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Cytokine Dynamics in Multiple Sclerosis: Modulating Adaptive Immunity in Neuroinflammation

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Abstract

Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system (CNS) characterized by immune system dysfunction, inflammation, and demyelination. This review examines the intricate roles of cytokines in regulating neuroinflammation and influencing adaptive immune responses in MS. Proinflammatory cytokines, including IL-6, IL-17, and IFNγ, drive pathological processes by promoting immune cell activation and tissue damage, whereas anti-inflammatory cytokines, such as IL-10 and IL-22, contribute to immune regulation and neuroprotection. Furthermore, the review explores the emerging role of novel cytokines in MS pathophysiology, shedding light on newly identified immune mediators and their potential implications for disease progression. By analyzing cytokine profiles and their interplay with adaptive immunity, this review provides valuable insights into the immunopathogenic mechanisms underlying MS. Overall, this comprehensive examination advances current understanding of the cytokine-mediated dynamics in MS and identifies potential biomarkers of disease activity while informing future research directions. In summary, dysregulation of pro- and anti-inflammatory cytokines plays a fundamental role in MS pathogenesis by promoting neuroinflammation and immune-mediated tissue damage. Future studies are required to clarify the contributions of emerging cytokines to disease activity and progression across different stages of MS.

Keywords: Cytokines | Adaptive immunity | Inflammation | Multiple sclerosis | Neurodegeneration

1. Introduction

1.1 Multiple sclerosis and theories on the immune system's role

Multiple Sclerosis (MS) is a chronic autoimmune disease characterized by inflammation and damage to the central nervous system (CNS), resulting in demyelination of nerve fibers [1]. In individuals with MS, the integrity of the blood-brain barrier (BBB) is compromised [2]. The breakdown mechanisms are not fully understood, but it is believed that proinflammatory

molecules produced by immune cells and brain endothelial cells contribute to this disruption. These unidentified antigen triggers the activation of specific immune cells (Th1 and Th17 cells), which adhere to the endothelial cells of the BBB, cross it, and initiate an immune response. This response can result in demyelination, nerve fiber damage, neurodegeneration, and irreversible neurological impairment [3]. Activation and migration of T lymphocytes from the bloodstream to the brain disrupt the BBB. If this barrier is compromised in a critical brain region, it can lead to a sudden worsening of clinical symptoms [3,4]. Multiple theories have been proposed to explain the role of the peripheral immune system in neurodegenerative processes such as MS. These theories include autoimmunity, molecular mimicry, dysregulated immune surveillance, and chronic activation of immune cells [5]. However, the BBB is the primary structure affected during neuroinflammation, with its integrity compromised due to astrocyte activation, excessive release of cytokines and chemokines, and infiltration of immune cells. Both the cellular and non-cellular components of the BBB are impaired under inflammatory conditions. In advanced stages, additional mechanisms come into play. Similar to other neurodegenerative disorders, such as Alzheimer's and Parkinson's disease, oxidative stress and the pathological generation of free radicals and reactive oxygen species (ROS) play a significant role in sustaining neuronal loss [6].

1.2 Role of adaptive immunity in Multiple Sclerosis: CD4+ and CD8+ T Cells in CNS inflammation and pathology

Adaptive immune responses play a pivotal role in the development and progression of MS, as observed in acute and active chronic lesions [7]. The development of MS pathology begins with activating CD4+ T cells specific to CNS antigens in the peripheral immune system. Once activated, CD4+ T cells increase the expression of integrins, such as lymphocyte function-associated antigen-1 (LFA-1) and very late antigen-4 (VLA-4), enabling their migration across the BBB [8]. Upon encountering antigens, autoreactive T cells reactivate and differentiate, leading to cytokine production. These cytokines then activate neighboring immune and neural cells, attracting inflammatory cells into the CNS. Among these, macrophages are notably activated, exerting detrimental effects on the CNS directly or indirectly [9].

