Public Summary:
Glioblastoma multiforme (GBM) is the most common and deadly brain tumor, with a mean survival time of only 21 months. Despite the dramatic improvements in our understanding of GBM fueled by recent revolutions in molecular and systems biology, treatment advances for GBM have progressed inadequately slowly, which is due in part to the wide cellular and molecular heterogeneity both across tumors and within a single tumor. Thus, there is increasing clinical interest in targeting cell-extrinsic factors as way of slowing or halting the progression of GBM. These cell-extrinsic factors, collectively termed the microenvironment, include the extracellular matrix, blood vessels, stromal cells that surround tumor cells, and all associated soluble and scaffold-bound signals. In this review, we will first describe the regulation of GBM tumors by these microenvironmental factors. Next, we will discuss the various in vitro approaches that have been exploited to recapitulate and model the GBM tumor microenvironment in vitro. We conclude by identifying future challenges and opportunities in this field, including the development of microenvironmental platforms amenable to high-throughput discovery and screening. We anticipate that these ongoing efforts will prove to be valuable both as enabling tools for accelerating our understanding of microenvironmental regulation in GBM and as foundations for next-generation molecular screening platforms that may serve as a conceptual bridge between traditional reductionist systems and animal or clinical studies.

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