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MAIN FIELDS OF RESEARCH; ABSTRACT

Glioblastoma multiforme (GBM) is a malignant brain tumor with a poor prognosis. Median overall survival with current standard therapy, including maximal safe resection and adjuvant radio-chemoradiotherapy is only 14 months. Brain metastases (BM) arise in 10-30% of patients diagnosed with systemic tumor burden and this number is expected to increase. Each year there are ~10 times as many brain cancer patients diagnosed with a metastatic brain tumor than with a primary brain tumor. Current therapies for BM include local treatments, and newer systemic approaches.

The inflammation research lab investigated the leukocyte landscape in brain cancer in a series of patient samples.[1] The results showed that the glioma microenvironment was dominated by tumor-associated macrophages (TAM), and the BM tumor microenvironment (TME) by lymphocyte infiltrates. The in-depth analysis of the myeloid compartment revealed that tumor types shape the differentiation of monocyte-derived macrophages (MDMs). Multiple experimental approaches confirmed that the origin of TAM populations originated either from embryonically derived CNS-resident microglia (GBM), or from blood derived MDMs (BM).

The aim of the current project is a deeper preclinical investigation of these findings and includes: 1) Preclinical modeling of the local monocyte to macrophage transformation within the brain tumor and the surrounding microenvironment, 2) Manipulation of TAM signatures and correlation with preclinical and clinical outcomes 3) Assessment of phenotypic lymphoid and TAM changes with Immunotherapy and identification of new targets.

SPECIAL TECHNIQUES AND EQUIPMENT

Orthotopic brain tumor mouse models, High dimensional flow cytometry, Single cell RNA sequencing, Mass cytometry

1. Friebel, E. et al. Single-Cell Mapping of Human Brain Cancer Reveals Tumor-Specific Instruction of Tissue Invading Leukocytes. Cell 181, 1626-1642 e1620 (2020).