P4

Mechanisms and intra-tumor interactions of skull bone-derived T cells

B. Scheffler, DKTK Translational Neurooncology

Background and central scientific questions or problem: The classic perception of the brain as an immune-privileged organ with very limited immune activity is outdated. Emerging scientific insights into the neuro-immune-interface and its associated anatomical structures open up disruptive therapeutic possibilities. We have recently discovered accumulation of active lymphoid populations in the skull bone marrow, in juxtaposition to treatment-naive glioblastoma tumors at the time of initial diagnosis. These populations contain T cell clonotypes that are also present in the tumor. Very little is known on their relationship to each other and on their interactions with the brain tumor microenvironment.

Technical and conceptual approach to address the research question: Our lab is embedded in the comprehensive cancer center's clinical neurooncology program with prospective access to patient-derived glioblastoma specimens via established ethics and informed consent procedures. We routinely recruit paired clinical samples of skull bone, blood, and tumor tissue of patients with glioblastoma. We are experienced in the study of tumor-, and immune cell-molecular and functional 28

profiles, and we know how to create and exploit patient-derived cellular ex-vivo and complex tissue models for the revealing and validation of novel mechanisms of cellular function and disease. These prerequisites enable the study of intra-tumor mechanisms and microenvironmental interactions of human skull bone-derived T cells in a co-clinical setting.

Scientific expertise within the group: neurooncology, immunology, hematopoiesis, fresh surgical samples, patient-derived cell- and tissue-models; molecular/cell biology incl. CRISPR; NGS incl. scRNA-Seq; patient-derived xenografts; drug discovery; early clinical trials.