Moreover, CNS-specific CD8+ T cells are crucial for damaging the CNS during both the relapse and chronic phases of MS. These cells are activated by antigen-presenting cells [APCs] that present CNS-derived peptides and accumulate in MS lesions. They attack axons and neurons that express MHC-I molecules, which recognize target antigens [9]. CD8+ T cells disrupt the BBB by releasing perforin, which damages endothelial cell membranes, and by producing proinflammatory cytokines such as interferon-gamma (IFNγ) and tumor necrosis factor-alpha (TNFα), which weaken the junctions between endothelial cells and increase BBB permeability with other inflammatory molecules such as vascular endothelial growth factor (VEGF). They also recruit and activate other immune cells, exacerbating CNS inflammation and increasing BBB permeability [3,9]. Additionally, CD8+ T cells can activate microglia, enhance their inflammatory responses, and further support T-cell activity, which amplifies the inflammatory response in MS lesions [10].

1.3 B Cells in Multiple Sclerosis: pathogenesis and immune mechanisms

B cells play a critical dual role in the pathogenesis of MS. They produce autoantibodies that damage the myelin sheath and act as APCs, facilitating immune activation and promoting inflammation [8]. Laboratory studies have demonstrated that B cells release substances capable of directly inducing the death of oligodendrocytes and neurons, further contributing to MS progression [11].

The migration of B cells into the CNS is thought to be regulated by T follicular helper (TFH) cells, a specialized type of immune cell detected in the cerebrospinal fluid (CSF) of MS patients [12]. Notably, B-cell clones exhibit bidirectional movement between the CNS and the peripheral immune system, guided by chemical attractants such as C-X-C motif chemokine ligands CXCL10, CXCL12, and CXCL13 [13].

Additionally, B cells release proinflammatory cytokines that activate other immune cells, amplifying CNS damage. However, they also produce anti-inflammatory cytokines that help regulate immune responses, reflecting their complex role in MS pathogenesis [14]. The presence of immunoglobulin G (IgG) oligoclonal bands (OCBs) in the CSF remains a major diagnostic marker for MS. In contrast, the less frequent IgM OCBs are associated with disease activity and responsiveness to B-cell-depleting therapies [15].

Recent advancements in MS treatment include approving B-cell-targeted therapies such as ocrelizumab and ofatumumab. These therapies selectively deplete B cells or inhibit their activity, leading to a reduction in both disease activity and progression. The pivotal role of B cells in MS pathogenesis has driven the development of highly effective treatments aimed at these cells [16]. For example, rituximab, an anti-CD20 monoclonal antibody, is effective in lowering both the activity and the frequency of relapses in MS patients [17]. However, the most common side effect associated with anti-CD20 monoclonal antibodies, such as ocrelizumab and ofatumumab, is infusion-related reactions, likely due to excessive complement activation. To reduce the risk of serious events, safety protocols such as pre-medication with antihistamines (e.g., diphenhydramine) and antipyretics (e.g., acetaminophen) are routinely implemented during intravenous administration [18].

In addition, SLAMF7, a member of the signaling lymphocytic activation molecule (SLAM) family expressed on B cells and other immune cells, has been implicated in regulating B-cell activation and adaptive immune responses. Evidence from experimental and clinical studies indicates that dysregulation of SLAMF7 signaling can enhance pathogenic B-cell–mediated immune responses and promote pro-inflammatory T-cell activation, thereby increasing susceptibility to CNS autoimmunity [19].

2. Investigating the involvement of proinflammatory cytokines in the pathogenesis of Multiple Sclerosis

2.1 Interferon-gamma (IFNγ)

IFNγ, a proinflammatory cytokine produced by immune cells such as CD8+ T cells, CD4+ Th1 cells, and natural killer (NK) cells, plays dual roles in MS. Notably, IFNγ contributes to inflammation and tissue damage by activating and recruiting immune cells to the CNS, allowing them to harm neurons, axons, and oligodendrocytes directly [20]. Moreover, IFNγ activates microglia, macrophages, and astrocytes, promoting the release of proinflammatory mediators and sustaining the inflammatory cycle. IFNγ further facilitates immune cell migration and

amplifies the inflammatory cascade by affecting the production of other proinflammatory cytokines [21]. While IFNγ is known primarily for its proinflammatory effects in MS, it also plays an important anti-inflammatory role in this disease. It can inhibit the production of proinflammatory cytokines and promote the differentiation of CD4+ T cells into regulatory T cells (Tregs), which have immunosuppressive functions [22]. These dual effects of IFNγ are mediated through the activation of JAK/STAT proteins, which regulate genes involved in inflammation and immune activation [23].

