

1477 NEURONAL MODULATION OF MYELOID CELLS IN GLIOBLASTOMA

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Background Cancer neuroscience is emerging as an important field in glioblastoma (GBM) research. Immuno-oncology has never had a successful phase III clinical trial treating GBM patients and we hypothesize that neuronal drivers of immune cells can change patient outcomes. While most of the cancer neuroscience work in GBM has focused on the neuron-glioma interaction, little has been done to establish the neuron-immune relationship within these tumors. Myeloid (microglia and bone marrow-derived macrophages) cells have previously been shown to be the most significant players in driving GBM tumor immunosuppression. We hypothesized that neurons play a role in driving pro-tumor myeloid cells and the interaction can be exploited for therapeutic benefit.

Methods We used a combination of RNA sequencing, immunofluorescence of formalin-fixed tissue, calcium imaging, electron microscopy, and in vitro cell-based assays to determine the effect that neurons and neurotransmitters have on tumor-derived CD11b+ cells. We also sought to identify how neuromodulatory medications such as gabapentin and levetiracetam impact the neuron-myeloid interaction and the subsequent phenotype of these immune populations.

Results Here we show that neuron-myeloid interactions are present and functional within GBM tumors. Neurotransmitter receptors are expressed on CD11b+ cells. The neuronal influence causes a functional change among myeloid cells that is altered by the presence of neuromodulatory medications.

Conclusions Neuromodulatory medications are an important adjuvant to consider for future immunotherapy clinical trials in GBM patients.

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