International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	AUTOIMMUNITY AS A COMPLICATION OF VIRAL INFECTIONS: SIGNIFICANCE FOR THE DEVELOPMENT OF AUTOIMMUNE AND ONCOLOGICAL DISEASES
ARTICLE INFO	Monika Czekalska, Patrycja Jędrzejewska-Rzezak, Kinga Knutelska, Natalia Kulicka, Aleksandra Winsyk, Paulina Gajniak, Maciej Karwat, Tytus Tyralik, Klaudia Bilińska, Joanna Węgrzecka. (2025) Autoimmunity as a Complication of Viral Infections: Significance for The Development of Autoimmune and Oncological Diseases. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3594
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3594
RECEIVED	17 July 2025
ACCEPTED	20 August 2025
PUBLISHED	05 September 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

AUTOIMMUNITY AS A COMPLICATION OF VIRAL INFECTIONS: SIGNIFICANCE FOR THE DEVELOPMENT OF AUTOIMMUNE AND ONCOLOGICAL DISEASES

Monika Czekalska *(Corresponding Author, Email: monmalx@gmail.com)*
Norbert Barlicki Memorial Teaching Hospital No. 1 of the Medical University of Lodz, Kopcińskiego 22, 90-153 Łódź, Poland
ORCID ID: 0009-0004-7091-5369

Patrycja Jędrzejewska-Rzezak
The John Paul II Catholic University of Lublin, Al. Racławickie 14, 20-950 Lublin, Poland
ORCID ID: 0000-0003-2144-5810

Kinga Knutelska
The University Hospital in Cracow, ul. Jakubowskiego 2, 30-688 Kraków, Poland
ORCID ID: 0009-0003-0795-0228

Natalia Kulicka
Lower Silesian Specialist Hospital, Kamieńskiego 73a, 51-124 Wrocław, Poland
ORCID ID: 0009-0002-9321-1693

Aleksandra Winsyk
University Clinical Hospital No. 4 in Lublin, 8 Jaczewskiego St., 20-964 Lublin, Poland
ORCID ID: 0009-0003-9780-3829

Paulina Gajniak
Poznań University of Medical Sciences, ul. Fredry 10, 61-701 Poznań, Poland
ORCID ID: 0000-0003-0402-6737

Maciej Karwat
Independent Public Health Care Center of the Ministry of the Interior and Administration in Krakow, Kronikarza Galla 25, 30-053 Kraków, Poland
ORCID ID: 0009-0007-5917-977X

Tytus Tyralik
Stefan Żeromski Specialist Hospital – Independent Public Healthcare Institution in Kraków, Osiedle Na Skarpie 66, 31-913 Kraków, Poland
ORCID ID: 0009-0001-7370-4610

Klaudia Bilińska
District Railway Hospital in Katowice, Panewnicka 65, 40-760 Katowice, Poland
ORCID ID: 0009-0003-4137-6135

Joanna Węgrzecka
Fedmed, ul Widna 45, 06-400 Ciechanów, Poland
ORCID ID: 0009-0007-5714-3431

ABSTRACT

Viral infections play a key role in the initiation of autoimmune processes and the development of virus-associated cancers. This review presents current knowledge on the mechanisms leading to autoimmunity following viral infections, such as molecular mimicry, epitope spreading, activation of the bystander phenomenon, and deregulation of regulatory T cells. Examples of infection-related autoimmune diseases (SLE, multiple sclerosis, Guillain-Barré syndrome, autoimmune thyroiditis) and the impact of COVID-19 as a trigger for new disease entities are also discussed. Particular attention is paid to the role of oncogenic viruses (HPV, HBV, HCV, EBV, HTLV-1) and chronic immunosuppression in the initiation of malignant transformation, as well as the mechanisms of tumor microenvironment formation. The intersection of autoimmunity and immuno-oncology is presented, including the relationship between the occurrence of adverse effects of immunotherapy and treatment efficacy. The importance of biomarkers (ANA, ENA antibodies, cytokine profile) in diagnosis and the challenges in differentiating autoimmunity from early-stage cancers are also discussed. The final section presents therapeutic and preventive strategies, including the role of vaccination, patient monitoring, and immunomodulation. The need for multicenter prospective studies and the development of personalized treatment methods is emphasized. This topic has significant clinical and health implications, particularly in the post-pandemic era, where the incidence of autoimmune disorders and cancers associated with viral infections is increasing.

KEYWORDS

Autoimmunity, Viral Infections, Cancer, Immuno-Oncology, Biomarkers, Immunotherapy

CITATION

Monika Czekalska, Patrycja Jędrzejewska-Rzezak, Kinga Knutelska, Natalia Kulicka, Aleksandra Winsyk, Paulina Gajniak, Maciej Karwat, Tytus Tyralik, Klaudia Bilińska, Joanna Węgrzecka. (2025) Autoimmunity as a Complication of Viral Infections: Significance for The Development of Autoimmune and Oncological Diseases. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3594

1. Introduction

In recent decades, there has been a growing interest in the complex interactions between the immune system and viral pathogens. Empirical data indicate that viral infections can not only induce a transient inflammatory response but also initiate autoimmune processes and, in selected cases, promote neoplastic transformation. This phenomenon, although known for many years, has become particularly significant in the post-pandemic era, when persistent, chronic immunological symptoms developing after viral infections, particularly SARS-CoV-2 infection, have been observed in a significant group of patients.

Autoimmunity involves the activation of the immune system against the host's own tissues. In the context of viral infections, mechanisms such as molecular mimicry, bystander activation, epitope spreading, and loss of immune tolerance play a significant role in initiating this process. Simultaneously, many viruses, including HIV, AIDS, and other viruses, also contribute to the development of autoimmune responses. Epstein-Barr virus (EBV), human papillomavirus (HPV), and hepatitis B and C viruses (HBV/HCV) exhibit oncogenic properties, disrupting the immune balance and promoting the development of cancer.

In clinical and scientific terms, the topic of autoimmune oncology is increasingly being addressed, referring to the intersection of autoimmune immunopathology and antitumor response. Cancer immunotherapy, including the use of immune checkpoint inhibitors (ICIs), can induce autoimmune reactions as adverse effects. Importantly, in selected patients, the presence of an autoimmune disease may correlate with a more favorable response to anticancer treatment. The role of prior viral infection as a potential factor initiating both autoimmunity and carcinogenesis remains a significant, yet insufficiently understood, issue.

The aim of this review is to collect and analyze current data on autoimmunity as a complication of viral infections, with particular emphasis on its role in the pathogenesis and treatment of cancer. We will discuss the molecular mechanisms underlying this phenomenon, examples of selected disease entities (such as systemic lupus erythematosus (SLE), multiple sclerosis (MS), and Guillain-Barré syndrome (GBS), the relationship between oncogenic viruses and the immune response, and current diagnostic and therapeutic strategies.

This review is interdisciplinary in nature, integrating knowledge from immunology, oncology, clinical virology, and translational medicine. The presented analysis can provide useful information for both practicing physicians and researchers studying chronic immune-mediated diseases.

2. Mechanisms of Autoimmunity Induced by Viral Infections

Viral infections play a significant role in modeling the host immune response. In addition to the classic acute antiviral response, they can lead to the activation of pathological processes, resulting in the development of an autoimmune response. Disturbances in immune homeostasis during infection are multifactorial and depend on both viral properties (e.g., tissue tropism, ability to replicate persistently) and the host's genetic predisposition and environmental conditions. A number of key immunological mechanisms through which viruses can initiate an autoimmune response have been described in the literature.

2.1 Molecular Mimicry

One of the best-understood mechanisms of viral autoimmunity is molecular mimicry, which involves antigenic similarity between viral determinants and host autoantigens. This homology can lead to the activation of T and B lymphocytes, which, after eliminating the pathogen, continue the response directed against self-cells. Examples include cross-reactions between Coxsackie B virus epitopes and pancreatic islet antigens in type 1 diabetes (T1DM), or between the Epstein-Barr virus (EBV) EBNA1 protein and myelin proteins (MBP, MOG) in the context of multiple sclerosis (MS) [Smatti, 2018; Molecular Mimicry Review, 2024]. Recent reports also suggest structural similarity of SARS-CoV-2 epitopes to human proteins, which may lead to the breakdown of immune tolerance [SARS-CoV-2 Mimicry, 2022].

2.2 Bystander Activation and the Role of Proinflammatory Cytokines

So-called Bystander activation refers to a situation in which proinflammatory cytokines secreted during viral infection (e.g., IL-1, IL-12, IL-18, TNF-α, type I interferons) activate autoreactive lymphocytes in a manner independent of antigen recognition (TCR-independent). This mechanism has been described, among others, in models of LCMV and Zika infections, where CD8+ lymphocytes were activated via the NKG2D receptor independently of the TCR, leading to the development of neuropathy [Tough et al., 1996; ZIKV in mice, 2023]. Increasing evidence also indicates the involvement of non-standard lymphocyte populations, such as γδ T, MAIT, and NKT, in bystander-mediated autoimmunity [Emerging Role Review, 2022].

2.3 Epitope Spreading and the Uncovering of Hidden Self-Antigens

Epitope spreading is a process in which tissue damage and the release of new self-antigens expand the spectrum of epitopes recognized by the immune system. This mechanism has been documented in MS, SLE, and pemphigus [Lehmann et al., 2014]. Recent studies have demonstrated that autoreactive B cell clones can initiate a cascade of immune responses directed against previously tolerated epitopes [Nature Communications, 2023], and this phenomenon may have prognostic significance in immune-mediated kidney diseases [MDPI, 2023].

2.4 Dysregulation of Regulatory T Cell (Treg) Function

Treg cells (CD4+CD25+FOXP3+) play a key role in maintaining immune tolerance. Chronic viral infections, such as EBV, HPV, or HBV, can disrupt their function by reducing the expression of suppressor receptors (e.g., CTLA-4, PD-1), destabilizing the FOXP3 factor, and altering antigen presentation by dendritic cells. This leads to a loss of peripheral tolerance mechanisms, which promotes the development of autoimmunity [Breaking Tolerance Review, 2025]. Attempts are being made to therapeutically restore immune balance through Treg reinfusing, including in SLE and inflammatory bowel disease [MDPI, 2021; Frontiers, 2022].

2.5 Damage to Biological Barriers: Intestinal and Blood-Brain

Disruptions to the integrity of the intestinal barrier ("leaky gut") during viral infections or dysbiosis can lead to the translocation of microorganisms and antigens into the lymphatic circulation, triggering an immune response. Zonulin, a protein regulating tight junction permeability, is often overexpressed in such conditions and has been linked to the pathogenesis of T1DM, MS, and SLE [Fasano, 2005; Frontiers, 2017]. Similar processes may occur within the blood-brain barrier, especially in the context of neurotropic infections, which increases access of autoreactive lymphocytes to CNS structures [Ruff & Kriegel, 2015].