2.2 Tumor necrosis factor (TNF)

TNF is produced by various immune cells, such as macrophages, T cells, and microglia. In the context of MS, TNF triggers specific cellular pathways like NF-Kb and mitogen-activated protein kinase (MAPK) pathways, which result in the expression of genes that promote inflammation and activate immune cells in the CNS [24]. A common genetic variation associated with MS inflammation is the TNF receptor superfamily member 1A (TNFRSF1A) gene, which contributes to processes such as the breakdown of the BBB, allowing immune cells to enter the CNS. TNF also stimulates the production of other proinflammatory cytokines like IL-1 and IL-6, further intensifying the inflammatory response in the CNS [25]. Additionally, TNF plays a role in the destruction of myelin by promoting the production of matrix metalloproteinases (MMPs), which degrade the extracellular matrix and cause myelin damage [26]. Moreover, evidence supporting the involvement of TNF in MS includes its detection in astrocytes, microglia, and endothelial cells, particularly within acute and chronic active brain lesions in MS patients [27–29].

2.3 Interleukin-17 (IL-17)

IL-17 is a proinflammatory cytokine produced primarily by Th17 cells, gamma-delta T cells [γδ T cells], and natural killer T [NKT] cells, and plays a crucial role in MS. IL-17 contributes to inflammation and immune-mediated damage in the CNS by activating immune cells and promoting the release of other inflammatory molecules and chemokines [30]. IL-17 disrupts the BBB, allowing immune cells and inflammatory substances to enter the CNS and worsening inflammation. Studies have shown elevated levels of IL-17 and Th17 cells in blood, CSF, and MS lesions, particularly during active disease stages [31]. Moreover, Elevated levels of IL-17 and Th17-related transcripts, such as IL-6 and IL-17a, have been observed in MS plaques obtained during autopsy. Additionally, IL-17 was identified as the most prominently expressed gene in the CNS of MS patients at autopsy [32].

2.4 Interleukin-6 (IL-6)

IL-6, a proinflammatory cytokine produced by various immune cells, contributes to the development and progression of MS [22]. Elevated levels of IL-6 are observed in blood, CSF, and MS lesions [33]. Patients diagnosed with secondary progressive MS (SPMS) demonstrated higher IL-6 levels than those with relapsing-remitting MS (RRMS) or primary-progressive MS (PPMS)[34]. IL-6 activates immune cells, promotes the production of proinflammatory molecules, and enhances immune cell entry into the CNS. It interacts with other cytokines to sustain inflammation in the CNS and disrupts the BBB, facilitating immune cell infiltration [35].

However, IL-6 also has protective functions within the CNS. It supports the survival and differentiation of oligodendrocytes, which produce the myelin sheath and are involved in neurons' growth, repair, and regeneration [36]. The leukemia inhibitory factor (LIF)-IL-6 axis, formed by the interaction between IL-6 and LIF [37], facilitates neural repair and regeneration processes (Figure 1).

