Abstract

Glioblastoma multiforme (GBM), the most common intracranial tumor in adults, is characterized by extensive heterogeneity at the cellular and molecular levels. This insidious feature arises inevitably in almost all cancers and has great significance for the general outcome of the malignancy, because it confounds our understanding of the disease and also intrinsically contributes to the tumor's aggressiveness and poses an obstacle to the design of effective therapies. The classic view that heterogeneity arises as the result of a tumor's "genetic chaos" and the more contemporary cancer stem cell (CSC) hypothesis tend to identify a single cell population as the therapeutic target: the prevailing clone over time in the first case and the CSC in the latter. However, there is growing evidence that the different tumor cell populations may not be simple bystanders. Rather, they can establish a complex network of interactions between each other and with the tumor microenvironment that eventually strengthens tumor growth and increases chances to escape therapy. These differing but complementary ideas about the origin and maintenance of tumor heterogeneity and its importance in GBM are reviewed here. Cancer Res; 71(12); 4055-60. ©2011 AACR.