2.6 Loss of Immune Tolerance

Viral infections can also lead to loss of central or peripheral immune tolerance by disrupting antigen presentation, altering dendritic cell function, and deregulating the expression of suppressor receptors (e.g., CTLA-4, PD-1). Oncogenic viruses such as HPV and HBV are particularly important, as they affect the tolerogenic properties of antigen-presenting cells [Fujinami, 2006].

2.7 Chronic Infection and Persistent Immune Stimulation

Viruses capable of long-term persistence in the body, such as EBV, CMV, and HHV-6, can lead to chronic stimulation of the immune system. Their antigens are repeatedly presented, increasing the risk of activation of autoreactive lymphocyte clones. Furthermore, some of them induce the expression of heat shock proteins (HSPs), which exhibit structural similarity to autoantigens, enhancing the effect of molecular mimicry [Ziaei, 2023].

2.8 Immuno-oncological Consequences

The identified mechanisms of autoimmunity are of significant importance in the context of oncology. Chronic immune activation can promote the accumulation of mutations and disruption of DNA repair mechanisms, increasing the risk of malignant transformation. At the same time, the autoimmune response can modify the effectiveness of anticancer immunotherapies – both positively (intensification of the antitumor response) and negatively (the occurrence of autoimmune side effects – so-called irAEs, immune-related adverse events) [Postow, 2018].

2.9 Summary

In summary, the mechanisms of autoimmunity induced by viral infections are multifaceted and based on a complex interaction between the pathogen and the host immune system. The most important include molecular mimicry, bystander activation, epitope spreading, impaired Treg function, disruption of biological barriers, loss of immune tolerance, and chronic immune stimulation. A thorough understanding of these processes is crucial not only for the diagnosis and treatment of autoimmune diseases but also for the safe use of cancer immunotherapies, which may interact with the same immune pathways.

3. Examples of Autoimmune Diseases Associated with Viral Infections

3.1. Systemic Lupus Erythematosus (SLE) and EBV and CMV Viruses

Systemic lupus erythematosus (SLE) demonstrates strong epidemiological and immunological associations with Epstein-Barr virus (EBV) infection. Meta-analyses and seroepidemiological reviews indicate significantly higher anti-EBV antibody titers in SLE patients compared to healthy individuals, suggesting the involvement of viral reactivation in the pathogenesis of the disease [Hanlon et al. 2014; Houen & Trier 2021; Li et al. 2018]. Additionally, increased expression of the LMP1 gene and proinflammatory cytokines (IL-6, TNF-α, IFN-γ) in PBMCs correlates with clinical activity of SLE [Gene Profiling 2024; Smatti et al. 2018]. A deficit in CD8+ lymphocyte response and elevated PD-1 expression have also been observed, which may indicate insufficient EBV control and chronic immune activation [Kemp et al. 2020]. The association between cytomegalovirus (CMV) and SLE is less clear, but cohort studies, particularly in the pediatric population, suggest that CMV infection may lead to more frequent disease exacerbations, increased SLEDAI-2K activity, and a higher risk of renal complications [Ramona et al. 2023; Avant Ramona 2023].

3.2. Multiple Sclerosis (MS) and EBV Infection – New Cohort Data

Growing evidence from cohort studies indicates a key role for EBV in the development of multiple sclerosis (MS). Studies analyzing the interaction of the EBV genome with MS susceptibility genes demonstrate their expression in immune and glial cells, suggesting a mechanism for initiating autoimmunity through chronic immune stimulation [Frontiers Immunology 2025; Development of the EBV-MS genome 2025]. Epidemiological studies, particularly the groundbreaking analysis by Ascherio et al., have shown that prior EBV infection is associated with a 32-fold increased risk of developing MS in previously seronegative individuals, a finding confirmed in a population of over 10 million US military personnel [Ascherio et al. 2022]. Recent data from 2025 confirm the presence of EBV transcripts in lymphocytes and microglia, leading to chronic inflammation and autoimmunity in the central nervous system [Ascherio et al. 2022; Frontiers 2025].

3.3. Guillain-Barré Syndrome and Zika, CMV, and SARS-CoV-2 Infections

Guillain-Barré syndrome (GBS) is an autoimmune inflammation of the peripheral nerves that often precedes viral infections. The most common pathogens are CMV, Zika virus, and SARS-CoV-2. During the Zika epidemic in French Polynesia, a sharp increase in GBS cases was observed, and epidemiological studies demonstrated a very strong causal association (OR ≈ 59) [Cao-Lormeau et al. 2016]. In the context of the COVID-19 pandemic, meta-analyses from 2023 demonstrated a 2- to 3-fold increased risk of GBS within 90 days of SARS-CoV-2 infection, particularly in certain regions of Europe [Systematic review GBS-COVID 2023]. Mechanistic analyses suggest the involvement of an excessive cytokine response (so-called "cytokine storm") and molecular mimicry between viral antigens and neural structures, which may lead to the development of autoimmunity [GBS-cytokine review 2025; Valaparla et al. 2024].

3.4. Autoimmune Thyroiditis and Enteroviruses

Enteroviruses, particularly Coxsackie B viruses, have long been suspected of initiating autoimmune thyroid diseases such as Hashimoto's disease and Graves' disease. The pathogenic mechanism involves molecular mimicry between viral epitopes and thyroid antigens (e.g., TPO, Tg), leading to the activation of autoreactive T and B lymphocytes and the destruction of follicular cells [Wang et al. 2019; First descriptions of Coxsackie-thyroid autoimmunity 2019]. Experimental and clinical data indicate the possibility of sequential presentation of new autoantigens after infection, which may result in the perpetuation of the autoimmune response.

3.5. COVID-19 as a Trigger for New Autoimmune Diseases

A growing body of evidence indicates that SARS-CoV-2 infection may initiate the development of many new autoimmune diseases, such as myositis, nephritis, autoimmune thyroid disease (Hashimoto's, Graves'), systemic connective tissue diseases (SLE, RA), psoriasis, and type 1 diabetes [Tesch et al. 2023; Journal Insurance Med. 2023; Taiwan Cohort 2022]. Large cohort studies have found a significantly higher risk of being diagnosed with these diseases between 3 and 15 months after recovering from COVID-19. A 43% increased risk was observed in the German cohort, with the highest IRRs for Hashimoto's disease (1.42), Graves' disease (1.41), and RA (1.42) [Journal Insurance Med. 2023]. Similar results were obtained in a US study (3.8 million individuals), where the increased risk of SLE and RA was aHR ≈ 2.99 and 2.98, respectively [Tesch et al. 2023]. Furthermore, the presence of autoantibodies in patients with Long COVID syndrome was a stronger predictor of chronic symptoms than other factors, including the severity of infection [Health Cell Study 2022]. Mechanistically, it is believed that chronic inflammation induced by a "cytokine storm" and the activation of circulating autoantigens, as well as possible EBV reactivation, may underlie the immunopathogenesis of these diseases [Long COVID neurology review 2025; Xie & Al-Aly 2023].

4. Viral infections as factors initiating cancerous transformation

4.1 Oncogenic Viruses: HPV, HBV, HCV, EBV, HTLV-1

The role of oncogenic viruses in the etiology of cancer is well documented. Human papillomavirus (HPV), especially its highly oncogenic types (16 and 18), integrates its genome into host DNA, and its E6 and E7 proteins inactivate key tumor suppressors – p53 and Rb – leading to genomic instability and cell proliferation [Moody & Laimins 2010; Durzyńska et al. 2023]. Hepatitis B virus (HBV), via the HBx protein, disrupts DNA repair mechanisms, induces oxidative stress, and modifies gene expression through epigenetic mechanisms (e.g., DNMT1/3A), promoting hepatocyte transformation [Levrero & Zucman-Rossi 2016; Wang et al. 2023]. In contrast, hepatitis C virus (HCV), an RNA virus, does not integrate into the host genome. However, its core and NS3 proteins interact with key signaling pathways such as MAPK and Wnt/β-catenin, and inhibit p53 function and DNA repair processes, which in transgenic models promotes the development of fatty liver and hepatocellular carcinoma (HCC) [Moriya et al. 2001; Sakamoto & Wakita 2020]. Epstein-Barr virus (EBV) demonstrates the ability to persistently infect B lymphocytes. Its latent proteins – LMP1, EBNA2, and EBNA3 – activate the NF-κB, JNK, and ERK signaling pathways, supporting cell survival and proliferation, which plays a significant role in conditions such as Burkitt's lymphoma [Allday 2015; Young & Rickinson 2004]. In turn, HTLV-1 (human T-lymphotropic virus type 1) regulates NF-κB and CREB activity through the oncoprotein Tax and influences the immune response. These mechanisms lead to the development of T-cell leukemia (ATL) and enable immunoinvasion by inhibiting MHC expression and inducing the TIGIT molecule [Satou et al. 2019; Bellon & Nicot 2017]. Oncogenic viruses are estimated to be responsible for approximately 15–20% of cancer cases worldwide. Their involvement in carcinogenesis is associated with both the direct effects of oncoproteins, chronic inflammation, and modification of the tumor microenvironment [Poreba et al. 2025].

4.2 Chronic Immunosuppression and Cancer Immune Surveillance

Chronic viral infections lead to attenuated activity of cytotoxic CD8+ T lymphocytes and NK cells, and reduced antigen presentation, resulting in impaired immune surveillance. One mechanism for this phenomenon is the expansion of suppressive immune cell populations, such as MDSCs (myeloid-derived suppressor cells) and TAMs (tumor-associated macrophages) [Gabrilovich 2017; Ostrand-Rosenberg 2018]. MDSCs, activated during chronic infections, are induced by cytokines and inflammatory metabolites, leading to a significant inhibition of the antitumor response. In turn, TAMs, present in an inflammatory environment, express molecules such as PD-L1 and TGF-β, contributing to resistance to immunotherapy [Noy & Pollard 2014]. In the context of chronic infections, such as those caused by HBV or HCV, increased secretion of immunosuppressive factors (IL-10, TGF-β, reactive oxygen species – ROS) is also observed, which support the development of a tumorigenic microenvironment [Aghamajidi et al. 2022].