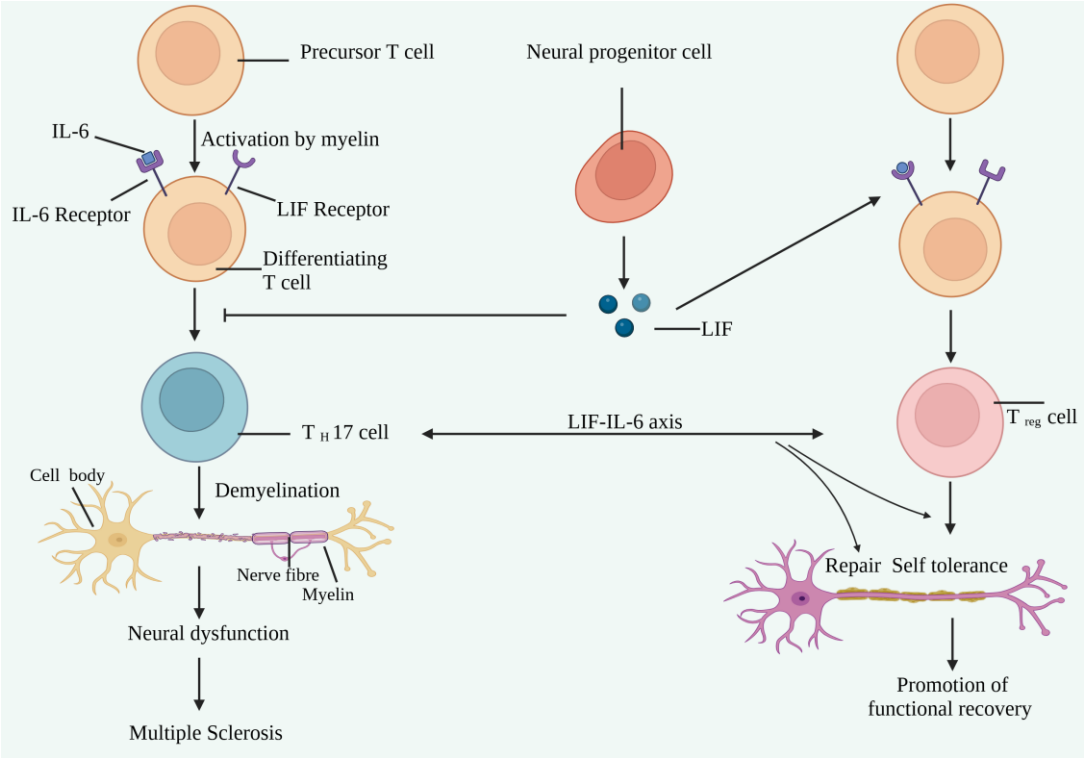

Figure 1. The LIF–IL-6 axis regulates multiple sclerosis. IL-6 promotes Th17 cell differentiation, causing myelin damage, while LIF inhibits Th17 cells, enhances Treg cell differentiation, and supports CNS repair and self-tolerance, presenting a therapeutic approach for autoimmune damage (figure created by BioRender).

2.5 Interleukin-12 (IL-12)

IL-12, a cytokine produced by APCs, plays a significant role in the development of MS. IL-12 plays a proinflammatory role by promoting the differentiation of CD4+ T cells into Th1 cells, which produce proinflammatory cytokines such as IFNγ [38]. This Th1-driven immune response targets myelin, resulting in its destruction and contributing to MS lesions [8]. IL-12 also enhances the production of other proinflammatory cytokines, such as IL-17, which is associated with inflammation in the CNS and is implicated in MS pathogenesis [30]. IL-12 not only contributes to the development of MS through its pro-inflammatory effects but also plays a role in the activation and proliferation of NK cells, which are involved in immune surveillance and defense against pathogens. NK cells can enter the CNS and participate in the immune response during MS [20]. Owing to its pro-inflammatory nature, IL-12 has been targeted as a potential therapeutic strategy for MS. Clinical trials have examined the ability of inhibitors of IL-12 to modulate the immune response and decrease inflammation in individuals with MS [39].

2.6 Interleukin 1β (IL-1β)

IL-1β is a proinflammatory cytokine produced primarily by activated immune cells, contributing to inflammation and immune dysregulation in MS. IL-1β activates pathways that lead to the production of other proinflammatory cytokines and the recruitment and activation of immune cells. It also promotes the breakdown of the BBB, allowing immune cells to enter the CNS and damage myelin and neural tissue [40]. IL-1β can enhance the activation and survival of autoreactive T cells and modulate the activity of other immune cells, such as B cells and microglia [41]. Elevated levels of IL-1β have been observed in MS patients, particularly during active phases of the disease, and genetic variations in genes related to IL-1β signaling have been associated with increased MS risk [42]. Genetic variations in IL-1β signaling genes impact the risk of developing MS. For example, a well-studied variant called rs1143634 in the IL1B gene increases IL-1β production and MS risk. Another gene, IL1RN, produces the IL-1 receptor antagonist (IL-1RA), which inhibits IL-1β signaling. IL1RN variations, such as VNTR polymorphisms, affect IL-1RA levels and increase MS risk. However, the relationship between IL1RN gene variations and MS risk is complex and involves interactions with other genes and the environment [43].

