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Molecular and Immunological Mechanisms Linking EBV Infection to Multiple Sclerosis: Literature Review

Michał Czechowski

Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland

michat.czechowski@gmail.com

https://orcid.org/0009-0009-7038-6731

Gabriela Sikora

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

gabriela.sikora1029@gmail.com

https://orcid.org/0009-0002-4627-7403

Martyna Woźniak

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

m.wozniak912@gmail.com

https://orcid.org/0009-0002-2518-4531

Karolina Kutnik

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakutnik98@gmail.com

https://orcid.org/0009-0008-2250-1232

Karolina Koguc

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakoguc@gmail.com

https://orcid.org/0009-0004-0762-7356

Karolina Kusibab

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakusibab00@gmail.com

https://orcid.org/0009-0004-9743-8734

Gabriela Skórska

Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland

gabrielaskorska12@gmail.com

https://orcid.org/0009-0008-2197-3414

Marcela Słomianny

Medical University of Silesia, Poniatowskiego 15, 40-055 Katowice, Poland

slomiannymarcela@gmail.com

https://orcid.org/0009-0004-8029-1422

Karolina Kolada

Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland

karolinakolada2001@gmail.com

https://orcid.org/0009-0005-4960-9604

Małgorzata Sajda

Medical University of Lublin Aleje Racławickie 1, 20-059 Lublin, Poland

m.skura15@gmail.com

https://orcid.org/0009-0004-6836-0704

Abstract:

Background: Epstein–Barr virus (EBV), a ubiquitous herpesvirus, has been increasingly implicated as a key environmental factor in the pathogenesis of multiple sclerosis (MS). Nearly all individuals with MS are EBV-seropositive and mounting epidemiological and immunological evidence suggests a causal relationship.

Objective: This review aims to summarize current knowledge on the potential mechanisms by which EBV infection contributes to MS development, with a particular focus on immunopathology, genetic susceptibility and therapeutic implications.

Methods: A literature search was conducted using PubMed, Google Scholar, and ResearchGate. Key terms included “Epstein–Barr virus,” “EBV,” “multiple sclerosis,” “EBNA1,” “molecular mimicry,” “autoimmunity,” and “HLA-DRB1*15:01.” Studies published between 2005 and 2024 were reviewed, with emphasis on high-impact research articles and recent findings.

Results: Several mechanisms have been proposed to explain the association between EBV and MS, including molecular mimicry between viral and CNS antigens, chronic latent infection of B cells, and the activation of autoreactive T cells in genetically predisposed individuals. The strong association with the HLA-DRB1*15:01 allele suggests a gene–environment interaction facilitating aberrant antigen presentation and loss of tolerance. Emerging therapies targeting EBV, including EBV-specific T cell immunotherapy and vaccination strategies offer promising avenues for disease modification.

Conclusion: EBV likely plays a crucial role in MS pathogenesis, acting as a trigger of autoimmunity in susceptible individuals. Understanding the mechanisms of EBV-mediated immune dysregulation may enable the development of more targeted and preventive treatments for MS.

Keywords: Epstein–Barr virus, multiple sclerosis, EBNA1, molecular mimicry, HLA-DRB1*15:01, autoimmunity, B cells, T cells, neuroinflammation, immunotherapy

Introduction:

Multiple sclerosis (MS) is a chronic, immune-mediated demyelinating disease of the central nervous system (CNS), characterized by inflammation, neurodegeneration, and progressive neurological dysfunction. While the exact etiology of MS remains elusive, it is widely accepted that the disease results from a complex interplay between genetic predisposition and environmental exposures. Among the latter, viral infections—particularly Epstein-Barr virus (EBV)—have emerged as leading candidates in the pathogenesis of MS (1,2).

EBV is a ubiquitous human gammaherpesvirus that infects over 90% of the global population, establishing lifelong latency in B lymphocytes (3). A large body of evidence suggests that EBV infection not only precedes MS onset but may play a direct role in disease development. Nearly all MS patients are EBV-seropositive, and elevated titers of antibodies against EBV

nuclear antigen 1 (EBNA1) and viral capsid antigen (VCA) have been consistently observed in individuals who later develop MS (4,9).