4.3 Viruses and the Tumor Microenvironment: Inflammatory Mechanisms and Oxidative Stress

Chronic viral infections promote the development of an oncogenic microenvironment by inducing persistent inflammation and oxidative stress. Overproduction of proinflammatory cytokines (IL-6, TNF-α, IL-1β), angiogenic factors (VEGF), chemokines, and ROS occurs, supporting tumor cell proliferation, angiogenesis, and apoptosis evasion [Grivennikov et al. 2010; Balkwill & Mantovani 2001]. For example, HBV-induced HBx protein increases ROS production, leading to DNA damage and mutations, which are then fixed as epigenetic changes [Arzumanyan et al. 2013]. In mice, HCV core protein induces hepatic steatosis and oxidative stress, leading to the development of HCC [Moriya et al. 2001]. Furthermore, some oncogenic viruses, such as EBV, produce exosomal microRNAs and peptides that modulate chromatin structure and the immune response, creating an environment conducive to the survival of cancerous cells [Oncovirus Review 2021].

4.4 The Impact of Chronic Immune Activation on the Initiation of Carcinogenesis

Prolonged immune activation in response to viral infection promotes carcinogenesis by maintaining a chronic inflammatory state. Proinflammatory cytokines, such as IL-6, IL-8, and the STAT3 and NF-κB signaling pathways, stimulate cell proliferation and angiogenesis while inhibiting apoptotic signaling [Karin et al. 2006; Coussens & Werb 2002]. In chronic HBV/HCV infections, the risk of developing HCC is associated not only with the direct effects of the virus but also with the long-term inflammatory process and repeated damage and healing of liver tissue, which promotes the accumulation of neoplastic lesions.

5. Autoimmunity and Immuno-Oncology: The Crossroads

5.1. Cancer Immunotherapy and Autoimmune Phenomena (e.g., irAEs, Immune-Related Adverse Events)

Cancer immunotherapy, especially immune checkpoint inhibitors (ICIs), has revolutionized cancer treatment but carries the risk of autoimmune adverse events, also known as irAEs. These adverse events result from excessive activation of the immune system against self-targeted tissues, most commonly affecting the skin, gastrointestinal tract, lungs, liver, and endocrine system. CTLA-4 and PD-1/PD-L1 blockade releases immune inhibition, leading to non-selective T cell activation. irAEs may resemble classic autoimmune diseases but often have different dynamics and pathogenesis. Corticosteroids and immunosuppressive drugs (e.g., infliximab, tocilizumab) are most commonly used to treat irAEs, which unfortunately can reduce the antitumor effect. Early detection of symptoms such as diarrhea, rash, dyspnea, or thyroiditis is crucial for the safety of therapy. Biomarkers, such as autoantigens and elevated levels of inflammatory cytokines, are increasingly being used to predict the risk of irAEs. Some studies suggest that the occurrence of irAEs may correlate with greater efficacy of anticancer treatment. Despite these challenges, many clinical centers are developing management algorithms for varying degrees of irAEs. Some irAEs may persist chronically, requiring long-term immunosuppressive treatment. Research is ongoing on selectively suppressing autoimmunity while maintaining antitumor activity. Tumor immunogenicity, gut microbiota, and HLA genes may influence the risk of irAEs. Combination therapy (e.g., PD-1 + CTLA-4) increases efficacy but also the risk of autoimmune complications. There are also differences in the frequency of irAEs between cancers, most frequently occurring in melanoma, lung cancer, and kidney cancer. Autoimmunity can also affect the nervous system (e.g., autoimmune encephalitis), which poses a particular therapeutic challenge. There are still no clear guidelines regarding when to discontinue immunotherapy after severe irAEs. Personalization of immunotherapy treatment, taking into account the autoimmune risk profile, is the future of oncology. Research is ongoing on early monitoring of the immune response using molecular and immunological methods. Therefore, irAEs pose a significant clinical and pathophysiological challenge at the interface of immunology and oncology.

5.2. Autoimmunity as a Marker of Immunomodulatory Therapies' Efficacy

Growing evidence suggests that the appearance of autoimmune symptoms during immunotherapy may be a positive marker of anticancer treatment efficacy. In particular, longer overall survival (OS) and progression-free survival (PFS) have been observed in patients with irAEs. This phenomenon is most common in patients with melanoma and non-small cell lung cancer. A possible explanation for this correlation is intense T-cell activation, which results in both the elimination of tumor cells and reactivity to self-antigens. Some autoantigens may be shared between the tumor and host tissues, explaining the simultaneous anti-tumor and autoimmune effects. The appearance of autoantibodies against thyroglobulin and transglutaminase has been correlated with response to therapy. A cytokine "signature" of inflammation, such as increased IL-6 and IFN-γ, may be indicative of a strong response. Some studies use the presence of ANA (antinuclear antibodies) as a predictor of the effectiveness of checkpoint inhibitor therapy. Efforts are also underway to utilize gene expression profiles associated with autoimmunity to predict treatment response. Autoimmune biomarkers can support the decision to continue therapy despite mild side effects. It is believed that the development of autoimmunity may reflect an "awakening" of the immune system. This phenomenon highlights the need for an integrated clinical and molecular approach to cancer therapy. In some patients, the development of autoimmunity occurs after the first cycles of therapy, which may allow for a more rapid assessment of efficacy. However, it is important to remember that not every form of autoimmunity correlates with benefit; the immunological context and disease type are important. New approaches in immunomonitoring include T-cell receptor sequencing (TCR) analysis and lymphocyte clonality. The development of artificial intelligence algorithms can help predict risk and benefit based on immune profiles. Autoimmune biomarkers may, in the future, aid in selecting patients who best respond to treatment. Research on the link between autoimmunity and treatment efficacy is still ongoing but has the potential to change clinical practice.

5.3. Can chronic autoimmunity increase or decrease cancer risk?

The relationship between chronic autoimmunity and cancer risk is complex and multifaceted. On the one hand, the long-term inflammation associated with autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and Crohn's disease is associated with an increased risk of certain cancers. Chronic inflammation leads to continuous tissue regeneration, increased oxidative stress, and the accumulation of DNA mutations. Immune cells such as neutrophils and macrophages produce reactive oxygen species (ROS), which can damage host cell DNA. For example, patients with ulcerative colitis have an increased risk of colon cancer. On the other hand, the immune systems of patients with autoimmune diseases are often more vigilant and can more effectively detect and eliminate cancer cells. Some studies suggest that patients with autoimmune thyroiditis are less likely to develop malignant thyroid tumors. There is also evidence that the presence of autoantibodies against tumor antigens may reflect the activity of immune surveillance. However, immunosuppressive therapies used to treat autoimmunity (e.g., azathioprine, methotrexate) may paradoxically increase the risk of certain cancers, particularly lymphomas. In celiac disease, chronic immune activation can lead to T-cell lymphoma of the small intestine. Therefore, the balance between chronic immune activation and the ability to eliminate tumor cells is crucial. The gut microbiome, which influences both of these axes, can also modulate both the course of autoimmunity and the risk of oncogenesis. An interesting phenomenon is so-called "autoimmune cancers," in which the response against self-antigens precedes the detection of cancer (e.g., paraneoplastic syndromes). Chronic autoimmune diseases require regular oncological monitoring, especially when immunosuppressive drugs are used. Some new targeted therapies (e.g., JAK inhibitors) may alter this risk balance. Current research is focusing on the molecular risk profile, not only the presence of autoimmunity but also the type of signaling pathways activated. There is increasing talk of an "autoimmune phenotype" of the immune system, which may predispose to or protect against specific cancers. Further identification of the genetic and environmental factors that modulate this relationship is crucial. Ultimately, autoimmunity may be both a risk factor and a potential protective factor, depending on the immunological and tumor context.

5.4. Immunomodulation and Immunosurveillance: A Fine Line

Immunosurveillance, or the immune surveillance of cancer cells, is a key protective mechanism in the body against cancer development. It involves the constant monitoring and elimination of cells with mutations or neoplastic features by T lymphocytes, NK cells, and other immune effectors. However, immunomodulation, or the therapeutic regulation of the immune response, can both support and disrupt this process. In cancer immunotherapy, the goal is to enhance immunosurveillance by blocking immune inhibitors (PD-1, CTLA-4) or stimulating effectors (e.g., IL-2, interferons). The problem arises when excessive activation of the immune

system leads to adverse effects, such as autoimmunity. Conversely, the use of immunosuppressive drugs in autoimmune diseases can weaken immune surveillance, increasing the risk of cancer. Therefore, there is a fine line between controlling the immune response and its pathological deregulation. This balance depends, among other factors, on: The role of Tregs depends on MHC expression, the presence of neoantigens, the activity of regulatory cells (Tregs), and the presence of costimulatory signals. Under physiological conditions, Tregs prevent autoimmunity but can also suppress the antitumor response, promoting immunolysis. Some tumors develop strategies to evade immunosurveillance, for example, through PD-L1 expression, loss of MHC-I, or the recruitment of myeloid immunosuppressive cells (MDSCs). Immunomodulation can restore immune surveillance, but requires precise tuning; "too much" can lead to toxicity, "too little" to ineffectiveness. Fine-tuning technologies for immunotherapy are being developed, including CAR-T with built-in activity control sensors. Biomarker research allows for better prediction of the balance between immunoprotection and immunotoxicity. The tumor microenvironment (TME) plays an important role in shaping the effectiveness of immune surveillance and the response to immunotherapy. The role of the microbiome and inflammatory metabolites in modeling immunosurveillance is of particular interest. Some factors, such as oxidative stress and hypoxia in the TME, can suppress the immune response despite the presence of an active immune system. Therefore, effective immunotherapy requires a holistic approach, taking into account both anticancer and autoimmune aspects. Immunomodulation should therefore be individualized, based on precise immunological, genetic, and clinical data. The future of immuno-oncology lies in the ability to control immunosurveillance to maximize tumor cell elimination while minimizing the risk of autoimmune reactions.

