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MAIN FIELDS OF RESEARCH; ABSTRACT

Glioblastoma is the most common and most malignant primary brain tumor with a poor prognosis despite surgery and chemo-radiotherapy. A major challenge is the fact that tumor cells infiltrate the healthy brain tissue, precluding complete surgical resection. Thus, innovative treatment approaches for glioblastoma are urgently needed. Among these, immunotherapy receives increasing attention, also because glioblastoma is paradigmatic for cancer-associated immunosuppression. The overall objective of my PhD project is to uncover the characteristics of tumor infiltrating lymphocytes (TIL) in human glioblastoma samples to be able to develop novel specific T cell-based therapies for glioblastoma.

This goal will be achieved by:

1. mapping the antigenic landscape of glioblastoma with the aim to identify novel and common tumor-exclusive class I and class II ligands presented by human leukocyte antigen (HLA) molecules. HLA class I and II ligands of snap frozen primary glioblastoma samples will be isolated applying a standard immunoaffinity purification protocol and sequenced using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) (Kowalewski and Stevanović, Methods Mol Biol. 2013;960:145-157).
2. characterizing, both at the functional and the phenotypic level, freshly isolated TIL and compare them with autologous circulating lymphocytes. We aim at functionally characterizing TIL by investigating their antigen specificity against candidate peptides and assessing their cytotoxic potential against autologous tumor cells. For the phenotypic characterization, mass cytometry and high dimensional flow cytometry analysis will be applied.
3. investigating the clonal diversity of infiltrating T cells in order to identify clonally expanded T cells in the tumor compared to the circulatory system. For this purpose, ultra deep sequencing of the T cell receptor (TCR) using snap frozen glioblastoma, blood samples and antigen-specific T cell clones will be performed in order to determine the repertoire of TIL in glioblastoma and to detect the clonal frequency of antigen-specific clones in the original samples.

SPECIAL TECHNIQUES AND EQUIPMENT

Mass spectrometry, cell culture, mass cytometry, flow cytometry, immunogenicity and cytotoxicity assays