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Junior Clinician Scientist
nTTP-GCT-Cohort 2025

HTCC, Clinic for Dermatology
CHARITÉ - UNIVERSITÄTSMEDIZIN BERLIN

Fields of Research:

- Critical Illnesses
- Autoimmunity
- Biomarkers
- Trace Elements

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Translational Scientist
nTTP-GCT-Cohort 2025

BERLIN INSTITUTE OF HEALTH IN DER CHARITÉ
(BIH)

Fields of Research:

- Immunology
- T cells
- SARS-CoV-2
- Skin Organoids
- Cancer Immunotherapy

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Project Description:

Effective T cell responses are crucial for tumor control and elimination and are significantly influenced by the avidity of the T cell receptor (TCR) for the antigen-MHC complex. Current technologies for measuring TCR avidity are time consuming, complex and not scalable. We have introduced an antigen-specific T cell receptor avidity assay, the CATCH (chasing antigen-specific T cells with high avidity) assay, which enables rapid and high-throughput identification of different avidities for defined antigens without prior knowledge of the MHC-antigen complex. Since the TCR avidity for their antigen correlates directly with the T cell effector function, the presence of T cells with medium to high avidity against tumor antigens is a prerequisite for the therapeutic success of adoptive T cell therapy (ACT), but also for immune checkpoint inhibitor (ICI) therapies. In this project, the benefits of the CATCH assay will be investigated at two levels of tumor therapy:

1) CATCH as a predictive biomarker in ACT and ICI therapy

ICI therapy is based on the blockade of inhibitory immune receptors and is used primarily for the treatment of metastatic melanoma. The success of treatment (remission rates of up to 58%) is offset by frequent, potentially chronic immune-related side effects. In the absence of a response to ICI, Lifileucel, the first cell therapy from tumor-infiltrating lymphocytes (TIL), is about to be approved for melanoma. Expanded TILs from the patient's tumor tissue are administered intravenously to destroy remaining cancer cells. We want to evaluate whether the CATCH assay is suitable as a predictive biomarker for TIL and ICI treatment of melanoma to identify patients with a good chance of therapeutic success before treatment in order to enable customized therapies.

2) CATCH as a high-throughput tool for the identification of TCRs for ACTs

Further, we will investigate whether CATCH can support both customized ACTs and the construction of a global TCR library. The patient cohort will be subdivided according to ICI response rates and observed side effects and tumor-specific T cells will be isolated by CATCH assay. After subsequent single-cell RNA sequencing, the repertoire of TCR will be examined for clonal expansion of tumor-specific receptors and newly identified candidates will be tested for their effector function. This methodology will confirm that the CATCH assay can rapidly and reliably expand the known repertoire of individual and global TCRs.