2.7 Interleukin-18 (IL-18)

IL-18 is a critical proinflammatory cytokine involved in regulating the immune response against infections and influencing various immune cells [22]. It collaborates with IL-12 and IL-2 to stimulate the production of specific cytokines. IL-18 is produced by both immune and non-immune cells, highlighting its diverse roles in cell differentiation and survival [44]. In MS, IL-18 plays a significant role in promoting inflammation and tissue damage. Its elevated levels in MS patients and genetic variations in the IL-18 gene associated with MS susceptibility highlight its involvement in the disease [45]. Additionally, Nicoletti et al. reported significantly higher IL-18 levels during the acute phase compared to the stable phase and observed elevated levels in SPMS compared to RRMS, suggesting a potential association between IL-18 levels and disease progression [46]. Furthermore, IL-18 activates immune cells, compromises the BBB, and enhances the survival and activation of autoreactive T cells, contributing to the development of MS [44].

2.8 Interleukin 16 (IL-16)

IL-16 is a proinflammatory cytokine produced primarily by CD4+ and CD8+ cells, as well as other cell types, such as monocytes, macrophages, dendritic cells, mast cells, fibroblasts, and microglia [47]. It functions by binding to the CD4 receptor on immune cells, influencing various biological processes. The active form of IL-16, released through caspase 3-mediated cleavage, promotes the migration of CD4+ Th1 cells, facilitating T-cell proliferation and B-cell development [48]. Moreover, IL-16 suppresses inflammation mediated by antigen-triggered Th2 cells and hinders the chemotactic effects of certain proteins on T cells. It also regulates migration, activation, molecular expression, cytokine synthesis, coordination with dendritic cells, collaboration with B cells, interactions among T cells, and the production of inflammatory

cytokines, and modulates T-cell migration by affecting chemokine receptors such as C-C chemokine receptor type 5 (CCR5), C-X-C chemokine receptor type 4 (CXCR4), and CXCR3 [49].

IL-16 has been implicated in the development of autoimmune disorders, including MS and systemic lupus erythematosus (SLE) [50–52]. Research on the levels of IL-16 in the blood of individuals with MS is limited. In contrast, other studies have reported elevated levels of IL-16 in the CSF and brain lesions of MS patients, suggesting its potential involvement in the disease process [47]. Additionally, studies have demonstrated that interferon β-1 therapy reduces IL-16 levels among individuals with MS. These findings support the existence of significant disparities in IL-16 levels between MS patients and control individuals. Furthermore, IL-16 plays a vital role in recruiting and activating CD4+ T cells, which contribute to the inflammatory response in MS by attracting them to CNS inflammation sites through binding to the CD4 receptor. This recruitment of CD4+ T cells may contribute to the immune-mediated damage to myelin and subsequent neuroinflammation observed in MS [53,54].

2.9 Interleukin 23 (IL-23)

IL-23 is a proinflammatory cytokine produced by immune cells in response to inflammation and plays a significant role in MS. It is involved in the differentiation and activation of Th17 cells, which contribute to immune-mediated damage in the CNS [55]. IL-23 increases the growth and persistence of Th17 cells, resulting in increased production of inflammatory cytokines such as IL-17. It also strengthens the stability and harmful potential of Th17 cells, amplifying their role in inflammation and tissue damage in MS [30,31]. IL-23 can also drive the production of other proinflammatory cytokines, such as IL-6 and TNF-α, further contributing to immune-mediated damage in MS [56].

Gene variations in IL-23 signaling are associated with increased MS susceptibility. Targeting IL-23 has emerged as a potential therapy for MS. Clinical trials using IL-23-blocking monoclonal antibodies have shown promising results, reducing disease activity and slowing disability progression. These treatments inhibit IL-23 to decrease Th17 cell production and function, thereby alleviating the inflammatory response in the central nervous system in MS [45,56]. Furthermore, IL-23's clinical potential is primarily evident in two ways. One is its role as a disease biomarker, which can support early diagnosis and timely treatment. The other is its use as a therapeutic target, for example, through IL-23 inhibitors [57], as shown in Figure 2.

