The Role of Tissue Immune Dysregulation in Cancer and Systemic Diseases

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Abstract: Tissue immune homeostasis is essential for the prevention of pathological inflammation and the preservation of organ integrity. However, when immune regulation at the tissue level is disrupted, it can trigger or aggravate a wide array of diseases, including cancer and systemic inflammatory disorders. This review looks into the pathophysiology of autoimmune and chronic systemic disorders, as well as the emerging understanding of how tissue-specific immune dysregulation contributes to oncogenesis, tumor progression, and metastasis. Dysfunctional interactions between tissue-resident immune cells, stromal components, cytokine networks, and the local microenvironment are at the core of this dysregulation. The failure of immune tolerance, chronic low-grade inflammation, and aberrant activation of immune checkpoints are identified as critical mechanisms. Additionally, the role of tissue-specific immune niches in shaping disease outcomes emphasizes the need for localized therapeutic approaches. Understanding the molecular and cellular basis of tissue immune dysregulation opens new insights into targeted immunotherapies and precision medicine for both malignant and non-malignant diseases.

Keywords: Tissue, Immune Dysregulation, Cancer, Systemic Diseases.

1. Introduction to Tissue Immune Dysregulation

Scientists are working to gain a deeper understanding of the dysregulation of the immune system in order to enhance treatment options by discovering important

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cellular and molecular processes. This investigation is essential for preserving a robust immune reaction [1].

The growing area of research holds the promise of leading to revolutionary findings and progress in treating different diseases, ultimately enhancing the lives of numerous people around the world. Scientists are working hard to unravel the complexities of immune cell signaling pathways and to study the impact of genetic and environmental factors, with the ultimate goal of gaining a thorough understanding of immune dysregulation [2].

By elucidating the underlying causes and mechanisms, scientists aim to develop novel therapies that can restore immune equilibrium and prevent the progression of diseases such as cancer, chronic inflammation, and fibrosis. With each new breakthrough, we inch closer to a future where immune dysregulation is no longer a formidable adversary, but a challenge that can be overcome through scientific exploration and innovation. For years, the mechanisms of immune responses have been studied, but the context of responses ultimately depended on the tissue, which aligned a different strategy of approach, compared to systemic responses classified more on the basis of the organ [3].

Several organs have been studied to understand the main mechanisms of immune response evasion and dysregulation, specifically promoting the disease-typing process. It is important to pinpoint those immune responses cannot function properly if cells are dysregulated in terms of immune biology, and tissue sites allow for this interaction by providing signals. The majority of biomedical studies are mainly focused on the interaction between immune cells and diseased populations, or in the tumor microenvironment [4]. Inside historic buildings, breakdown usually occurs gradually or suddenly, from the weakest joint to the weakest in a form of chain of structural elements. [5]. There is limited discussion regarding the interaction of the immune system with various tissue sites and organs, especially in relation to its reactivity under stressful conditions to effectively control the killing mechanism in specific tissue environments. Many unanswered questions remain, particularly regarding the immune response responsible for inducing and protecting tissue-site regulatory proteins, as well as the factors that lead to dysregulated immune responses. A comprehensive analysis of this topic would greatly benefit the scientific community in developing therapeutic strategies that combine drug treatments for the primary disease with tissue-specific therapies, which directly target the underlying cause of the disease [6].

1.1 Definition and Overview

Tissue immune dysregulation is a localized discoordination of immune function with changing tissue dynamics. An interconnected network mediates this dynamic

coordination between local tissue dynamics and immune function. Like tissues, local immune networks may lose fidelity in adaptive responses. Immune dysregulation drives cancers, predisposing individuals to specific tumor types. Developing strategies to eliminate these cancers could provide new clues to the principles of precision medicine [7].

Understanding immune tissue discoordination begins with defining immune dysregulation. Related terms include immune response or tolerance, in which immune cells and tissues have a limited set of possible configurations. In adaptive immune responses, the increasing variability of immune repertoire via VDJ recombination creates immune effector and memory cells. Within tissues and lymphoid tissues, immune maladaptation can lead to focal or systemic immune phenotypes, such as organ-specific autoimmune diseases [8].

In the context of immune cytokine and surface receptor signaling, this could also contribute to tissue vitiligo location, although immune cell access and some restriction are due to immune chemokine and trafficking molecule expression rather than signal dysfunction. Regulatory cytokines are necessary for adaptive immune tissue specificity as well. An increasing morphological correlate of immune dysregulation is in the case of lymphoid follicles, increasingly found in autoimmune disease onset and cancer resistance areas [9].

1.2 Importance in Cancer and Systemic Diseases

Chronic tissue immune-related dysregulation has turned out to play a critical role in cancer. Though often initially designed to contain and suppress neoplastic cells, immune responses develop in response to tumor growth, sometimes proliferating and facilitating a 'smoldering state' of tumor development and progression. Modulating tissue immune responses to tumors often determines survival, and a better understanding of tissue immunopathology is providing novel forms of cancer therapeutics. In oncology, the involvement of immune cells in malignant tumors is getting progressively recognized [10].

This is primarily because the composition, function, and positioning of immune infiltrates are powerfully connected to clinical outcomes in a way that surpasses that of age-old and classical staging systems. The archetypal example is the association between tumor-infiltrating lymphocytes in triple-negative breast cancer, which led to responses to treatment and better survival. Moreover, different tissue sites, even at the scale of individual cancer types, display distinct patterns of tissue immune dysregulation [11].

Immune-related cellular changes in cancers are commonly observed in systemic diseases. Systemic diseases, including cardiovascular and renal diseases, microbial

infections, granuloma-forming diseases, and, still controversially, chronic inflammation-associated diseases such as type 2 diabetes, are molecularly associated with immune dysregulation. This implies that studies of the tissue immunopathology within cancer can also inform how to study chronic systemic diseases. Moreover, immune cells can become immunosuppressed to permit the progression of chronic systemic diseases [12].