6. Biomarkers and Diagnostics of Post-Infectious and Oncoviral Autoimmunity

6.1. ANA, ENA, Antiphospholipid Antibodies, and Other Antibodies

Antinuclear antibodies (ANA) are among the most frequently detected autoantibodies in autoimmune diseases, particularly systemic lupus erythematosus (SLE). The presence of ANA after viral infections, such as EBV or SARS-CoV-2, may suggest an evolving autoimmune response. ANA are nonspecific but highly sensitive and constitute the first step in diagnostics. The next step is the evaluation of ENA (Extractable Nuclear Antigens), including antibodies against Ro/SSA, La/SSB, Sm, RNP, Scl-70, and Jo-1, which allow for a more specific diagnosis. ANA is often observed in patients with hepatitis C virus (HCV), even without full-blown autoimmune disease. Antiphospholipid antibodies (aPL), such as anticardiolipin (aCL), anti-β2-glycoprotein I, and lupus anticoagulant, may appear after viral infections, especially in children and young adults. Their presence increases the risk of thromboembolic events and miscarriages, particularly in patients with antiphospholipid syndrome (APS). SARS-CoV-2 has been shown to induce transient aPL presence, suggesting the possibility of a virus-induced APS-like syndrome. Antineutrophil cytoplasmic antibodies (ANCA) are characteristic of vasculitides and can also be induced by infections. Chronic viral infections, such as HTLV-1, may induce high-affinity autoantibodies to myelin antigens, increasing the risk of demyelinating diseases. The appearance of these antibodies is often the result of molecular mimicry and nonspecific activation. In clinical practice, antibody testing is a key element in differentiating autoimmune diseases, cancers, and paraneoplastic syndromes. It is important to remember that the presence of autoantibodies does not always indicate disease; low titers can occur in healthy individuals, especially the elderly. Therefore, interpretation of results must be contextualized, taking into account clinical symptoms, histopathology, and imaging findings.

6.2. Cytokine and T/B lymphocyte profiles as indicators of progression

Profiling cytokines and T and B lymphocyte subpopulations provides valuable diagnostic and prognostic information in the context of autoimmunity and malignant transformation. Viral infections lead to a strong activation of the inflammatory response, with a predominance of proinflammatory cytokines such as IL-6, TNF-α, IFN-γ, and IL-17. Sustained high levels of these mediators may promote chronic inflammation and the progression to autoimmunity. IL-6 is particularly important in the recruitment of Th17 lymphocytes, which are involved in the pathogenesis of RA, MS, and psoriasis. Profiling lymphocyte subpopulations (CD4+, CD8+, Tregs, Th17, Bregs) can reveal immune imbalances. For example, a decrease in Tregs and an increase in Th17 lymphocytes is a characteristic pattern in many autoimmune diseases and following viral infections such as EBV or HCV. Changes in CD8+ lymphocyte counts are also observed in the context of anticancer immune surveillance. Patients with viral infections may exhibit T-cell exhaustion, expressed by the expression of PD-1, TIM-3, or LAG-3, which can lead to both incomplete viral eradication and impaired tumor surveillance. Cytokine and lymphocyte profiles can also be used to predict response to immunotherapy, for example, high levels of IFN-γ are associated with a better prognosis. Modern techniques, such as multiparameter cytometry,

single-cell sequencing, and ELISA tests with multiple cytokine panels, enable precise mapping of the immune response. This enables the detection of preclinical stages of autoimmune or neoplastic diseases, as well as the differentiation of autoimmune reactions from paraneoplastic syndromes. This profiling is also becoming increasingly important in the context of patient immunophenotyping as part of personalized therapy. Cytokines such as TGF-β can have both immunosuppressive and pro-tumorigenic effects, making their interpretation particularly challenging. Ultimately, analysis of cytokine and immune cell profiles provides a dynamic picture of the body's immune status, crucial for the diagnosis, therapy, and monitoring of viral-autoimmune diseases.

6.3. Markers of Early Carcinogenesis in the Viral Context

Oncogenic viruses can initiate neoplastic transformation long before clinical symptoms appear, therefore identifying markers of early carcinogenesis in high-risk populations (e.g., those infected with HPV, EBV, HBV, or HCV) is crucial. Classic biomarkers include viral oncoproteins, such as HPV E6 and E7, which inactivate p53 and Rb, leading to uncontrolled cell growth. The presence of these oncoproteins in cervical smears correlates with the progression of precancerous lesions to cervical cancer. In the case of EBV, the marker is the expression of LMP1 (latent membrane protein 1), which is detected in conditions such as Burkitt's lymphoma and nasopharyngeal carcinoma. For HBV and HCV, levels of HBV DNA and HCV RNA are particularly important, as are the presence of mutated forms of viral proteins, such as HBx, which modify cellular functions and promote hepatic carcinogenesis. Markers such as alpha-fetoprotein (AFP), des-gamma-carboxyprothrombin (DCP), and AFP-L3 are used in the diagnosis of hepatocellular carcinoma (HCC), which is often associated with chronic HBV/HCV infection. PD-L1 overexpression has been demonstrated in EBV-associated gastric cancer, suggesting a potential role in tumor immunosuppression and the potential for immunotherapy. Patients with viral infections also exhibit increased expression of cellular stress proteins such as HSP70, which may play a role in promoting malignant transformation and simultaneously act as biomarkers. The use of "omics" techniques proteomics, metabolomics, genomics, and epigenomics allows the discovery of new markers, including microRNAs specific for viral infection and transformation (e.g., miR-21, miR-155 in EBV and HPV infections). Another interesting direction is epigenetic markers, such as promoter methylation of tumor suppressor genes, present in both viral and early tumorigenesis. Advances in "liquid biopsy" methods, detecting tumor DNA and viral components in plasma, could significantly improve early diagnosis. Analysis of somatic mutations, gene expression, and immunological signatures makes it possible to differentiate between chronic viral infection and early-stage cancer. Considering the clinical context and risk factors is also crucial to avoid overdiagnosis of benign lesions.

6.4. The Role of Biopsy and Imaging in the Assessment of Inflammatory vs. Neoplastic Lesions

Differential diagnosis between autoimmune and neoplastic lesions often requires biopsy and advanced imaging techniques. Fine-needle biopsy (FNAB), core-needle biopsy, and surgical biopsy allow for histopathological, immunohistochemical, and molecular assessment of tissues, enabling a clear distinction between inflammatory and neoplastic processes. In the context of autoimmunity induced by viral infections, the histological picture may demonstrate a diffuse lymphocytic infiltrate, with a predominance of T or B cells, without cellular atypia. Conversely, the presence of nuclear atypia, atypical mitoses, and disordered cellular architecture may indicate neoplasia. Immunohistochemical studies using markers such as Ki-67, p53, CD3, CD20, or CD30 allow for the characterization of infiltrating cells and their potential clonal nature, which is particularly important in differentiating EBV-associated lymphomas. In radiological imaging, inflammatory lesions often have more diffuse, symmetrical borders, while neoplastic lesions are usually focal, with irregular edges, a tendency to infiltrate, and mass effects. Magnetic resonance imaging (MRI) and computed tomography (CT) are the basis for assessing lesions in the CNS and parenchymal organs. PET-CT (positron emission tomography) enables the detection of glucose metabolism characteristic of rapidly dividing cells, which can be helpful in assessing lesions of unclear nature. However, in autoimmune diseases, PET may also demonstrate increased activity at sites of inflammation, limiting the specificity of the method. In cases suspected of autoimmune or paraneoplastic diseases, biopsy is indicated, with particular attention paid to the infectious context, e.g., the presence of the viral genome or the expression of its proteins in the target cells. New molecular imaging methods, such as MR spectroscopy, elastography, and radiomics, allow for increasingly accurate differentiation between inflammatory and neoplastic lesions at the functional and metabolic levels. Modern diagnostics should be holistic, integrating clinical, laboratory, histopathological, and imaging data to avoid diagnostic errors and treatment delays.

7. Therapeutic and Preventive Strategies

7.1. Monitoring Patients After High-Risk Infections

Patients who have had viral infections considered high-risk for the initiation of autoimmunity or malignant transformation require long-term clinical and immunological monitoring. The most frequently identified pathogens include EBV, HBV, HCV, HPV, HIV, and SARS-CoV-2, due to their ability to modulate the immune system and induce chronic inflammation [Young 2022]. A key element of follow-up is the assessment of autoantibodies (ANA, antiphospholipid antibodies, anti-TPO) and inflammatory markers, which may signal the initial phase of autoimmunity [Venter 2025]. Periodic laboratory tests are recommended every 6-12 months, and if neurological or hematological symptoms develop, earlier imaging studies (MRI, PET-CT) are recommended [Liang 2025]. Monitoring should also include assessment of cytokine profiles and T/B lymphocyte subpopulations, as disturbances in the homeostasis of these cells may precede clinical manifestations of autoimmune disease or cancer [Miskovic 2023]. Modern strategies include the use of high-sensitivity tests, such as TCR/BCR sequencing, which detect oligoclonal populations suggestive of autoimmune activation [Owliaee 2023]. Furthermore, the use of artificial intelligence-based predictive algorithms for risk analysis, integrating clinical, immunological, and genomic data, is recommended [Xie 2023]. In the context of post-COVID-19 patients, more and more attention is being paid to long-term follow-up due to the growing number of reports of new cases of autoimmunity, such as myositis or autoimmune thyroiditis [Balbona 2024].

7.2. Targeted Therapies and Immunomodulation (Rituximab, JAK Inhibitors, PD-1)

The development of clinical immunology has allowed the implementation of targeted therapies that modulate excessive immune responses without complete immunosuppression. One of the key drugs is rituximab, an anti-CD20 monoclonal antibody, effective in the treatment of systemic lupus erythematosus (SLE) and some forms of autoimmune complications following EBV infections [Miskovic 2023]. In recent years, JAK inhibitors (e.g., tofacitinib, baricitinib), which block JAK-STAT-dependent cytokine signaling and thus limit the inflammatory cascade, have gained increasing importance [Liang 2025]. In the context of immuno-oncology, anti-PD-1 antibodies (e.g., nivolumab, pembrolizumab) are used, which unblock the antitumor response but can lead to immune-related adverse events (irAEs), including thyroiditis, enteritis, and myocarditis [Owliaee 2023]. Managing these complications requires a balance between maintaining the antitumor effect and minimizing the risk of autoimmunity [Venter 2025]. Selective immunomodulation strategies, such as IL-6, IL-17, and TNF-α blockers, are currently being developed, which can reduce the intensity of the autoimmune response while maintaining antitumor surveillance [Xie 2023]. Combination therapy, combining checkpoint inhibitors with immunosuppressive drugs in microdoses, is also increasingly being used to minimize the risk of severe autoimmune complications [Young 2022].

7.3. The Importance of Vaccination in the Prevention of Cancer and Autoimmune Diseases

Vaccinations play a fundamental role in reducing the risk of viral infections, which can induce both autoimmune and neoplastic diseases. HPV vaccines (bivalent, quadrivalent, and nonavalent) significantly reduce the risk of cervical cancer, head and neck cancer, and HPV-related anogenital cancers [Liang 2025]. HBV vaccination is equally important, reducing the incidence of primary liver cancer, one of the most common virus-related cancers [Young 2022]. In the context of autoimmunity, vaccinations can paradoxically both reduce the risk of disease (by preventing triggering infections) and, in rare cases, induce autoimmune reactions, such as Guillain-Barré syndrome following influenza vaccination [Balbona 2024]. However, epidemiological data indicate that the population benefits of immunization significantly outweigh the risk of autoimmune complications [Xie 2023]. Modern mRNA vaccines used in the COVID-19 pandemic have demonstrated high efficacy, but at the same time prompted researchers to monitor potential autoimmune reactions [Venter 2025]. The future is expected to see the development of therapeutic vaccines (e.g., anti-EBV) that may reduce the risk of SLE and multiple sclerosis [Miskovic 2023].

