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Advances in the Study of Multiple Sclerosis and the Immune Microenvironment

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1. Introduction

Multiple sclerosis is a heterogeneous multifactorial disease influenced by genetic and environmental factors. Its pathogenesis involves many different immune cells, of which T cells are the most critical cell type in the pathogenesis, and in recent years, studies have also reported the influence of the innate immune system on the disease. Thus, the immune microenvironment plays a crucial role in the amelioration and exacerbation of multiple sclerosis disease.

Multiple sclerosis and the blood-brain barrier

An important finding in multiple sclerosis lesions is the disruption of the blood-brain barrier, which is critical to the immune microenvironment and the pathogenesis of multiple sclerosis. The blood-brain barrier is dynamic and allows for immune surveillance. Lesions occur when leukocytes migrate into the brain with subsequent inflammation, a process that involves two steps, first leukocytes migrate through small post-capillary veins into the perivascular space and then further through the neuroglial boundary membrane into the brain parenchyma.

Multiple sclerosis and immune cells

The role of T cells is central to the pathogenesis of multiple sclerosis and has been confirmed by experimental models of metaplastic encephalomyelitis. CD4+ T cells, which secrete the interferon IFN-γ, are the main mediators of inflammation leading to multiple sclerosis lesions, and further studies have shown that Th17 cells play a secondary role. These T cells secrete the pro-inflammatory cytokines IL-17 and IL-6 and are regulated by IL-23. Multiple sclerosis results when the above-mentioned inflammatory cells and/or other cell types become dysregulated and shift from physiological immune surveillance to pathological immune response. Studies of lesions from patients with multiple sclerosis have shown that IL-17-secreting CD4+ cells are present in large numbers of inactive lesions and that the chemokine receptor CCR6 expressed on Th17 cells facilitates cell transit through the choroid plexus into the cerebrospinal fluid and perivascular space by interacting with CCL20/MIP-3α expressed on the endothelium. Th17 cells, by secreting IL-17 and IL 22, disrupt endothelial tight junctions and further attract CD4+ subpopulations and other immune cells by interacting with the endothelium, thereby further increasing the permeability of the blood-brain barrier, thereby initiating the pathological cascade of inflammation, perivascular infiltration, and neuronal and glial cell damage. To enter thin-walled tissue, T cells must cross the glial boundary membrane, a process mediated by perivascular antigen-presenting cells and macrophages, which cleave the transmembrane receptor dystroglycan by secreting MMP-2 and MMP-9. in summary, the above cascade is a stepwise model, with Th17 cells initially being attracted and migrating into the cerebrospinal fluid and perivascular space. This then increases the permeability of the blood-brain barrier, allowing additional inflammatory cells to enter, which in turn completely disrupts the blood-brain barrier causing damage to the central nervous system, leading to active lesions and potential clinical deterioration of the disease.

The presence of inflammatory T cells in the perivascular space and parenchyma triggers the recruitment of additional T cells as well as B cells, dendritic cells, microglia, and NK cells, which secrete cytokines that may cause damage to surrounding tissues. CD8+ T cells are usually present at the margins of lesions and in perivascular infiltrates, indicating a specific antigenic response, and may also cause damage to neurons through cell-dependent cytotoxicity. damage through cell-dependent cytotoxicity. In addition, γδ T cells are present in multiple sclerosis lesions; B cells may contribute to the pathology through antigen presentation, cellular interactions, or immunoglobulin production from plasma cells; NK cells can modify or lyse T cells, so NK cells may also be involved in regulating the immune system in multiple sclerosis patients.

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