Microglia

Microglia are the primary innate immune effector cells of the CNS and they represent a unique myeloid cell population whose origin and function must be clearly distinguished from other phagocytes in the brain (Ransohoff and Cardona, 2010).

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Related terms:

Multiple Sclerosis, Oligodendrocyte, Glial Cells, Tumor Necrosis Factor Alpha, Astrocyte, Eicosanoid Receptor, Central Nervous System, Alzheimer's Disease, Protein, Blood Brain Barrier

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Microglia

A.E. Cardona, ... K. Akassoglou, in Patterning and Cell Type Specification in the Developing CNS and PNS, 2013

41.7 Concluding Remarks

Microglia are cells of mesodermal/mesenchymal origin that migrate into the CNS to become resident macrophages within the unique brain microenvironment. Microglia are highly dynamic cells that interact with neurons and nonneuronal cells. Microglia patrol the brain parenchyma via continuous process extension and retraction and are also capable of transitioning from a ramified to an amoeboid morphology, a feature consistent with cell activation. Microglia express a wide array of receptors and thus respond to pleiotropic stimuli ranging from neurotransmitters to cytokines and plasma proteins. They play a crucial role in the healthy brain as regulators of synaptic functions and phagocytosis of newborn neurons, with important implications in synaptic plasticity and adult neurogenesis. In disease, they play a crucial role in neurodegenerative and neuroinflammatory conditions. Their interactions with T cells are a major component of the development of brain autoimmunity, while their pathogenic interactions with neurons via induction of ROS and iNOS play a crucial role in neurodegeneration. Emerging genetic tools and animal models have shed new light on the origin of microglia, their link to

peripheral monocytes, and their contribution to disease pathogenesis. As microglia might exert beneficial and pathogenic functions in the CNS, understanding their contribution in disease-specific context would be necessary for the identification of novel microglia-targeted therapies for CNS diseases.

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Microglia

Manuel B. Graeber, in Encyclopedia of the Neurological Sciences, 2003

Microglia as a Sensor of Tissue Pathology

Activated microglia are found in a large number of pathological conditions and, due to their low threshold of activation, have been proposed as a sensitive marker of early tissue damage. This can be exploited in diagnostic neuropathology and neuroimaging. Classic examples of microglial involvement in CNS diseases include the formation of rod-shaped microglia in the cerebral cortex in "general paralysis of the insane" (neurosyphilis) or subacute sclerosing panencephalitis and also the formation of "microglial nodules" by neuronophagic microglia clustering around affected neurons in poliomyelitis and other neuronotropic viral infections. The pathological hallmark of HIV-1 encephalitis is the multinucleated giant cell, which may derive from microglia. In Alzheimer's disease, microglia are prominent not only in the core but also around the outer border of amyloid plaques. Some authors believe that microglial cells are actively involved in the formation of amyloid deposits. Demyelinating activity in multiple sclerosis and in its animal model, experimental autoimmune encephalomyelitis, is largely attributable to phagocytically active macrophages. Many of them are microglia derived. Macrophages in ischemic brain tissue actively remove tissue debris. However, the significance of the large number of microglia in some gliomas remains enigmatic.

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Microglia

U.-K. Hanisch, in Encyclopedia of the Neurological Sciences (Second Edition), 2014

Microglia as a Sensor of Tissue Pathology

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Microglia

Guido Stoll, ... Michael Schroeter, in Encyclopedia of the Human Brain, 2002

II Origin of Microglia

The origin of ramified microglia has been a long-standing controversial issue, although most authorities would accept that microglia are bone marrow derived and belong to the monocyte/macrophage lineage. The observation that the decline of blood-derived ameboid cells (macrophages) in the CNS during the first postnatal weeks was accompanied by a dramatic increase in the number of ramified microglia was suggestive for a transition of ameboid cells into resident ramified microglia. Based on morphological grounds, however, transitional forms between these brain macrophages and resting microglia could not be detected in the developing brain. Moreover, in an attempt to directly address the issue of transition, young mice received bone marrow transplants from transgenic mice, thereby allowing the distinction between host and donor cells in tissues. In these chimeric animals only 10% of parenchymal microglia in the CNS displayed the transgenic signal. In adult animals attempts to directly demonstrate the replacement of ramified parenchymal microglia from bone marrow-derived precursors have so far yielded inconclusive results. Ramified microglia in the adult CNS are an extremely sessile cell population

exhibiting virtually no turnover from circulating monocytic precursor cells. In contrast to the parenchymal microglia, the perivascular microglia are definitely bone marrow derived and regularly replaced in the adult CNS as demonstrated by use of chimeric rats by Hickey and Kimura.

The view that parenchymal microglia are bone marrow derived has been challenged. Based on their finding that astroglial cultures initiated from newborn mouse neopallium contained bipotential progenitor cells that could give rise to both astrocytes and microglia, Fedoroff and colleagues put forward the idea that parenchymal microglia are of neuroectodermal origin, as are all other glia. This view was further supported by the observation that the majority of microglia lacked the transgenic signal after bone marrow transplantation as described previously. Despite the uncertainty about their origin, microglia share most surface molecules with bone marrow-derived monocytes/macrophages.