Recent mechanistic studies have provided compelling insights into how EBV may contribute to MS. These include molecular mimicry between EBNA1 and CNS proteins such as GlialCAM (6), chronic activation and dysregulation of EBV-infected memory B cells within the CNS (2,7), and EBV-driven induction of endogenous retroviral elements such as HERV-W, which can amplify neuroinflammation (2,8). The discovery of clonally expanded B cells in the cerebrospinal fluid of MS patients producing antibodies reactive to both EBNA1 and GlialCAM strongly supports a direct autoimmune link (10).

This review aims to summarize the current understanding of the role of EBV in MS pathogenesis. We will explore the epidemiological and immunological evidence connecting EBV with MS, elucidate key molecular and cellular mechanisms involved, and discuss emerging strategies for prevention and treatment targeting EBV infection.

Methodology:

A literature review was conducted using PubMed, Google Scholar, and ResearchGate. Search terms included: *Epstein-Barr virus*, *EBV*, *multiple sclerosis*, *MS*, *autoimmunity*, *EBNA1*, *GlialCAM*, *molecular mimicry*, and *neuroinflammation*. Articles published between 2005 and 2024 were considered. Priority was given to peer-reviewed original research articles, systematic reviews, and meta-analyses written in English. Reference lists of selected papers were also screened to identify additional relevant sources. Only studies addressing the role of EBV in the pathogenesis of MS at the epidemiological, immunological, or molecular level were included in this review.

3. What is Multiple Sclerosis?

Multiple sclerosis (MS) is a chronic, immune-mediated demyelinating disorder of the central nervous system (CNS) that primarily affects young adults, particularly women, and represents one of the leading causes of non-traumatic neurological disability in this population. The

disease typically manifests between the ages of 20 and 40 and shows a female-to-male predominance of approximately 3:1 (12,13).

Epidemiologically, MS exhibits a clear geographical distribution, with higher prevalence in temperate regions of Europe and North America, and lower rates in equatorial regions. The global prevalence of MS is estimated at over 2.8 million cases, with increasing incidence observed over the past decades, possibly due to improved diagnostics and environmental factors (9). Both genetic predisposition (e.g., HLA-DRB1*15:01 allele) and environmental triggers, including low vitamin D levels, smoking, and viral infections—particularly Epstein-Barr virus—are thought to contribute to MS susceptibility (4,5).

Pathophysiologically, MS is characterized by immune-mediated damage to the myelin sheath, axons, and eventually neurons within the CNS. The disease involves an aberrant activation of autoreactive $CD4^+$ T cells, especially Th1 and Th17 subsets, along with a dysregulated B-cell response and innate immune cell participation. This leads to inflammation, demyelination, and subsequent neurodegeneration (18,19). Formation of demyelinating lesions (plaques) predominantly in the white matter of the brain, spinal cord, and optic nerves underlies the clinical symptoms, which can range from visual disturbances and limb weakness to cognitive impairment and ataxia.

MS is classically divided into several clinical subtypes: relapsing-remitting MS (RRMS), the most common form; secondary progressive MS (SPMS); primary progressive MS (PPMS); and progressive-relapsing MS (PRMS), though classification continues to evolve with advances in biomarkers and imaging techniques (29).

4. Immunological Mechanisms in Multiple Sclerosis

The pathogenesis of multiple sclerosis (MS) is driven by a complex and dysregulated immune response targeting components of the central nervous system (CNS), primarily myelin and oligodendrocytes. Both innate and adaptive immune systems contribute to this process, with autoreactive T and B cells playing central roles in initiating and sustaining inflammation, demyelination, and axonal damage (23,24).

