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Glioblastoma revisited: from neuronal-like invasion to pacemaking

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Abstract

In recent years, two developments have helped us to better understand the fundamental biology of glioblastoma: the description of a striking intratumoral heterogeneity including gene expression-based cell states, and the discovery that neuro-cancer interactions and cancer-intrinsic neurodevelopmental mechanisms are fundamental features of glioblastoma. In this opinion article, we aim to integrate both developments. We explain how two key disease features are characterized by different neural mechanisms related to distinct but plastic cancer cell states: first, the single cell-dominated invasive parts and second, the more solid parts which are dominated by communicating cell networks constantly activated by pacemaker-like glioblastoma cells. The resulting integrative roadmap of molecular and functional heterogeneity contributes to the Cancer Neuroscience of glioblastoma and suggests novel therapeutic strategies.

Keywords: cancer neuroscience; cellular heterogeneity; glioblastoma; invasion; neuron-glioma synapse; tumor cell network.