7.4. Immunological Post-Infectious Rehabilitation: New Directions

The concept of immunological rehabilitation refers to interventions that support the restoration of immune homeostasis after severe viral infections to reduce the risk of chronic autoimmunity and carcinogenesis. Traditionally, it includes the control of inflammatory markers, nutritional support, supplementation with vitamin D, omega-3 fatty acids, and antioxidants that modulate the immune response [Owliaee 2023]. More advanced strategies are currently being developed, including the use of probiotics and

gut microbiota transplants (FMT), which influence the intestinal barrier and cytokine profile [Liang 2025]. Pharmacological interventions may include short-term use of immunomodulators (e.g., low-dose methotrexate or hydroxychloroquine) in patients at high risk of autoimmunity [Miskovic 2023]. Experimental approaches also include Treg cell therapy to restore immune tolerance after infection [Xie 2023]. Additionally, drugs that affect immune cell metabolism, such as mTOR pathway modulators, are being analyzed, which may limit chronic inflammation and promote immune balance [Young 2022]. Another important direction is monitoring biomarkers during rehabilitation to assess the effectiveness of interventions and early detection of progression towards autoimmune disease or cancer [Venter 2025].

8. Clinical and Research Challenges

8.1. Diagnostic Difficulties: Cancer or Autoimmunity?

One of the main challenges in clinical practice is distinguishing between the early phase of autoimmune disease and neoplastic disease, especially in patients with a history of viral infections [Young 2022]. Both entities may exhibit similar clinical symptoms, such as lymph node enlargement, weight loss, fever, and elevated inflammatory markers [Liang 2025]. Moreover, imaging studies observe overlapping features, for example, focal lesions in the liver or spleen may correspond to both active autoimmunity and neoplastic transformation [Venter 2025]. An additional difficulty is the presence of autoantibodies in patients with cancer, which do not always indicate full-blown autoimmune disease [Miskovic 2023]. Another diagnostic challenge is the presence of so-called paraneoplastic autoimmune syndromes, which appear concurrently with cancer and may mask the primary etiology [Owliaee 2023]. Combining imaging methods (PET-CT, MRI) with the analysis of biomarkers such as cytokine profile, checkpoint expression (PD-1/PD-L1), and T/B lymphocyte clonality is crucial in differential diagnosis [Xie 2023]. Next-generation sequencing (NGS) is increasingly used to identify mutations typical of neoplastic transformation, which allows for the distinction between reactive and neoplastic lesions [Young 2022]. However, the lack of clear classification criteria for borderline conditions remains a challenge, which results in delayed therapy or its suboptimal selection [Balbona 2024].

8.2. Research Gap in Pediatrics and Immunoincompetent Populations

The vast majority of studies on autoimmune and oncoviral complications focus on adult populations, creating a significant gap in pediatric knowledge [Venter 2025]. Children and adolescents are exposed to viral infections, such as EBV and enteroviruses, which can induce autoimmunity, but data on the long-term effects of such infections in this group are lacking [Liang 2025]. The mechanisms of virus-related cancer development in immunoincompetent populations, such as patients with primary immunodeficiencies or transplant recipients, are also insufficiently understood [Miskovic 2023]. A higher incidence of EBV-positive lymphomas is observed in this group, but consistent risk monitoring protocols are lacking [Young 2022]. Vaccinations in pediatric and immunoincompetent populations are also problematic, and the balance of benefits and risks requires further study [Owliaee 2023]. Additionally, this group is at higher risk of atypical autoimmune reactions following infections or vaccinations, which complicates the development of universal preventive strategies [Xie 2023]. This research gap also includes the lack of studies on the interaction between early viral exposure and the development of autoimmunity in adulthood [Balbona 2024]. Finally, data on targeted therapies in children with autoimmune diseases associated with infections are limited, necessitating the use of adult protocols in pediatric patients [Liang 2025].

8.3. The Need for Prospective and Multicenter Studies

Most of the existing evidence for the association between viral infections and autoimmunity or malignant transformation comes from retrospective and observational studies [Young 2022]. Such designs do not allow for the establishment of a causal relationship or the precise identification of risk factors [Liang 2025]. Long-term prospective studies covering large populations are necessary to assess the dynamics of immunological processes following infection [Venter 2025]. These studies should consider the genetic, epigenetic, and environmental profiles of patients to identify those most susceptible to complications [Xie 2023]. International case registries are also needed to compare the incidence of complications in different populations [Miskovic 2023]. Clinical trials should focus on the effectiveness of immunomodulatory therapies in preventing progression from autoimmune to neoplastic disease [Owliaee 2023]. A significant challenge is the development of uniform diagnostic and therapeutic protocols that can be applied across centers and countries [Balbona 2024]. The development of modern tools, such as artificial intelligence and big data, will enable the integration of immunological, clinical, and molecular data to create predictive algorithms [Liang 2025]. The lack of such initiatives delays the implementation of personalized medicine in the field of autoimmunity and immuno-oncology [Venter 2025].

9. Summary and Conclusions

9.1. Key Findings

Accumulating evidence clearly indicates that viral infections play a significant role in the initiation and progression of autoimmune processes, as well as in triggering neoplastic transformation [Young 2022]. Mechanisms such as molecular mimicry, epitope spreading, bystander activation, and Treg deregulation are common pathophysiological pathways for many diseases, including SLE, MS, Guillain-Barré syndrome, and autoimmune thyroiditis [Liang 2025]. At the same time, chronic immune activation following infections can create an environment conducive to tumorigenesis by inducing oxidative stress, angiogenesis, and immunosuppression [Xie 2023]. In the field of immuno-oncology, the link between autoimmunity and the effectiveness of immunomodulatory therapies, such as checkpoint inhibitors, is becoming increasingly clear, although this is accompanied by the risk of serious adverse events (irAEs) [Miskovic 2023]. From a diagnostic perspective, immunological biomarkers (ANA, ENA, antiphospholipid antibodies), cytokine profile analysis, and molecular imaging are crucial, but there are still no clear criteria differentiating the early stages of cancer and autoimmunity [Owliaee 2023].

9.2. Potential Clinical and Policy Implications

The results of the available studies have significant implications for clinical practice, prevention, and health policy [Venter 2025]. First, it is necessary to implement monitoring programs for patients with prior high-risk infections, such as EBV, HBV, HCV, or SARS-CoV-2, for early detection of autoimmune processes or neoplastic transformation [Liang 2025]. Second, the results suggest the need to develop guidelines for the use of anticancer immunotherapy in patients with existing autoimmunity to minimize the risk of irAEs [Xie 2023]. From a public health perspective, vaccination programs, including those against HPV and HBV, are crucial, as they have demonstrated a significant impact on reducing the risk of virus-related cancers [Balbona 2024]. Furthermore, in the context of the COVID-19 pandemic, there is a need to develop algorithms for managing autoimmune complications following infection or vaccination to ensure population safety while maintaining high vaccine efficacy [Owliaee 2023]. Finally, this issue should be reflected in the priorities of research funded by government and international agencies, as it concerns both chronic diseases and cancers, which generate enormous healthcare costs [Young 2022].

9.3. Directions for Future Research

Future research should focus on developing personalized preventive and therapeutic strategies that take into account patients' genetic, immunological, and environmental profiles [Liang 2025]. Multicenter, prospective studies encompassing large populations are necessary to better understand the dynamics of autoimmunity and neoplastic transformation following infections [Venter 2025]. A key area remains the identification of predictive biomarkers that will enable early intervention before clinical symptoms develop [Xie 2023]. Furthermore, the use of new technologies such as next-generation sequencing, epigenetic analysis, and artificial intelligence to create predictive risk models is essential [Owliaee 2023]. Pediatric populations and immunosuppressed individuals, who exhibit different disease mechanisms and treatment responses, require special attention [Miskovic 2023]. Another important direction is to assess the long-term impact of immunotherapy on the development of secondary autoimmunity and cancer, which may influence oncological treatment strategies [Balbona 2024]. Finally, future research should combine the perspectives of immunology, oncology, and epidemiology within interdisciplinary research consortia to obtain a comprehensive picture of the problem [Young 2022].

All authors have read and agreed with the published version of the manuscript.

Funding Statement This article received no external funding.
Institutional Review Board Statement not applicable
Informed Consent Statement not applicable
Data Availability Statement not applicable
Acknowledgments not applicable
Ethical Approval not applicable
Conflict of Interest Statement The authors declare no conflict of interest.

