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Cancer stem cell hypothesis 2.0 in glioblastoma: Where are we now and where are we going?

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Abstract

Over the past 2 decades, the cancer stem cell (CSC) hypothesis has provided insight into many malignant tumors, including glioblastoma (GBM). Cancer stem cells have been identified in patient-derived tumors and in some mouse models, allowing for a deeper understanding of cellular and molecular mechanisms underlying GBM growth and therapeutic resistance. The CSC hypothesis has been the cornerstone of cellular heterogeneity, providing a conceptual and technical framework to explain this longstanding phenotype in GBM. This hypothesis has evolved to fit recent insights into how cellular plasticity drives tumor growth to suggest that CSCs do not represent a distinct population but rather a cellular state with substantial plasticity that can be achieved by non-CSCs under specific conditions. This has further been reinforced by advances in genomics, including single-cell approaches, that have used the CSC hypothesis to identify multiple putative CSC states with unique properties, including specific developmental and metabolic programs. In this review, we provide a historical perspective on the CSC hypothesis and its recent evolution, with a focus on key functional phenotypes, and provide an update on the definition for its use in future genomic studies.

Keywords: cancer stem cell; glioblastoma; heterogeneity; proliferation.