$CD4^+$ T cells, especially Th1 and Th17 subsets, are believed to be major effectors in early MS pathogenesis. Th1 cells produce interferon-gamma (IFN-γ), while Th17 cells secrete

interleukin-17 (IL-17), both of which enhance the recruitment of inflammatory cells and disrupt the blood-brain barrier (BBB), facilitating immune cell infiltration into the CNS (25,26). Additionally, regulatory T cells (Tregs), which normally suppress autoreactive responses, are often functionally impaired in MS patients (19).

$CD8^+$ cytotoxic T cells are also abundant in MS lesions and may contribute directly to neuronal and oligodendrocyte injury via release of perforin and granzymes (19). These cells are increasingly recognized for their pathogenic role, particularly in progressive MS, where they may persist in the CNS and drive chronic damage.

B cells play a multifaceted role in MS. Beyond antibody production, B cells can act as antigen-presenting cells (APCs) and secrete pro-inflammatory cytokines such as IL-6 and TNF-α. The detection of oligoclonal bands (OCBs) in the cerebrospinal fluid (CSF) of ~90–95% of MS patients is a hallmark of intrathecal B-cell activation (15). Importantly, B-cell depleting therapies (e.g., anti-CD20 monoclonal antibodies) have demonstrated substantial efficacy in reducing MS disease activity, underscoring the central role of B cells in MS immunopathogenesis (16).

The innate immune system, including microglia and macrophages, contributes to lesion formation and expansion by releasing pro-inflammatory mediators, reactive oxygen species (ROS), and matrix metalloproteinases (MMPs), which exacerbate tissue injury and impair remyelination (17).

Collectively, these immune mechanisms result in the formation of demyelinating plaques, axonal transection, and eventually neurodegeneration, which underlie the clinical progression of MS. The interplay between peripheral immune activation and compartmentalized inflammation within the CNS creates a self-perpetuating cycle that is challenging to interrupt in advanced stages of the disease (21).

5. Virology of Epstein-Barr Virus

Epstein-Barr virus (EBV), also known as human herpesvirus 4 (HHV-4), is a ubiquitous double-stranded DNA virus belonging to the *Herpesviridae* family, *Gammaherpesvirinae* subfamily. EBV infects over 90% of the global population, typically during childhood or adolescence, and establishes a lifelong latent infection in host B lymphocytes (5,6).

EBV exhibits a biphasic life cycle consisting of a lytic phase and a latent phase. During primary infection, the virus enters the oropharyngeal epithelium and subsequently infects naive B cells via CD21 (complement receptor 2) and MHC class II molecules. In the lytic phase, EBV expresses immediate-early, early, and late genes, leading to the production of new virions and viral dissemination. This phase is responsible for symptoms of acute infection, such as infectious mononucleosis (3).

Following primary infection, EBV transitions into latency, where it persists in memory B cells in a transcriptionally restricted form. Three major latency programs have been described (latency I, II, and III), characterized by differential expression of EBV-encoded nuclear antigens (EBNAs) and latent membrane proteins (LMPs) (4). In healthy individuals, viral latency is tightly regulated by host immune surveillance, particularly cytotoxic $CD8^+$ T cells.

Among EBV latent antigens, EBNA1 is uniquely expressed across all latency types and plays a critical role in viral episome maintenance. Notably, EBNA1 has been implicated in molecular mimicry mechanisms, whereby cross-reactivity between EBNA1-derived peptides and CNS autoantigens may contribute to autoimmune diseases such as multiple sclerosis (5,6).

EBV also encodes a variety of non-coding RNAs and microRNAs that modulate host immune responses, inhibit apoptosis, and support immune evasion (7). Viral latency in B cells may result in their abnormal activation, survival, and antigen presentation, forming a potential link to B-cell dysregulation observed in MS.

Due to its capacity to modulate host immunity, evade immune detection, and persist in B cells—key players in MS pathogenesis—EBV remains a prime candidate as an environmental trigger in the etiology of multiple sclerosis.

6. Epidemiological Evidence Linking Epstein-Barr Virus to Multiple Sclerosis

A growing body of epidemiological research supports a strong association between Epstein-Barr virus (EBV) infection and the risk of developing multiple sclerosis (MS). Virtually all individuals diagnosed with MS show evidence of prior EBV infection, making EBV seronegativity exceedingly rare among MS patients 20,21).