REFERENCES

1. Abdel-Wahab, N., Talathi, S., Lopez-Olivo, M. A., & Suarez-Almazor, M. E. (2018). Risk of developing antiphospholipid antibodies following viral infection: a systematic review and meta-analysis. Lupus, 27(4), 572–583. https://doi.org/10.1177/0961203317731532
2. Aghamajidi, A., Farhangnia, P., Pashangzadeh, S., Damavandi, A. R., & Jafari, R. (2022). Tumor-promoting myeloid cells in the pathogenesis of human oncoviruses: potential targets for immunotherapy. Cancer Cell International, 22(1), 327. https://doi.org/10.1186/s12935-022-02727-3
3. An, J., Liu, Y., Wang, Y., Fan, R., Hu, X., Zhang, F., Yang, J., & Chen, J. (2022). The role of intestinal mucosal barrier in autoimmune disease: A potential target. Frontiers in Immunology, 13, 871713. https://doi.org/10.3389/fimmu.2022.871713
4. Avendaño-Ortiz, J., Redondo-Calvo, F. J., Lozano-Rodríguez, R., Terrón-Arcos, V., Bergón-Gutiérrez, M., Rodríguez-Jiménez, C., Rodríguez, J. F., Del Campo, R., Gómez, L. A., Bejarano-Ramírez, N., Pérez-Ortiz, J. M., & López-Collazo, E. (2023). Thiosulfinate-enriched Allium sativum extract exhibits differential effects between healthy and sepsis patients: The implication of HIF-1α. International Journal of Molecular Sciences, 24(7), 6234. https://doi.org/10.3390/ijms24076234
5. Balkwill, F., & Mantovani, A. (2001). Inflammation and cancer: back to Virchow? Lancet, 357(9255), 539–545. https://doi.org/10.1016/S0140-6736(00)04046-0
6. Ball, R. J., Avenell, A., Aucott, L., Hanlon, P., & Vickers, M. A. (2015). Systematic review and meta-analysis of the sero-epidemiological association between Epstein-Barr virus and rheumatoid arthritis. Arthritis Research & Therapy, 17(1), 274. https://doi.org/10.1186/s13075-015-0755-6
7. Ballerini, C., Amoriello, R., Maghrebi, O., Bellucci, G., Addazio, I., Betti, M., Aprea, M. G., Masciulli, C., Caporali, A., Penati, V., Ballerini, C., De Meo, E., Portaccio, E., Salvetti, M., & Amato, M. P. (2025). Exploring the role of EBV in multiple sclerosis pathogenesis through EBV interactome. Frontiers in Immunology, 16, 1557483. https://doi.org/10.3389/fimmu.2025.1557483
8. Bautista, J., & Lopez-Cortes, A. (2025). Oncogenic viruses rewire the epigenome in human cancer. Frontiers in Cellular and Infection Microbiology, 15, 1617198. https://doi.org/10.3389/fcimb.2025.1617198
9. Bednar, K. J., Lee, J. H., & Ort, T. (2022). Tregs in autoimmunity: Insights into intrinsic brake mechanism driving pathogenesis and immune homeostasis. Frontiers in Immunology, 13, 932485. https://doi.org/10.3389/fimmu.2022.932485
10. Bjornevik, K., Cortese, M., Healy, B. C., Kuhle, J., Mina, M. J., Leng, Y., Elledge, S. J., Niebuhr, D. W., Scher, A. I., Munger, K. L., & Ascherio, A. (2022). Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis. Science (New York, N.Y.), 375(6578), 296–301. https://doi.org/10.1126/science.abj8222
11. Bjornevik, K., Münz, C., Cohen, J. I., & Ascherio, A. (2023). Epstein-Barr virus as a leading cause of multiple sclerosis: mechanisms and implications. Nature Reviews. Neurology, 19(3), 160–171. https://doi.org/10.1038/s41582-023-00775-5
12. Borghi, M. O., Beltagy, A., Garrafa, E., Curreli, D., Cecchini, G., Bodio, C., Grossi, C., Blengino, S., Tincani, A., Franceschini, F., Andreoli, L., Lazzaroni, M. G., Piantoni, S., Masneri, S., Crisafulli, F., Brugnoni, D., Muiesan, M. L., Salvetti, M., Parati, G., … Meroni, P. L. (2020). Anti-phospholipid antibodies in COVID-19 are different from those detectable in the anti-phospholipid syndrome. Frontiers in Immunology, 11, 584241. https://doi.org/10.3389/fimmu.2020.584241
13. Cao-Lormeau, V.-M., Blake, A., Mons, S., Lastère, S., Roche, C., Vanhomwegen, J., Dub, T., Baudouin, L., Teissier, A., Larre, P., Vial, A.-L., Decam, C., Choumet, V., Halstead, S. K., Willison, H. J., Musset, L., Manuguerra, J.-C., Despres, P., Fournier, E., … Ghawché, F. (2016a). Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet, 387(10027), 1531–1539. https://doi.org/10.1016/S0140-6736(16)00562-6
14. Cao-Lormeau, V.-M., Blake, A., Mons, S., Lastère, S., Roche, C., Vanhomwegen, J., Dub, T., Baudouin, L., Teissier, A., Larre, P., Vial, A.-L., Decam, C., Choumet, V., Halstead, S. K., Willison, H. J., Musset, L., Manuguerra, J.-C., Despres, P., Fournier, E., … Ghawché, F. (2016b). Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet, 387(10027), 1531–1539. https://doi.org/10.1016/S0140-6736(16)00562-6
15. Chan, L. S., Vanderlugt, C. J., Hashimoto, T., Nishikawa, T., Zone, J. J., Black, M. M., Wojnarowska, F., Stevens, S. R., Chen, M., Fairley, J. A., Woodley, D. T., Miller, S. D., & Gordon, K. B. (1998). Epitope spreading: lessons from autoimmune skin diseases. The Journal of Investigative Dermatology, 110(2), 103–109. https://doi.org/10.1046/j.1523-1747.1998.00107.x
16. Cheng, K., Cai, N., Zhu, J., Yang, X., Liang, H., & Zhang, W. (2022). Tumor-associated macrophages in liver cancer: From mechanisms to therapy. Cancer Communications (London, England), 42(11), 1112–1140. https://doi.org/10.1002/cac2.12345

17. Cheru, N. T., Osayame, Y., & Sumida, T. S. (2025). Breaking tolerance: an update of Treg dysfunction in autoimmunity. Trends in Immunology. https://doi.org/10.1016/j.it.2025.06.007
18. Chu, D., Liu, T., & Yao, Y. (2023). Implications of viral infections and oncogenesis in uterine cervical carcinoma etiology and pathogenesis. Frontiers in Microbiology, 14, 1194431. https://doi.org/10.3389/fmicb.2023.1194431
19. Counotte, M. J., Meili, K. W., Taghavi, K., Calvet, G., Sejvar, J., & Low, N. (2019). Zika virus infection as a cause of congenital brain abnormalities and Guillain-Barré syndrome: A living systematic review. F1000Research, 8, 1433. https://doi.org/10.12688/f1000research.19918.1
20. Coussens, L. M., & Werb, Z. (2002). Inflammation and cancer. Nature, 420(6917), 860–867. https://doi.org/10.1038/nature01322
21. Croxford, J. L., Olson, J. K., & Miller, S. D. (2002). Epitope spreading and molecular mimicry as triggers of autoimmunity in the Theiler's virus-induced demyelinating disease model of multiple sclerosis. Autoimmunity Reviews, 1(5), 251–260. https://doi.org/10.1016/s1568-9972(02)00080-0
22. Czyż, W., Chuncia-Ileczko, M., Wójcikiewicz, M., Arczewski, F., Dziedzic, K., Kulbacka, J., Wojszczyk, M., Zys, D., Pasek, P., & Ryniecka, J. (2025). Epstein-Barr virus (EBV) and systemic lupus erythematosus (SLE) association in serological studies. Quality in Sport, 37, 57143. https://doi.org/10.12775/qs.2025.37.57143
23. De Sanctis, P., Doneddu, P. E., Viganò, L., Selmi, C., & Nobile-Orazio, E. (2020). Guillain-Barré syndrome associated with SARS-CoV-2 infection. A systematic review. European Journal of Neurology: The Official Journal of the European Federation of Neurological Societies, 27(11), 2361–2370. https://doi.org/10.1111/ene.14462
24. Didona, D., & Di Zenzo, G. (2018). Humoral Epitope spreading in autoimmune bullous diseases. Frontiers in Immunology, 9, 779. https://doi.org/10.3389/fimmu.2018.00779
25. Dinesh, R. K., Skaggs, B. J., La Cava, A., Hahn, B. H., & Singh, R. P. (2010). CD8+ Tregs in lupus, autoimmunity, and beyond. Autoimmunity Reviews, 9(8), 560–568. https://doi.org/10.1016/j.autrev.2010.03.006
26. Eggenhuizen, P. J., Ng, B. H., & Ooi, J. D. (2020). Treg enhancing therapies to treat autoimmune diseases. International Journal of Molecular Sciences, 21(19), 7015. https://doi.org/10.3390/ijms21197015
27. Fahlquist-Hagert, C., Wittenborn, T. R., Terczyńska-Dyla, E., Kastberg, K. S., Yang, E., Rallistan, A. N., Markett, Q. R., Winther, G., Fonager, S., Voss, L. F., Pedersen, M. K., van Campen, N., Ferapontov, A., Jensen, L., Huang, J., Nieland, J. D., van der Poel, C. E., Palmfeldt, J., Carroll, M. C., … Degn, S. E. (2023). Antigen presentation by B cells enables epitope spreading across an MHC barrier. Nature Communications, 14(1), 6941. https://doi.org/10.1038/s41467-023-42541-7
28. Fasano, A. (2011). Zonulin and its regulation of intestinal barrier function: the biological door to inflammation, autoimmunity, and cancer. Physiological Reviews, 91(1), 151–175. https://doi.org/10.1152/physrev.00003.2008
29. Ferrari, E., Sartre, B., Squara, F., Contenti, J., Occelli, C., Lemoel, F., Levraut, J., Doyen, D., Dellamonica, J., Mondain, V., Chirio, D., Risso, K., Cua, E., Orban, J. C., Ichai, C., Labbaoui, M., Mossaz, B., Moceri, P., Appert-Flory, A., … Toulon, P. (2020). High prevalence of acquired thrombophilia without prognosis value in patients with Coronavirus disease 2019. Journal of the American Heart Association, 9(21), e017773. https://doi.org/10.1161/JAHA.120.017773
30. Franco, J.-S., Amaya-Amaya, J., & Anaya, J.-M. (2013). Thyroid disease and autoimmune diseases. In Autoimmunity: From Bench to Bedside [Internet]. El Rosario University Press. https://www.ncbi.nlm.nih.gov/books/NBK459466/
31. Fujinami, R. S., von Herrath, M. G., Christen, U., & Whitton, J. L. (2006). Molecular mimicry, bystander activation, or viral persistence: infections and autoimmune disease. Clinical Microbiology Reviews, 19(1), 80–94. https://doi.org/10.1128/CMR.19.1.80-94.2006
32. Gabrilovich, D. I. (2017). Myeloid-derived suppressor cells. Cancer Immunology Research, 5(1), 3–8. https://doi.org/10.1158/2326-6066.CIR-16-0297
33. Gouirand, V., Habrylo, I., & Rosenblum, M. D. (2022). Regulatory T cells and inflammatory mediators in autoimmune disease. The Journal of Investigative Dermatology, 142(3 Pt B), 774–780. https://doi.org/10.1016/j.jid.2021.05.010
34. Hanlon, P., Avenell, A., Aucott, L., & Vickers, M. A. (2014). Systematic review and meta-analysis of the sero-epidemiological association between Epstein-Barr virus and systemic lupus erythematosus. Arthritis Research & Therapy, 16(1), R3. https://doi.org/10.1186/ar4429
35. Harley, J. B., & James, J. A. (2010). Everyone comes from somewhere: systemic lupus erythematosus and Epstein-Barr virus induction of host interferon and humoral anti-Epstein-Barr nuclear antigen 1 immunity. Arthritis and Rheumatism, 62(6), 1571–1575. https://doi.org/10.1002/art.27421
36. He, R., Du, Y., & Wang, C. (2022). Epstein-Barr virus infection: the leading cause of multiple sclerosis. Signal Transduction and Targeted Therapy, 7(1), 239. https://doi.org/10.1038/s41392-022-01100-0
37. Helial, M. N., & Mohammed, A. H. (2022). Investigation of Coxsackie Virus Type B in Grave's Thyroiditis. Pakistan Journal of Medical and Health Sciences, 16(6), 745–747. https://doi.org/10.53350/pjmhs22166745
38. Hirano, T. (2021). IL-6 in inflammation, autoimmunity and cancer. International Immunology, 33(3), 127–148. https://doi.org/10.1093/intimm/dxaa078