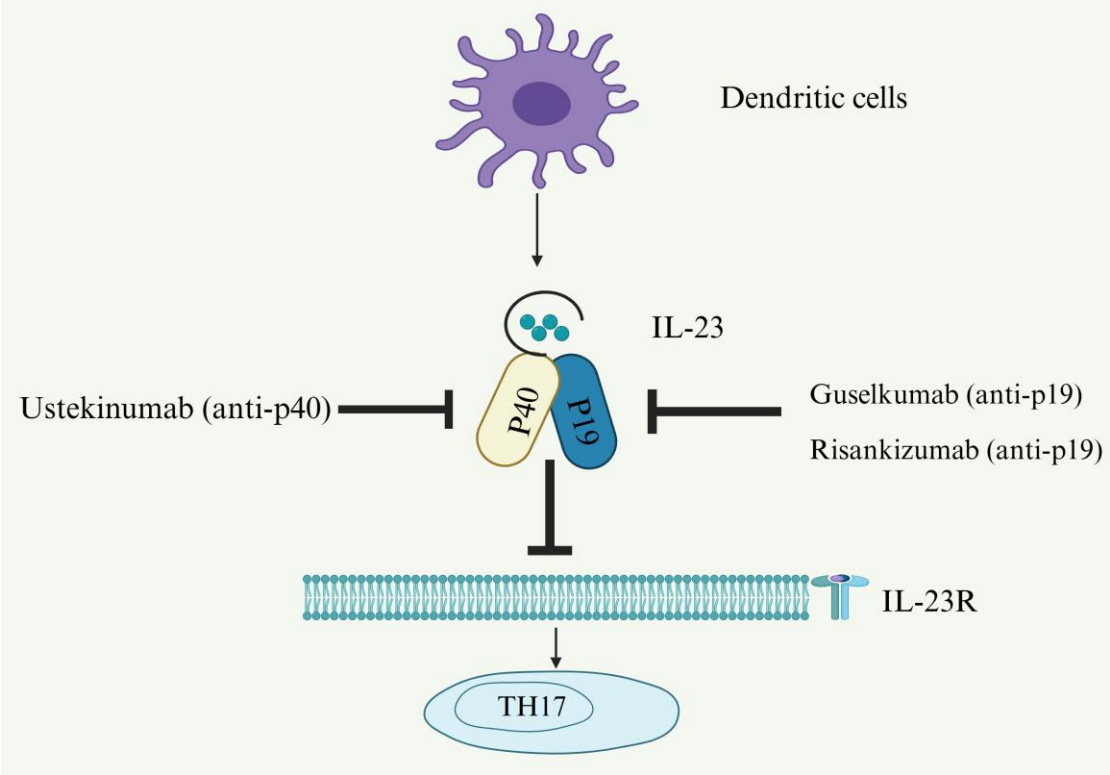

Figure 2. Therapeutic targeting of IL-23 in autoimmune diseases. IL-23 inhibitors have proven to be effective in modulating immune responses. Ustekinumab acts on the IL-23p40 subunit, whereas Guselkumab and Risankizumab selectively inhibit IL-23p19. By binding to these subunits, these drugs block the IL-23 signaling pathway and reduce TH17-driven immune activity (figure created by BioRender).

3. Investigating the involvement of anti-inflammatory cytokines in the pathogenesis of Multiple Sclerosis

3.1 Interleukin-10 (IL-10)

IL-10 is an important cytokine that regulates inflammation and immune responses, with anti-inflammatory effects that help suppress excessive immune reactions. It can reduce the production of proinflammatory cytokines, inhibit immune cell proliferation, and have neuroprotective effects [39]. While some studies have not found a significant association between IL-10 gene variations and cytokine levels in the development of MS [58], other research suggests that genetic variations leading to decreased IL-10 expression are associated with MS symptom onset [59]. Higher IL-10 levels are now associated with less severe disability in MS patients, indicating its potential as a therapeutic target. Furthermore, IL-10 secretion decreases before relapse and increases during remission in MS patients. Additionally, IL-10 expression in the CNS is linked to the recovery phase in experimental autoimmune encephalomyelitis (EAE) [60].