Several longitudinal cohort studies have demonstrated that seroconversion to EBV positivity significantly precedes the onset of MS symptoms, often by several years or even decades, suggesting a temporal relationship consistent with a causal link (20,21). In particular, elevated levels of antibodies against EBV nuclear antigen 1 (EBNA1) have been consistently observed in individuals prior to MS diagnosis and are associated with an increased risk of disease development (5,6).

Moreover, a history of infectious mononucleosis (IM), a symptomatic manifestation of primary EBV infection, has been linked to approximately a twofold increased risk of MS, supporting the notion that the immune response to EBV plays a critical role in disease pathogenesis (7,8).

Geographical and demographic data further corroborate the EBV-MS connection. Both EBV prevalence and MS incidence increase with latitude and show similar patterns of distribution, implicating shared environmental or genetic susceptibility factors (31). Additionally, variations in HLA genotypes—particularly the MS-associated HLA-DRB1*15:01 allele—interact with EBV serostatus to modulate MS risk, highlighting the complex interplay between viral infection and host genetics (10).

Recent advances in large-scale seroepidemiological studies have reinforced these findings, demonstrating that elevated EBV-specific immune responses are among the strongest identifiable risk factors for MS, surpassing other environmental factors such as vitamin D deficiency and smoking (30).

Collectively, these epidemiological data provide compelling evidence that EBV infection is a necessary, though not solely sufficient, factor in MS etiology, warranting further investigation into the underlying biological mechanisms that translate EBV infection into autoimmune CNS damage.

7. Proposed Pathogenetic Mechanisms Linking EBV Infection to Multiple Sclerosis

Although the epidemiological association between Epstein-Barr virus (EBV) infection and multiple sclerosis (MS) is well established, the precise biological mechanisms underlying this relationship remain an area of intense research. Several interrelated hypotheses have been

proposed to explain how EBV may contribute to MS pathogenesis, drawing on both molecular and immunological findings (Soldan & Lieberman, 2023; Lanz et al., 2022).

The leading theories suggest that EBV may act as a trigger of CNS-directed autoimmunity through multiple mechanisms, including molecular mimicry, epitope spreading, bystander activation, and the expansion of autoreactive B cells (Guan et al., 2019; Lanz et al., 2022). One notable observation is the presence of clonally expanded B cells in the cerebrospinal fluid (CSF) of MS patients that recognize both EBV antigens and CNS autoantigens such as GlialCAM, supporting the idea of antigenic cross-reactivity (Lanz et al., 2022).

Moreover, EBV's ability to establish latency in memory B cells, evade cytotoxic T cell responses, and persist in the host for life creates an immunological environment favorable for chronic CNS inflammation (Kuchroo & Weiner, 2022; Hedström, 2023). The detection of EBV-infected B cells within meningeal ectopic lymphoid structures in MS brain tissue further supports the concept that the virus may promote compartmentalized immune responses within the CNS (Soldan & Lieberman, 2023).

Recent immunological and genomic studies have also highlighted the interaction between EBV latent proteins (especially EBNA1) and MS risk alleles, such as HLA-DRB1*15:01, indicating a gene–environment synergy in MS pathogenesis (Lanz et al., 2023; Morawiec et al., 2025).

In the following subsections, we will examine each of these proposed mechanisms in detail, incorporating evidence from experimental models, post-mortem analyses, and recent immunological studies.

8. Molecular Mimicry

Molecular mimicry is one of the most extensively studied mechanisms by which Epstein-Barr virus (EBV) may trigger autoimmunity in multiple sclerosis (MS). This hypothesis proposes that viral antigens share sequence or structural similarities with self-proteins in the central nervous system (CNS), leading to a misdirected immune response where the host immune system attacks its own tissues.