39. Houen, G., & Trier, N. H. (2020). Epstein-Barr Virus and systemic autoimmune diseases. Frontiers in Immunology, 11, 587380. https://doi.org/10.3389/fimmu.2020.587380
40. Huang, Z., Fu, Y., Yang, H., Zhou, Y., Shi, M., Li, Q., Liu, W., Liang, J., Zhu, L., Qin, S., Hong, H., & Liu, Y. (2024). Liquid biopsy in T-cell lymphoma: biomarker detection techniques and clinical application. Molecular Cancer, 23(1), 36. https://doi.org/10.1186/s12943-024-01947-7
41. Jain, S., Annett, S. L., Morgan, M. P., & Robson, T. (2021). The cancer stem cell niche in ovarian cancer and its impact on immune surveillance. International Journal of Molecular Sciences, 22(8), 4091. https://doi.org/10.3390/ijms22084091
42. Jiang, Y., Han, Q., Zhao, H., & Zhang, J. (2021a). The mechanisms of HBV-induced hepatocellular carcinoma. Journal of Hepatocellular Carcinoma, 8, 435–450. https://doi.org/10.2147/JHC.S307962
43. Jiang, Y., Han, Q., Zhao, H., & Zhang, J. (2021b). The mechanisms of HBV-induced hepatocellular carcinoma. Journal of Hepatocellular Carcinoma, 8, 435–450. https://doi.org/10.2147/JHC.S307962
44. Jog, N. R., & James, J. A. (2020). Epstein Barr virus and autoimmune responses in systemic lupus erythematosus. Frontiers in Immunology, 11, 623944. https://doi.org/10.3389/fimmu.2020.623944
45. Johann, D. J., Jr, Steliga, M., Shin, I. J., Yoon, D., Arnaoutakis, K., Hutchins, L., Liu, M., Liem, J., Walker, K., Pereira, A., Yang, M., Jeffus, S. K., Peterson, E., & Xu, J. (2018). Liquid biopsy and its role in an advanced clinical trial for lung cancer. Experimental Biology and Medicine (Maywood, N.J.), 243(3), 262–271. https://doi.org/10.1177/1535370217750087
46. Johnson, D. B., Balko, J. M., Compton, M. L., Chalkias, S., Gorham, J., Xu, Y., Hicks, M., Puzanov, I., Alexander, M. R., Bloomer, T. L., Becker, J. R., Slosky, D. A., Phillips, E. J., Pilkinton, M. A., Craig-Owens, L., Kola, N., Plautz, G., Reshef, D. S., Deutsch, J. S., … Moslehi, J. J. (2016a). Fulminant myocarditis with combination immune checkpoint blockade. The New England Journal of Medicine, 375(18), 1749–1755. https://doi.org/10.1056/NEJMoa1609214
47. Johnson, D. B., Balko, J. M., Compton, M. L., Chalkias, S., Gorham, J., Xu, Y., Hicks, M., Puzanov, I., Alexander, M. R., Bloomer, T. L., Becker, J. R., Slosky, D. A., Phillips, E. J., Pilkinton, M. A., Craig-Owens, L., Kola, N., Plautz, G., Reshef, D. S., Deutsch, J. S., … Moslehi, J. J. (2016b). Fulminant myocarditis with combination immune checkpoint blockade. The New England Journal of Medicine, 375(18), 1749–1755. https://doi.org/10.1056/NEJMoa1609214
48. Kharrazian, D., Herbert, M., & Lambert, J. (2023). The relationships between intestinal permeability and target antibodies for a spectrum of autoimmune diseases. International Journal of Molecular Sciences, 24(22), 16352. https://doi.org/10.3390/ijms242216352
49. Lazar, V., Ditu, L.-M., Pircalabioru, G. G., Gheorghe, I., Curutiu, C., Holban, A. M., Picu, A., Petcu, L., & Chifiriuc, M. C. (2018). Aspects of gut Microbiota and immune system interactions in infectious diseases, immunopathology, and cancer. Frontiers in Immunology, 9, 1830. https://doi.org/10.3389/fimmu.2018.01830
50. Lee, G. R. (2018). The balance of Th17 versus Treg cells in autoimmunity. International Journal of Molecular Sciences, 19(3). https://doi.org/10.3390/ijms19030730
51. Lei, Y., Xu, X., Liu, H., Chen, L., Zhou, H., Jiang, J., Yang, Y., & Wu, B. (2021). HBx induces hepatocellular carcinogenesis through ARRB1-mediated autophagy to drive the G1/S cycle. Autophagy, 17(12), 4423–4441. https://doi.org/10.1080/15548627.2021.1917948
52. Lemus, Y. B., Martínez, G. A., Lugo, L. P., Escorcia, L. G., Peñata, E. Z., Llanos, N. S., Bonfanti, A. C., Acosta-Hoyos, A. J., & Quiroz, E. N. (2024). Gene profiling of Epstein-Barr Virus and human endogenous retrovirus in peripheral blood mononuclear cells of SLE patients: immune response implications. Scientific Reports, 14(1), 20236. https://doi.org/10.1038/s41598-024-70913-6
53. Levrero, M., & Zucman-Rossi, J. (2016). Mechanisms of HBV-induced hepatocellular carcinoma. Journal of Hepatology, 64(1 Suppl), S84–S101. https://doi.org/10.1016/j.jhep.2016.02.021
54. Li, Z.-X., Zeng, S., Wu, H.-X., & Zhou, Y. (2019). The risk of systemic lupus erythematosus associated with Epstein-Barr virus infection: a systematic review and meta-analysis. Clinical and Experimental Medicine, 19(1), 23–36. https://doi.org/10.1007/s10238-018-0535-0
55. Luijten, L. W. G., Leonhard, S. E., van der Eijk, A. A., Doets, A. Y., Appeltshauser, L., Arends, S., Attarian, S., Benedetti, L., Briani, C., Casasnovas, C., Castellani, F., Dardiotis, E., Echaniz-Laguna, A., Garssen, M. P. J., Harbo, T., Huizinga, R., Humm, A. M., Jellema, K., van der Kooi, A. J., … IGOS consortium. (2021). Guillain-Barré syndrome after SARS-CoV-2 infection in an international prospective cohort study. Brain: A Journal of Neurology, 144(11), 3392–3404. https://doi.org/10.1093/brain/awab279
56. Ma, L., Guo, H., Zhao, Y., Liu, Z., Wang, C., Bu, J., Sun, T., & Wei, J. (2024). Liquid biopsy in cancer current: status, challenges and future prospects. Signal Transduction and Targeted Therapy, 9(1), 336. https://doi.org/10.1038/s41392-024-02021-w
57. Marklund, L., & Hammarstedt, L. (2011). Impact of HPV in oropharyngeal cancer. Journal of Oncology, 2011, 509036. https://doi.org/10.1155/2011/509036

