Hosting group information for applicants

Name of DKFZ research division/group:
Neuroimmunology and Brain Tumor Immunology (D170)

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Group homepage: **https://www.dkfz.de/en/neuroimmunologie/index.php**

Please visit our website for further information on our research and recent publications.

RESEARCH PROFILE AND PROJECT TOPICS:

Please, add a short description of the research focus of your group and of a potential project for a postdoctoral fellow working in your group (max. 300-350 words in total)

The central nervous system (CNS) is considered an immune privileged organ, where immune responses are tightly controlled through an intensive cross-talk with the peripheral immune system despite the blood-brain barrier. Imbalance of such immune control is a hallmark of CNS autoimmunity, while on the other hand, active immunosuppression in the tumor microenvironment of CNS tumors like gliomas hampers effective antitumor immune responses. Our group aims to developing and improving novel immunotherapeutic approaches to gliomas based particularly in two focus areas.
Focus Area 1 (Identifying and targeting shared clonal neoepitopes in gliomas) represents a coordinated effort to probe shared mutations for immunogenicity. Using a syngeneic mouse tumor model we showed therapeutic efficacy of an IDH1 mutation-specific vaccine, providing the first evidence that mutation-specific T helper cell responses are capable to control solid tumors. On that basis we have successfully completed a phase I clinical trial to test immunogenicity and tolerability of this vaccine in brain tumor patients, showing strong immunogenicity, enhanced pseudoprogression as a surrogate marker for immune cell infiltration and successful anti-tumor immune response, and IDH1 mutation-specific T cells infiltrating into this post-vaccine lesion. Ongoing projects now focus on identification of further mutational antigens for specific immunotherapy and on specific TCR discovery for use in transgenic T cell therapy for glioma patients. Bioinformatics-based approaches for tumor-infiltrating reactive T cell selection for such TCR discovery based on high throughput state-of-the-art single cell RNA, single cell VDJ, as well as TCRbeta deep sequencing, are boosting these processes and progress.

Focus Area 2 (Targeting the immunosuppressive glioma microenvironment) has aimed at a more detailed understanding of metabolic constraints to tumor-reactive T cells in the glioma microenvironment. A central goal is the identification of drugs e.g. interfering with

tryptophan catabolism as potential therapeutics for malignant glioma. Our findings that IDH-mutant glioma cell-derived 2HG actively and directly inhibits adaptive cellular and innate immune responses by affecting immune cell function in the tumor microenvironment pave the way towards novel concepts of immunotherapeutic combination treatments which we are currently investigating in preclinical animal glioma models and chaperoning on their clinical translation.