3.2 Interleukin-22 (IL-22)

IL-22, a member of the IL-10 cytokine family, plays a complex role in MS. It is primarily produced by Th17 and NK cells and acts on CNS target cells [30]. IL-22 has both protective and

detrimental effects on MS. On one hand, it exhibits anti-inflammatory actions by inhibiting proinflammatory cytokines and promoting the production of anti-inflammatory molecules [61]. It also helps maintain BBB integrity, protecting the CNS from immune cell infiltration. On the other hand, it contributes to inflammation and tissue damage in MS [62]. It stimulates the production of enzymes, including MMPs, that degrade the extracellular matrix, destroying myelin. IL-22 also activates astrocytes, contributing to neuroinflammation and neuronal damage [63]. Furthermore, recent investigations have found that IL-22 levels correlate with MS disease activity and progression, suggesting its potential as a biomarker for treatment response [64]. However, some evidence suggests a protective role. One study demonstrated that IL-22 improved motor and behavioral performance in EAE and significantly enhanced remyelination. These results provide valuable insights into the potential for developing targeted therapeutic strategies for MS [65].

3.3 Interleukin-20 (IL-20)

IL-20 is a cytokine belonging to the IL-10 family and has a vital influence on immune cell communication. Activated T cells, monocytes, and keratinocytes produce it. IL-20 operates through the JAK-STAT signaling pathway, influencing genes involved in inflammation, immune responses, and tissue repair [66]. The IL-20 subfamily includes cytokines such as IL-19, IL-22, IL-24, and IL-26, which connect the immune system with epithelial tissues. These cytokines bind specific receptors on epithelial cells and are produced by immune cells [67]. IL-20 promotes immune cell activation and migration to the CNS, contributing to inflammation. It also stimulates the production of proinflammatory molecules, supports immune cell survival, and may affect BBB integrity [31]. Furthermore, A study found that PPMS patients had lower IL-20 levels than RRMS patients [68]; however, ocrelizumab treatment increased IL-20 and IL-19 levels in PPMS patients compared to untreated individuals [68]. Additionally, a significant association between specific genotypes in the IL-20 gene and a protective role against MS development has been reported [69].

3.4 Interleukin-36 (IL-36)

IL-36 is a subgroup of the IL-1 family consisting of IL-36α, IL-36β, IL-36γ, and IL-36Ra. It is expressed in various cell types and triggers the production of several cytokines, chemokines, and proinflammatory mediators [70]. IL-36 agonists stimulate the generation of IFN-γ, IL-4, and IL-17 in T cells and induce the maturation of dendritic cells. Activated dendritic cells under IL-36 stimulation produce cytokines and chemokines that promote Th1 and Th17 immune responses [71]. Aberrant production and activity of IL-36 cytokines have been associated with autoimmune disorders such as psoriasis, RA, and primary Sjögren's syndrome [45].

The specific role of IL-36 in MS is not yet fully understood, as most research has focused on its involvement in other autoimmune disorders. However, it is possible that IL-36, with its proinflammatory properties and ability to promote Th1 and Th17 immune responses, may contribute to the inflammation observed in MS [45]. While limited, one study reported higher levels of IL-36 in individuals with MS than in healthy controls, suggesting a potential association between IL-36 and the disease [71].

3.5 Interleukin 38 (IL-38)

IL-38, a recently discovered cytokine, was first identified in 2001 and is classified within the IL-36 subfamily along with IL-36α, IL-36β, IL-36γ, and IL-36R [72]. IL-38 can interact with different receptors, leading to the suppression of pro-inflammatory factors [73]. Various cell types, including epithelial cells, monocytes, macrophages, and immune cells, release this cytokine [74]. IL-38 can be expressed in various tissues, such as the heart, placenta, fetal liver, skin, spleen, and thymus, as well as in proliferating B cells of the tonsils [75]. While IL-38 has been recognized for its immunosuppressive role in inflammatory infectious diseases, it is also considered a promising target for therapeutic intervention. However, there are still significant knowledge gaps regarding the biology of IL-38 in infections [76]. Key questions about IL-38 include whether natural human variants exist, how it responds to pathogens, and its role in pathogen clearance and inflammation resolution. Additionally, the reasons why lower concentrations of IL-38 have a more pronounced effect remain unclear, leaving its precise role in infections uncertain [77]. Given the limited number of studies investigating this topic, the role of IL-38 in MS is not fully understood. It is considered an anti-inflammatory cytokine that may impact inflammatory responses in MS [78]. Studies have shown no significant differences in overall serum levels of IL-38 between MS patients and healthy controls [78,79]. However, newly diagnosed MS patients have significantly higher levels of IL-38 than those who have received previous treatment [79].