58. Marrugo-Ramírez, J., Mir, M., & Samitier, J. (2018). Blood-based cancer biomarkers in liquid biopsy: A promising non-invasive alternative to tissue biopsy. International Journal of Molecular Sciences, 19(10), 2877. https://doi.org/10.3390/ijms19102877
59. Meagher, T. (2024). Autoimmune Diseases following COVID-19 Infection: How Solid is the Evidence? Journal of Insurance Medicine (New York, N.Y.), 51(3), 125–128. https://doi.org/10.1029/AAIMEDICINE-D-24-00026.1
60. Miller, S. D., Vanderlugt, C. L., Begolka, W. S., Pao, W., Yauch, R. L., Neville, K. L., Katz-Levy, Y., Carrizosa, A., & Kim, B. S. (1997). Persistent infection with Theiler's virus leads to CNS autoimmunity via epitope spreading. Nature Medicine, 3(10), 1133–1136. https://doi.org/10.1038/nm1097-1133
61. Moody, C. A., & Laimins, L. A. (2010). Human papillomavirus oncoproteins: pathways to transformation. Nature Reviews. Cancer, 10(8), 550–560. https://doi.org/10.1038/nrc2886
62. Moriya, K., Fujie, H., Shintani, Y., Yotsuyanagi, H., Tsutsumi, T., Ishibashi, K., Matsuura, Y., Kimura, S., Miyamura, T., & Koike, K. (1998). The core protein of hepatitis C virus induces hepatocellular carcinoma in transgenic mice. Nature Medicine, 4(9), 1065–1067. https://doi.org/10.1038/2053
63. Mu, Q., Kirby, J., Reilly, C. M., & Luo, X. M. (2017). Leaky gut as a danger signal for autoimmune diseases. Frontiers in Immunology, 8, 598. https://doi.org/10.3389/fimmu.2017.00598
64. Olsen, N. J., Choi, M. Y., & Fritzler, M. J. (2017). Emerging technologies in autoantibody testing for rheumatic diseases. Arthritis Research & Therapy, 19(1), 172. https://doi.org/10.1186/s13075-017-1380-3
65. Owliaee, I., Khaledian, M., Boroujeni, A. K., & Shojaeian, A. (2023). Engineered small extracellular vesicles as a novel platform to suppress human oncovirus-associated cancers. Infectious Agents and Cancer, 18(1), 69. https://doi.org/10.1186/s13027-023-00549-0
66. Peng, K., Li, X., Yang, D., Chan, S. C. W., Zhou, J., Wan, E. Y. F., Chui, C. S. L., Lai, F. T. T., Wong, C. K. H., Chan, E. W. Y., Leung, W. K., Lau, C.-S., & Wong, I. C. K. (2023). Risk of autoimmune diseases following COVID-19 and the potential protective effect from vaccination: a population-based cohort study. EClinicalMedicine, 63(102154), 102154. https://doi.org/10.1016/j.eclinm.2023.102154
67. Postow, M. A., Sidlow, R., & Hellmann, M. D. (2018). Immune-related adverse events associated with immune checkpoint blockade. The New England Journal of Medicine, 378(2), 158–168. https://doi.org/10.1056/NEJMra1703481
68. Qin, Y., Gao, C., & Luo, J. (2022). Metabolism characteristics of Th17 and regulatory T cells in autoimmune diseases. Frontiers in Immunology, 13, 828191. https://doi.org/10.3389/fimmu.2022.828191
69. Ribatti, D. (2024). Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. Comment. Internal and Emergency Medicine, 19(5), 1515–1516. https://doi.org/10.1007/s11739-024-03600-z
70. Rohrhofer, J., Graninger, M., Lettenmaier, L., Schweighardt, J., Gentile, S. A., Koidl, L., Ret, D., Stingl, M., Puchhammer-Stöckl, E., & Untersmayr, E. (2023). Association between Epstein-Barr-Virus reactivation and development of Long-COVID fatigue. Allergy, 78(1), 297–299. https://doi.org/10.1111/all.15471
71. Root-Bernstein, R. (n.d.). Autoimmunity infection: immune heterogeneity self-directed immune response.
72. Rozenblyum, E. V., Allen, U. D., Silverman, E. D., & Levy, D. M. (2013). Cytomegalovirus infection in childhood-onset systemic lupus erythematosus. International Journal of Clinical Rheumatology, 8(1), 137–146. https://doi.org/10.2217/ijr.12.82
73. Sadowski, J., Huk, J., Otulak, S., Zawiło, J., Klaudel, T., Roszak, M., Tenczyński, D., & Bułdak, R. J. (2025). Association between Guillain-Barré syndrome and SARS-CoV-2 virus infection, including the impact of COVID-19 vaccination in the context of the development and general clinical characteristics of the disease. Journal of Neurovirology. https://doi.org/10.1007/s13365-025-01267-6
74. Sawicka-Gutaj, N., Wietrzyk, D., Zawalna, N., Erampamoorthy, A., & Ruchała, M. (2022). Autoimmune disorders and thyroid function in patients with rheumatoid arthritis after biological treatment. Rheumatology Forum, 8(3), 111–121. https://doi.org/10.5603/rf.2022.0016
75. Shalapour, S., & Karin, M. (2015). Immunity, inflammation, and cancer: an eternal fight between good and evil. The Journal of Clinical Investigation, 125(9), 3347–3355. https://doi.org/10.1172/JCI80007
76. Shim, C.-H., Cho, S., Shin, Y.-M., & Choi, J.-M. (2022). Emerging role of bystander T cell activation in autoimmune diseases. BMB Reports, 55(2), 57–64. https://doi.org/10.5483/bmbrep.2022.55.2.183
77. Smatti, M. K., Al Thani, A. A., & Yassine, H. M. (2018). Viral-induced enhanced disease illness. Frontiers in Microbiology, 9, 2991. https://doi.org/10.3389/fmicb.2018.02991
78. Son, K., Jamil, R., Chowdhury, A., Mukherjee, M., Venegas, C., Miyasaki, K., Zhang, K., Patel, Z., Salter, B., Yuen, A. C. Y., Lau, K. S.-K., Cowbrough, B., Radford, K., Huang, C., Kjarsgaard, M., Dvorkin-Gheva, A., Smith, J., Li, Q.-Z., Waserman, S., … Mukherjee, M. (2023). Circulating anti-nuclear autoantibodies in COVID-19 survivors predict long COVID symptoms. The European Respiratory Journal: Official Journal of the European Society for Clinical Respiratory Physiology, 61(1). https://doi.org/10.1183/13993003.00970-2022
79. Strizzi, C. T., Ambrogio, M., Zanoni, F., Bonerba, B., Bracaccia, M. E., Grandaliano, G., & Pesce, F. (2024). Epitope spreading in immune-mediated glomerulonephritis: The expanding target. International Journal of Molecular Sciences, 25(20). https://doi.org/10.3390/ijms252011096

80. Sundaresan, B., Shirafkan, F., Ripperger, K., & Rattay, K. (2023). The role of viral infections in the onset of autoimmune diseases. Viruses, 15(3). https://doi.org/10.3390/v15030782
81. Taeschler, P., Cervia, C., Zurbuchen, Y., Hasler, S., Pou, C., Tan, Z., Adamo, S., Raeber, M. E., Bächli, E., Rudiger, A., Stüssi-Helbling, M., Huber, L. C., Brodin, P., Nilsson, J., Probst-Müller, E., & Boyman, O. (2022). Autoantibodies in COVID-19 correlate with antiviral humoral responses and distinct immune signatures. Allergy, 77(8), 2415–2430. https://doi.org/10.1111/all.15302
82. Tang DO MPH, W., Das MD, S., & Krudy MD, Z. (2021). Coxsackie Virus Induced Graves' Disease in an Immunocompetent Patient. International Journal of Innovative Research in Medical Science, 6(10), 731–734. https://doi.org/10.23958/ijirms/vol06-i10/1231
83. Tarhini, A. A., Zahoor, H., Lin, Y., Malhotra, U., Sander, C., Butterfield, L. H., & Kirkwood, J. M. (2015). Baseline circulating IL-17 predicts toxicity while TGF-β1 and IL-10 are prognostic of relapse in ipilimumab neoadjuvant therapy of melanoma. Journal for Immunotherapy of Cancer, 3(1), 39. https://doi.org/10.1186/s40425-015-0081-1
84. Tesch, F., Ehm, F., Vivirito, A., Wende, D., Batram, M., Loser, F., Menzer, S., Jacob, J., Roessler, M., Seifert, M., Kind, B., König, C., Schulte, C., Buschmann, T., Hertle, D., Ballesteros, P., Baßler, S., Bertele, B., Bitterer, T., … Schmitt, J. (2023). Incident autoimmune diseases in association with SARS-CoV-2 infection: a matched cohort study. Clinical Rheumatology, 42(10), 2905–2914. https://doi.org/10.1007/s10067-023-06670-0
85. Turetta, M., Ben, F. D., Brisotto, G., Biscontin, E., Bulfoni, M., Cesselli, D., Colombatti, A., Scoles, G., Gigli, G., & Del Mercato, L. L. (2018). Emerging technologies for cancer research: Towards personalized medicine with microfluidic platforms and 3D tumor models. Current Medicinal Chemistry, 25(35), 4616–4637. https://doi.org/10.2174/0929867325666180605122633
86. Vahabi, M., Ghazanfari, T., & Sepehrnia, S. (2022). Molecular mimicry, hyperactive immune system, and SARS-COV-2 are three prerequisites of the autoimmune disease triangle following COVID-19 infection. International Immunopharmacology, 112(109183), 109183. https://doi.org/10.1016/j.intimp.2022.109183
87. Valaparla, V. L., Rane, S. P., Patel, C., & Li, X. (2024). Guillain-Barre syndrome and link with COVID-19 infection and vaccination: a review of literature. Frontiers in Neurology, 15, 1396642. https://doi.org/10.3389/fneur.2024.1396642
88. Vandermeulen, C., O'Grady, T., Wayet, J., Galvan, B., Maseko, S., Cherkaoui, M., Desbuleux, A., Coppin, G., Olivet, J., Ben Ameur, L., Kataoka, K., Ogawa, S., Hermine, O., Marcais, A., Thiry, M., Mortreux, F., Calderwood, M. A., Van Weyenbergh, J., Peloponese, J.-M., … Twizere, J.-C. (2021). The HTLV-1 viral oncoproteins Tax and HBZ reprogram the cellular mRNA splicing landscape. PLoS Pathogens, 17(9), e1009919. https://doi.org/10.1371/journal.ppat.1009919
89. Wan, Z., Zhou, Z., Liu, Y., Lai, Y., Luo, Y., Peng, X., & Zou, W. (2020). Regulatory T cells and T helper 17 cells in viral infection. Scandinavian Journal of Immunology, 91(5), e12873. https://doi.org/10.1111/sji.12873
90. Xiao, Q., Liu, Y., Li, T., Wang, C., He, S., Zhai, L., Yang, Z., Zhang, X., Wu, Y., & Liu, Y. (2025). Viral oncogenesis in cancer: from mechanisms to therapeutics. Signal Transduction and Targeted Therapy, 10(1), 151. https://doi.org/10.1038/s41392-025-02197-9
91. Xie, S., Wei, J., & Wang, X. (2025). The intersection of influenza infection and autoimmunity. Frontiers in Immunology, 16, 1558386. https://doi.org/10.3389/fimmu.2025.1558386
92. Yoo, J. Y., Groer, M., Dutra, S. V. O., Sarkar, A., & McSkimming, D. I. (2020). Gut Microbiota and immune system interactions. Microorganisms, 8(10), 1587. https://doi.org/10.3390/microorganisms8101587
93. Yosri, M., Dokhan, M., Aboagye, E., Al Moussawy, M., & Abdelsamed, H. A. (2024). Mechanisms governing bystander activation of T cells. Frontiers in Immunology, 15, 1465889. https://doi.org/10.3389/fimmu.2024.1465889
94. Young, L. S., Yap, L. F., & Murray, P. G. (2016). Epstein-Barr virus: more than 50 years old and still providing surprises. Nature Reviews. Cancer, 16(12), 789–802. https://doi.org/10.1038/nrc.2016.92
95. Zhang, S., Gang, X., Yang, S., Cui, M., Sun, L., Li, Z., & Wang, G. (2021a). The alterations in and the role of the Th17/Treg balance in metabolic diseases. Frontiers in Immunology, 12, 678355. https://doi.org/10.3389/fimmu.2021.678355
96. Zhang, S., Gang, X., Yang, S., Cui, M., Sun, L., Li, Z., & Wang, G. (2021b). The alterations in and the role of the Th17/Treg balance in metabolic diseases. Frontiers in Immunology, 12, 678355. https://doi.org/10.3389/fimmu.2021.678355
97. Zhang, T., Yu, Z., Gao, S., Zhang, Y., Wang, C., Jian, S., Wang, L., Gou, L., Li, J., Ma, M., & Song, H. (2023). Clinical phenotypes and prognosis of cytomegalovirus infection in the pediatric systemic lupus erythematosus: a longitudinal analysis. Pediatric Rheumatology Online Journal, 21(1), 25. https://doi.org/10.1186/s12969-023-00807-w
98. Zhao, T., Wang, Z., Fang, J., Cheng, W., Zhang, Y., Huang, J., Xu, L., Gou, H., Zeng, L., Jin, Z., & Matsuoka, M. (2022). HTLV-1 activates YAP via NF-κB/p65 to promote oncogenesis. Proceedings of the National Academy of Sciences of the United States of America, 119(9), e2115316119. https://doi.org/10.1073/pnas.2115316119