Therapeutic activation of macrophages and microglia to suppress brain tumor-initiating cells.


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Abstract

Brain tumor initiating cells (BTICs) contribute to the genesis and recurrence of gliomas. We examined whether the microglia and macrophages that are abundant in gliomas alter BTIC growth. We found that microglia derived from non-glioma human subjects markedly mitigated the sphere-forming capacity of glioma patient-derived BTICs in culture by inducing the expression of genes that control cell cycle arrest and differentiation. This sphere-reducing effect was mimicked by macrophages, but not by neurons or astrocytes. Using a drug screen, we validated amphotericin B (AmpB) as an activator of monocytoid cells and found that AmpB enhanced the microglial reduction of BTIC spheres. In mice harboring intracranial mouse or patient-derived BTICs, daily systemic treatment with non-toxic doses of AmpB substantially prolonged life. Notably, microglia and monocytes cultured from glioma patients were inefficient at reducing the sphere-forming capacity of autologous BTICs, but this was rectified by AmpB. These results provide new insights into the treatment of gliomas.