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### Glioblastoma Stem Cells: A Neuropathologist's View.

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#### Abstract

Glioblastoma (WHO Grade IV) is both the most common primary brain tumor and the most malignant. Advances in the understanding of the biology of the tumor are needed in order to obtain a clearer picture of the mechanisms driving these tumors. To neuropathologists, glioblastoma is a tumor that represents a complex system of migrating pleomorphic tumor cells, proliferating blood vessels, infiltrating inflammatory cells, and necrosis. This review will highlight how the glioma stem cell concept brings these elements together into a collective whole, interacting with microenvironmental influences in complex ways. Borrowing from chaos theory a vocabulary of "self organizing systems" and "complex adaptive systems" that seem useful in describing these pathologic features, a new paradigm of glioblastoma biology will be proposed that genetic changes should be understood in a three dimensional framework as they relate not only to the tumor cells themselves but also to the multicellular hierarchical unit, not isolated from, but responsive to, its local milieu. In this way we will come to better appreciate the impact our therapeutic interventions have on the regional phenotypic heterogeneity that exists within the tumor and the intercellular communications directing adaptation and progression.

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