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The role of microglia in central nervous system immunity and glioma immunology.

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The central nervous system (CNS) historically has been considered an immune-privileged organ, lacking a lymphatic system and shielded from the circulatory system by the blood-brain barrier. Microglia are an abundant portion of the CNS cell population, comprising 5% to 20% of the total glial cell population, and are as numerous as neurons. A crucial function of microglia is the ability to generate significant innate and adaptive immune responses. Microglia are involved in first line innate immunity of the CNS. Proper antigen presentation is critical in the generation of specific, durable responses by the adaptive immune system, and requires interaction between the T cell receptor and processed antigen peptide presented on major histocompatibility complex (MHC) molecules by the antigen presenting cells (APC). Microglia also have a large regulatory role in CNS immunity. Histopathologic studies of glioma tissue have consistently shown high levels of infiltrating microglia. Microglia are also localized diffusely throughout the tumor, rather than to the areas of necrosis, and phagocytosis of glioma cells or debris by microglia is not observed. Recent evidence indicates that glioma-infiltrating microglia/macrophages might be promoting tumor growth by facilitating immunosuppression of the tumor microenvironment. When activated, microglia can be potent immune effector cells, able to perform a broad range of functions, and they mediate both innate and adaptive responses during CNS injury and disease while remaining quiescent in the steady state. Their versatility in bridging the gap between the immune-privileged CNS and the peripheral immune system, in addition to their significant numbers in gliomas, makes them an attractive candidate in immunotherapy for gliomas. An enhanced understanding of microglia-glioma interaction may provide better methods to manipulate the glioma microenvironment to allow the generation of a specific and durable anti-glioma immunity. The role of microglia in CNS immunity is reviewed, with a focus on key advances made in glioma immunology.

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