ABSTRACT

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Regulation of Microglia for the Treatment of Glioma.

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Microglia are the resident macrophages of the central nervous system (CNS). They are derived from the erythromyeloid progenitors in the embryonic yolk sac, and they are maintained postnatally by limited self-renewal and longevity. As the most abundant immune cells in the CNS, they play critical roles in homeostasis and various CNS pathologies, including tumor, stroke, and neurodegenerative disease. For instance, in gliomas, up to more than 30% of cells in the tumor microenvironment can be microglia and tumor-associated macrophages. These cells are typically coopted by tumor cells to create a pro-tumorigenic microenvironment. The transcriptional regulation of the development and function of microglia in health and disease is not well understood. Transcription factors are master regulators of cell fates and functions and activate target genes that execute a genetic program typically initiated by external stimuli. Several transcription factors, not necessarily specific to microglia, have been shown to play roles in the development, function, and activation state of microglia. In this review, we summarize our current understanding of the roles of transcription factors in the functions of microglia in normal CNS homeostasis and in gliomas. A thorough understanding of the transcription factors and their target genes that mediate and regulate the functions of microglia in gliomas may help identify new targets for immune therapies. These stroma-directed therapies may be combined with tumor cell-directed therapies for more effective treatment of these diseases.

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