One of the most compelling examples involves EBV nuclear antigen 1 (EBNA1), a protein expressed during latent EBV infection, which contains peptide sequences that mimic epitopes found on GlialCAM, a glial cell adhesion molecule expressed in the CNS. This molecular similarity enables cross-reactive B and T cells, initially primed against EBNA1, to target GlialCAM, thereby contributing to CNS-directed autoimmunity (1).

In a landmark study, Lanz et al. (2022) demonstrated that clonally expanded B cells in the cerebrospinal fluid of MS patients bound both EBNA1 and GlialCAM, providing direct evidence of cross-reactivity consistent with molecular mimicry (1). Furthermore, these B cells produced antibodies that bound EBNA1 and CNS antigens with high affinity, reinforcing the notion that viral priming can elicit an autoimmune response.

In addition to B cell cross-reactivity, $CD4^+$ and $CD8^+$ T cells reactive to EBNA1 have been shown to recognize peptides derived from myelin proteins such as myelin basic protein (MBP) and myelin oligodendrocyte glycoprotein (MOG), suggesting a broader phenomenon of T cell–mediated mimicry contributing to demyelination (29,30).

Notably, individuals with the HLA-DRB1*15:01 allele, a major genetic risk factor for MS, present EBNA1-derived peptides more efficiently to T cells, which may potentiate the autoimmune cascade in genetically predisposed hosts (4,5). These findings underscore the importance of gene–environment interactions in MS pathogenesis and suggest that molecular mimicry may serve as the initial spark in a complex inflammatory process.

While molecular mimicry alone is unlikely to account for the full spectrum of MS immunopathology, it provides a biologically plausible and experimentally supported framework linking a ubiquitous viral infection with a rare autoimmune disease.

9. Expansion of Autoreactive B Cells and Ectopic Lymphoid Follicles

Another central mechanism proposed to link Epstein–Barr virus (EBV) infection with multiple sclerosis (MS) pathogenesis is the persistence and expansion of autoreactive B cells, particularly within the central nervous system (CNS). EBV has a unique tropism for B lymphocytes, where it establishes latency and promotes their survival, proliferation, and resistance to apoptosis (2,3).

In MS, clonally expanded B cells have been found not only in the periphery but also within the cerebrospinal fluid (CSF) and meningeal compartments, where they often reside in ectopic lymphoid follicles (ELFs) — organized immune aggregates resembling secondary lymphoid organs (1,2). These structures are frequently observed in the meninges of patients with progressive MS and are associated with adjacent cortical demyelination and neurodegeneration (18).

Evidence suggests that EBV-infected memory B cells may home to the CNS and contribute to local antigen presentation and cytokine secretion, perpetuating chronic inflammation. In the study by Lanz et al. (2022), B cell clones derived from MS CSF recognized both EBNA1 and GlialCAM, suggesting that EBV infection drives the selection of autoreactive B cell populations (1). These cells can then mature into plasma cells that secrete pathogenic antibodies, or function as antigen-presenting cells (APCs), supporting T cell activation and expansion (18,19).

Furthermore, studies have demonstrated that these EBV-infected B cells express elevated levels of CD80/CD86 and MHC class II, enhancing their capacity to activate autoreactive T cells and amplify the local autoimmune response (13,14). The chronic presence of such activated B cells within ELFs creates a self-sustaining inflammatory niche in the CNS, which is increasingly considered a hallmark of progressive MS pathology.

Altogether, the expansion of EBV-infected, autoreactive B cells in meningeal ELFs provides a plausible anatomical and immunological link between systemic EBV infection and compartmentalized CNS autoimmunity.

10. EBV Latency and Immune Evasion

Epstein–Barr virus (EBV) establishes a lifelong latent infection in the host, primarily within memory B cells, where it evades immune surveillance and periodically reactivates. This persistence of EBV in immunologically privileged niches, particularly in B cell subsets implicated in autoimmunity, is thought to play a critical role in multiple sclerosis (MS) pathogenesis (2,3).

