

Single cell mapping of human brain cancer reveals tumor-driven education of tumor-associated leukocytes

Among malignant primary brain tumors, glioblastoma is the most frequent and the most severe form. The brain tumor microenvironment (TME) actively prevents anti-tumor immunity and it is relatively unclear whether this immunosuppression is a feature of the brain or mediated by the tumor itself. To tackle this question, we here mapped the leukocyte landscape across gliomas and brain metastases (melanoma and non-small cell lung cancer) using high-dimensional single cell profiling with mass cytometry. We found a heterogeneous intratumor immune composition of the TME and could distinguish specialized tissue-resident leukocytes including microglia, as well as leukocytes invading the brain from the systemic circulation. The composition of immune cells within the TME alone permitted a clear distinction between primary brain tumors (gliomas) and secondary brain tumors (metastases). Among the most striking differences was the presence of tissue invading lymphocytes and myeloid cells in metastatic lesions, whereas gliomas presented with predominant tissue resident reactive microglia. Among gliomas, WHO grades were associated with a different composition of the TME. WHO Grade III-IV gliomas were invaded by monocyte-derived macrophages, which showed a signature trajectory indicative of tumor-driven education. Our study revealed the specific immunological signature across brain tumors, which is highly dependent on whether the tumor originated in the brain or invaded as a metastatic growth. This information can facilitate the rational design of targeted immunotherapy strategies.

Keywords : glioma, brain metastases, tumor microenvironment, macrophage, mass cytometry

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