (2–6). We also characterized clonally unique H3K27M-reactive TCRs from a glioma patient who achieved complete remission following H3K27M peptide vaccination (7).

In close collaboration with our immune monitoring and clinical teams, we continue to identify TCRs recognizing shared neoepitopes (8–9) and patient-specific antigens (2–3, 10–11). Furthermore, we developed **predicTCR**, a machine learning classifier that combines high-throughput TCR cloning, functional validation, and single-cell RNA sequencing to identify tumor-reactive tumor-infiltrating lymphocytes in an antigen-agnostic manner. PredicTCR outperforms previous approaches and will accelerate the development of personalized T cell therapies (12).



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We are seeking a highly motivated candidate with a strong interest in translational tumor immunology, excellent communication and teamwork skills, and enthusiasm for interdisciplinary research. Experience in bioinformatics, cell culture, flow cytometry, molecular cloning, animal experimentation, and programming (R and/or Python) is desirable but not required.

References*

1. A vaccine targeting mutant IDH1 induces antitumour immunity. Schumacher T, [...], Platten M. *Nature*. 2014
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4. Identification of a tumor-reactive T-cell repertoire in the immune infiltrate of patients with resectable pancreatic ductal adenocarcinoma. Poschke I, [...], Offringa R. *Oncoimmunology*. 2016
5. The Outcome of Ex Vivo TIL Expansion Is Highly Influenced by Spatial Heterogeneity of the Tumor T-Cell Repertoire and Differences in Intrinsic In Vitro Growth Capacity between T-Cell Clones. Poschke I, [...], Offringa R. *Clin Cancer Res*. 2020
6. A vaccine targeting mutant IDH1 in newly diagnosed glioma. Platten M, Bunse L, [...], Wick W. *Nature*. 2021
7. H3K27M neopeptide vaccination in diffuse midline glioma induces B and T cell responses across diverse HLA loci of a recovered patient. Boschert T., [...], Green EW. *Immunology* 2024
8. K27M-mutant histone-3 as a novel target for glioma immunotherapy. Ochs K, [...], Platten M. *Oncoimmunology*. 2017
9. T cell receptor therapy targeting mutant capicua transcriptional repressor in experimental gliomas. Kilian M, [...], Platten M, Bunse L. *Clin Cancer Res*.
10. Vaccine Strategies in Gliomas. Platten M, [...], Wick W. *Curr Treat Options Neurol*. 2018
11. Actively personalized vaccination trial for newly diagnosed glioblastoma. Hilf N, [...], Wick W. *Nature*. 2019
12. Prediction of tumor-reactive T cell receptors from scRNA-seq data for personalized T cell therapy. Tan CL, [...] Green EW. *Nature Biotechnology* 2024
13. Chih YC Platten M, Green EW, Bunse L. *Vaccine-induced T cell receptor T cell therapy targeting a glioblastoma stemness antigen*. *Nature Communications*. 2025



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