During latency, EBV expresses a restricted set of viral proteins — notably EBNA1, LMP1, and LMP2A — which promote B cell survival and proliferation while minimizing detection

by cytotoxic $CD8^+$ T cells. EBNA1, in particular, is poorly processed by the proteasome due to its glycine–alanine repeat domain, leading to reduced presentation on MHC class I molecules and diminished cytotoxic T cell recognition (2,8). This stealthy expression profile allows infected B cells to persist undetected in peripheral and possibly central compartments.

Importantly, EBV-infected B cells have been shown to modulate local immune responses. For instance, LMP1 mimics CD40 signaling, enhancing the expression of co-stimulatory molecules and cytokines such as IL-6 and IL-10, thereby skewing the immune milieu toward a pro-inflammatory and B cell–permissive environment (3). LMP2A, meanwhile, can promote B cell receptor (BCR)-independent survival signals, supporting the longevity of autoreactive clones (2,7).

These immune evasion strategies contribute to a "smoldering" infection, in which low-level viral activity is sustained over time without provoking a full antiviral immune response. In the context of MS, such persistent EBV activity may chronically stimulate autoreactive lymphocytes, leading to sustained CNS inflammation and demyelination (2,13).

Moreover, impaired $CD8^+$ T cell responses to EBV have been reported in MS patients, suggesting a host susceptibility factor that allows greater EBV persistence and the survival of pathogenic B cell clones (4). This dysfunction may be genetically mediated or arise from exhaustion due to chronic antigen exposure.

Taken together, EBV's ability to establish latency, evade immune surveillance, and modulate host immunity provides a mechanistic framework for its role as a persistent driver of autoimmunity in MS.

11. T Cell Responses and Genetic Susceptibility

The interplay between Epstein–Barr virus (EBV) infection and the host's genetic background — especially in the context of HLA class II alleles — plays a pivotal role in shaping the autoimmune responses observed in multiple sclerosis (MS). Among known susceptibility genes, HLA-DRB1*15:01 stands out as the strongest genetic risk factor for MS, significantly increasing disease risk in multiple populations (3,4).

This specific allele influences the antigen-presenting function of MHC class II molecules, especially in the presentation of EBNA1-derived peptides to $CD4^+$ T helper cells. Studies have demonstrated that EBNA1 peptides bind with high affinity to HLA-DRB1*15:01, facilitating robust T cell responses (1,2). This efficient antigen presentation may result in the activation of cross-reactive autoreactive T cells that also recognize structurally similar CNS antigens, such as GlialCAM or myelin proteins — a process that overlaps with molecular mimicry.

Additionally, patients with MS often exhibit increased frequencies of EBNA1-specific $CD4^+$ and $CD8^+$ T cells, some of which produce proinflammatory cytokines such as IFN-γ and IL-17, contributing to CNS inflammation (1,3). These T cells can cross the blood–brain barrier and participate directly in immune-mediated demyelination.

A study by Lanz et al. (2022) further illustrated that clonally expanded B cells in MS patients bind both EBV antigens and CNS proteins, supporting a model in which EBV-driven B cell activation and antigen presentation potentiates autoreactive T cell expansion within the CNS (18).

Moreover, impaired regulatory T cell (Treg) responses in MS patients may fail to suppress these autoreactive populations, creating an immunological environment conducive to sustained inflammation and neurodegeneration (28). This interaction between viral antigen, B cell presentation, and T cell effector function appears particularly potent in genetically predisposed individuals, such as HLA-DRB1*15:01 carriers.

In summary, the intersection of EBV-driven antigen presentation and host genetic susceptibility offers a compelling explanation for the selective development of MS in a small subset of EBV-infected individuals.

12. Therapeutic Perspectives Targeting EBV in MS

The growing body of evidence implicating Epstein–Barr virus (EBV) in the pathogenesis of multiple sclerosis (MS) has sparked increasing interest in therapies that directly or indirectly target EBV-related mechanisms. While current MS treatments largely modulate the immune system non-specifically, novel strategies aiming to disrupt EBV infection or its immunological consequences are emerging.