4. Materials and methods

This narrative review was conducted through a structured literature search across PubMed, NCBI, and MDPI. The search strategy combined predefined keywords, including multiple sclerosis, cytokines, adaptive immunity, pro-inflammatory cytokines, and anti-inflammatory cytokines. Studies were selected based on their relevance to MS immunopathogenesis and cytokine-mediated mechanisms. Both primary research and review articles were included to provide a comprehensive scientific context.

5. Conclusions

This review highlights the critical roles of cytokines and adaptive immunity in MS. Proinflammatory cytokines drive neuroinflammation and damage through interactions with T and B cells, while anti-inflammatory cytokines support immune regulation and repair. The balance between these processes is central to MS pathophysiology, offering biomarkers for disease activity and targets for therapy. Future research should focus on investigating emerging cytokines such as IL-19, IL-22, IL-23, and IL-38 to understand their roles in neuroinflammation and immune regulation. Understanding their mechanisms may help identify novel therapeutic targets, enhance treatment efficacy, and minimize adverse effects, ultimately improving patient outcomes.

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Y.M. wrote the original draft, prepared figures, and reviewed the manuscript. J.A. did the revisions and edited the final version of the manuscript. All the authors critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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Conflicts of Interest
The authors declare no conflicts of interest.

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Arabic translation of title page

ديناميكيات السيتوكينات في التصلب المتعدد: آليات تنظيم المناعة التكيفية في الالتهاب العصبي

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الملخص

يُعدّ التصلب المتعدد اضطرابًا مناعيًا ذاتيًا مزمنًا يصيب الجهاز العصبي المركزي، ويتّسم بخلل في التنظيم المناعي، وعمليات التهابية معقدة، وإزالة لغمد الميالين المحيط بالمحاور العصبية. تهدف هذه المراجعة إلى تحليل الأدوار المحورية للسيتوكينات في تنظيم الالتهاب العصبي وتأثيرها في الاستجابات المناعية التكيفية. إذ تساهم السيتوكينات المحفزة للالتهاب، مثل الانترلوكين ٦ والانترلوكين ١٧ والانترفيرون جاما في تعزيز تنشيط الخلايا المناعية وإحداث الضرر النسيجي، مما يسهم في تفاقم المسار المرضي. وعلى النقيض من ذلك، تُظهر السيتوكينات المضادة للالتهاب، مثل الانتر لوكين ١٠و٢٢، أدوارًا تنظيمية تسهم في كبح النشاط المناعي المرضي وتعزيز الحماية العصبية. كما تستعرض هذه المراجعة الدور الناشئ لسيتوكينات جديدة تم التعرف عليها مؤخرًا في فسيولوجيا مرض التصلب المتعدد، مع تسليط الضوء على دورها المحتمل في تعديل مسار المرض وآلياته المناعية. ومن خلال تحليل أنماط السيتوكينات وتفاعلها مع مكونات المناعة التكيفية، توفر هذه الدراسة فهمًا أعمق للآليات المناعية المرضية الكامنة وراء التصلب المتعدد، بما يفتح آفاقًا لتحديد مؤشرات حيوية دقيقة لنشاط المرض، ويُسهم في توجيه الأبحاث المستقبلية نحو استراتيجيات علاجية أكثر فاعلية. في الخلاصة، يُعدّ اختلال التوازن بين السيتوكينات المحفِّزة والمضادّة للالتهاب عاملًا أساسيًا في إمراضية التصلّب المتعدد، لما له من دور في تعزيز الالتهاب العصبي والتسبّب بتلف نسيجي ناجم عن الاستجابة المناعية. كما تبرز الحاجة إلى دراسات مستقبلية لتحديد الدور الدقيق للسيتوكينات المستجدة في نشاط المرض وتقدّمه عبر المراحل المختلفة للتصلّب المتعدد.

الكلمات المفتاحية: السيتوكينات | المناعة التكيفية | الالتهاب | التصلّب المتعدد | التنكّس العصبي.