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Neuroinflammation

Nicolas G. Bazan, ... Ludmila Belayev, in Basic Neurochemistry (Eighth Edition), 2012

Microglia in neurodegenerative diseases

Microglia are involved in multiple sclerosis, Alzheimer's disease, Parkinson's disease, HIV dementia, retinal degenerative diseases and many other conditions. In multiple sclerosis, phagocytic microglia are located in the lesion sites. In animal models, phagocytic microglia have been identified with lysosomes containing myelin degradation products. The overactivation and recruitment of microglia in Alzheimer's disease is due to accumulation of amyloid-□ proteins, which further activate microglia through neuronal damage. Activated microglia migrate to the site of plaque formation and penetrate the plaques, which leads to production of pro-inflammatory, cytotoxic molecules such as NO and TNF□. The dying dopaminergic neurons in Parkinson's disease result in overactivation of microglia through their release of matrix metalloproteinase-2, □-synuclein and neuromelanin—signals that subsequently trigger pro-inflammatory events in the activated microglia. In HIV dementia, microglia function as storage cells for the virus in the brain. The interaction of the HIV viral proteins with microglia results in their activation. Chronic activation of microglia in the retina leads to overactivation and results in retinal cell damage as an early event in retinal degenerative diseases.

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Microglia☆

G. Stoll, S. Jander, in Reference Module in Neuroscience and Biobehavioral Psychology, 2017

Abstract

Microglia, a major glial component of the central nervous system (CNS), serve as tissue-resident macrophages. Parenchymal microglia originate from the yolk sac during embryo-genesis and are extremely settled without significant turnover from outside in adults while the perivascular microglia, a subtype, are regularly replaced from the bone marrow. Microglia regularly sense the brain parenchyma by extending and retracting motile processes and, thereby, respond to virtually any, even minor pathological events in the CNS. There is increasing evidence that dysfunctional microglia play an active role in the progression of neurodegenerative as well as inflammatory CNS disorders.

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Nervous System

Catherine E. Hagan, ... C. Dirk Keene, in Comparative Anatomy and Histology, 2012

Microglia

Microglia are the resident histiocyte-type cell and the key innate immune effector of the CNS. They are often described as either resting (i.e., ramified) or activated, but these terms fail to convey the dynamic remodeling of their fine processes and constitutive immunosurveillance activity. Their origin is highly debated. Whereas some microglia are derived from circulating bone marrow-derived monocytes, particularly in the setting of acute or chronic injury, evidence suggests that early microglia are derived from yolk sac progenitors. Thus, microglia in adult mice and humans are the result of a combination of proliferation of the resident population and migration into the CNS by myeloid progenitors. In H&E-stained sections of normal brain, microglia are relatively few in number. Such “resting” microglia have small, dark, rod-shaped nuclei with condensed chromatin (Figure 11); they are smaller than the nuclei of astrocytes. The cytoplasm of surveying (not activated) microglia is inconspicuous. In contrast, activated microglia that have become distended by phagocytosed material

resemble foamy macrophages and are sometimes designated Gitter cells or foam cells. The markers frequently used to demonstrate microglia are CD68 in humans and CD11b or Iba-1 in mice.

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Neuroglia, Overview

Angus M. Brown, Bruce R. Ransom, in Encyclopedia of the Human Brain, 2002

VI.B Function

Microglia are the brain macrophages that respond to a variety of CNS injuries. There are three states of microglia: (1) resting, which are highly ramified cells, (2) activated microglia, which are cells responding to injury with morphological (enlarged cell bodies, contraction of processes) and immunophenotypic changes as well as proliferation, and (3) phagocytic microglia, which are full-blown brain macrophages with amoeboid morphology and expression of a number of immunomolecules. Activated microglia retract their processes followed by a rounding of the cell body. This is accompanied by increased expression of complement receptor 3. MHC class I and II antigens are up-regulated on the microglial cell surface, which enables the microglia to interact with immunocompetent cells such as T-cells. Once activated, phagocytic microglia are able to remove debris. The phagocytic microglia invade the area of damage and appear over a period of days, depending on the nature, severity, and location of the CNS damage. However, the process of debris removal can take from days to many weeks. This is in contrast to damage in the PNS, where macrophages have cleared debris within 2 weeks. As well as having a role in acute CNS injury, microglia may also play a role in neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. These conditions are characterized by the selective loss of neurons in distinct areas of the brain, areas in which microglia are activated. In Alzheimer plaques containing amyloid-β protein, microglia are present in the center of these plaques. It has been shown that amyloid-β protein precursor can activate microglia, which may act to enhance their toxicity.

Microglia are also involved in CNS autoimmunity and are activated by inflammatory signals such as LPS and interferon. Microglia are involved in HIV encephalitis, and although it is not clear how HIV interacts with microglia, it is thought that the HIV virus enters the CNS parenchyma hidden in infected monocytes and may subsequently spread to microglia.

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Advances in Cellular Neurobiology

Eng-Ang Ling, in Advances in Cellular Neurobiology, 1981

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Glial Cell Activation in PD

K. Wakabayashi, in Encyclopedia of Movement Disorders, 2010

Definition and History

Microglia, the antigen presenting immune cells in the brain, were discovered independently by Nissl (1899) and Robertson 1900, and first studied in detail by Rio-Hortega. Regarding the origin of microglia, the most widely accepted hypothesis is that they are bone marrow-derived cells. Microglia constitute □10% of all glial cells. Under normal conditions, microglia display a ramified morphology, but rapidly transform into an activated state displaying a plastic ameboid morphology in response to invading pathogens, the presence of foreign substances, or neuronal injuries inflicted by trauma, ischemia, or neurodegeneration. Activation of microglia begins within minutes after the insult and precedes the morphologically detectable neuronal damage. Activated microglia can destroy invading microorganisms and remove potentially deleterious debris by phagocytosis.