12.1. EBV-specific T Cell Immunotherapy

One of the most promising approaches involves the use of EBV-specific cytotoxic T lymphocytes (CTLs). Adoptive transfer of autologous or allogeneic EBV-reactive CTLs has shown safety and preliminary efficacy in small cohorts of progressive MS patients (29). These T cells target latent EBV antigens such as EBNA1 and LMP1/2, potentially reducing the reservoir of EBV-infected autoreactive B cells in the CNS (28). Ongoing trials aim to evaluate the long-term clinical benefits and optimal dosing strategies of this therapy.

12.2. Antiviral Therapies

Although traditional antivirals like acyclovir and valacyclovir have limited efficacy against latent EBV, some studies have suggested modest benefits in MS patients treated with long-term antiviral regimens (7). However, no approved antiviral therapy currently targets EBV latency, which remains a major obstacle. New drug candidates that interfere with EBV lytic cycle reactivation or epigenetic maintenance of latency are under investigation, but their clinical applicability in MS is still unclear (3,4).

12.3. B Cell-Depleting Therapies

Monoclonal antibodies targeting CD20+ B cells (e.g., ocrelizumab, rituximab) have demonstrated robust efficacy in reducing MS disease activity. While these therapies do not specifically target EBV, they may indirectly reduce the EBV reservoir by depleting infected memory B cells (2,4). Their success in MS supports the hypothesis that B cell–associated viral antigens play a pathogenic role.

12.4. Vaccination Strategies

The development of a prophylactic EBV vaccine is an area of intense research. Moderna has recently launched clinical trials using mRNA-based vaccines targeting EBV envelope and latency-associated proteins, aiming to prevent primary infection or reduce viral load upon infection. If successful, such vaccines could potentially reduce MS incidence by eliminating a major environmental trigger (5). Additionally, therapeutic vaccines targeting EBNA1 and LMP2 are in preclinical stages, aiming to stimulate immune clearance of infected cells.

12.5. Future Outlook

Targeting EBV in MS offers a promising etiology-specific approach, moving beyond generic immunosuppression. Challenges remain — including limited access of therapies to CNS-resident infected cells, potential off-target effects, and the ubiquity of EBV infection. Nevertheless, EBV-directed strategies, especially when combined with current disease-modifying therapies, may hold the key to modifying disease course and preventing progression.

13. Conclusion

Over the past decades, compelling evidence has accumulated linking Epstein–Barr virus (EBV) infection with the development of multiple sclerosis (MS). Virtually all MS patients are seropositive for EBV, and recent large-scale cohort studies have strengthened the temporal and causal association between primary EBV infection and subsequent MS risk.

Multiple mechanisms have been proposed to explain this relationship, including molecular mimicry, latent infection and immune evasion, and the activation of autoreactive B and T cells in genetically predisposed individuals, particularly carriers of the HLA-DRB1*15:01 allele. The detection of clonally expanded B cells in the central nervous system of MS patients that react to both EBV antigens and CNS autoantigens provides a direct immunological link.

Therapeutic strategies aimed at targeting EBV-infected cells — including EBV-specific T cell immunotherapy, B cell depletion, and prophylactic vaccination — offer promising avenues for future intervention. These approaches may allow for more targeted and etiology-based treatment, especially for patients in early or prodromal stages of MS.

While EBV is not the sole factor in MS pathogenesis, the virus appears to act as a critical environmental trigger that initiates and possibly sustains autoimmune processes in a genetically susceptible host. Continued research into the molecular and immunological interface between EBV and MS will be essential for translating these insights into effective preventive and therapeutic strategies.

Disclosure:

Author Contribution Statement

Conceptualization: Michał Czechowski, Marcela Słomianny, Małgorzata Sajda

Methodology: Martyna Woźniak, Karolina Kusibab, Gabriela Skórska, Małgorzata Sajda

Writing-rough preparation: Michał Czechowski, Karolina Kutnik, Karolina Koguc, Karolina Kolada

Writing-review and editing: Michał Czechowski, Martyna Woźniak, Karolina Kolada, Marcela Słomianny

Project administration: Michał Czechowski, Karolina Kutnik, Karolina Koguc, Gabriela Skórska

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