This process may protect the tissue site from collateral damage, or it may lead to direct tissue pathology, with immunosuppression permitting immune evasion of tissue damage and pathogen growth at the tissue site. Below, we discuss how chronic immune cell-associated dysregulation in non-immune privileged tissues, over time and in large numbers, is associated with systemic diseases [13].

This overview shows that non-cancer tissue immunopathology can be a systemic, and not just a local, risk factor and provide new areas where such an understanding would be beneficial. Clearly, a considerable cost arises from immune infiltration, but below we suggest the host may also gain from frequent cellular infiltration, which could explain why the immune response infiltrates tissue so commonly in chronic diseases, with chronic diseases fundamentally being associated with a great loss in immune homeostasis. Immune cells can either damage tissue directly or be targeted against standard cellular components, which leads to autoimmunity. Immune cell infiltration and autoimmunity are intimately linked. Treatments that control the former commonly treat the latter [14].

2. Immune System Basics

The immune system is a network of interacting cells, tissues, and organs that cooperates to recognize and fight invading pathogens. Its main goal is to maintain body homeostasis, defending against infection while minimizing immunopathology. The primary cells responsible for carrying out immune responses are divided into the innate and adaptive immune systems. Each of these systems is comprised of a myriad of subsets with distinct functions, but they all collaborate with non-immune cells to maintain homeostasis in an environment that includes up to 38 trillion cells in humans and is inhabited by complex interacting microbiota. Two important immune cell types are lymphocytes, which include B cells and T cells, and macrophages that can phagocytize bacteria and apply direct cytotoxicity to virus-infected and tumor cells [15].

The adaptive immune system also yields immunological memory, consisting of memory B and T lymphocytes that can better respond upon reinfection with a pathogen, or in the case of the elimination of cancer, resulting in enhanced and usually shorter immune responses than do naive lymphocytes. This immunity applies an inbuilt way to self-regulate and dampen immune responses, employing

clustered regulatory molecules and also the induction of immune inhibitory cells and cytokines. This ability to self-regulate immune status presents an opportunity to promote or suppress immune responses for therapeutic benefit, which has emerged as a key pillar of treating cancer over the past decade [16].

2.1. Components of the Immune System

The major types of T cells are T-helper cells, T-cytotoxic cells, and memory T cells. Additionally, there are suppressor or regulatory T cells, which serve to prevent or suppress autoimmune responses. Complement proteins are orchestrated by the immune system and have a variety of functions, including serving as opsonins, mediating chemotaxis, and facilitating phagocytosis. Antigen-presenting cells process information and share antigens via the major histocompatibility complex molecules with cells of the adaptive immune system. Dendritic cells are the strongest antigen-presenting cells of the immune system [17].

Secondary lymphoid organs, which include the spleen and the lymph nodes where cancer frequently metastasizes, are places in which adaptive immune responses can be generated. Data suggest that iNKT cells are involved in B-cell expansion and activation, potentially improving our understanding of how the immune system flags foreign and/or harmful substances. Immune responses are orchestrated by signaling molecules called cytokines and growth factors. Interactions among immune cells, as well as between cells and cytokine molecules, are critical elements in the discovery and eradication of cancers. In the next section, the fundamental process of immunity will be outlined, focusing on the role of immune cell dysregulation in cancer and systemic diseases. As part of a finely orchestrated network, these constructs rely on each other for optimal functionality [18].

2.2. Functions of the Immune System

There are numerous functions attributed to the immune system; one of the most important is the protection of the host from invading pathogens. The immune system has a multi-level system of pattern recognition dealing with not only the detection of pathogens but also with discernment for what type of pathogen is invading or if an infection is present. The immune system is also characterized by its ability to generate immune memory, which provides sustained protection and maintains the individual's health over a lifespan; self-tolerance and prevention of auto-reactivity; self-limitation; and the clearance phase of the response, removing the mechanisms once the infection or cancerous cells have been removed. Few of these functions operate in isolation; therefore, a dynamic and integrated immune response is essential for the optimal health of the individual [19].

To ensure homeostasis, the immune system remains unresponsive to all materials and cells that are not foreign to the host, a phenomenon known as immune tolerance. Although mainly designed to recognize and protect the body from foreign pathogens, informally referred to as "non-self," the immune system can also recognize and respond to self and damaged cells ("altered self") before elimination, including those that are undergoing malignant transformation. This balance between immune activation and regulation facilitates the host in avoiding self-destruction and overreaction to non-threatening stimuli [20].

The immune cells responsible for triggering immune responses are known as lymphocytes, and there are two broad groups: innate and adaptive immune responses. The first line of host defense is the innate immune response, which develops immediately on cell damage. However, prolonged tissue injury or infection will require a higher intensity of response. As a result, a more specific and intense immune response, known as the adaptive immune response, occurs. Both innate and adaptive immune responses complement each other in their features. For example, antigen nonspecific receptors bind to readily available molecules of pathogens in the innate response, whereas antigen-specific receptors bind to pathogens in the adaptive immune response [15].

3. Immune Dysregulation Mechanisms

Tissue immune dysregulation consists of two major components. In the inflamed tumor microenvironment, tumor exosome-derived products and other inflammatory mediators promote the local activation of bystander immune cells tasked with killing suddenly aberrant tissue cells. Over time, chronically reiterating bouts of cell necrosis and extension of damage-associated molecular patterns progress to induce those same immune cells to secrete cytotoxic molecules, pro-angiogenic factors, and matrix-remodeling enzymes while inducing mesenchymal cells to participate in the promotion of carcinogenesis [21]. If not detected and eradicated at early stages, disseminating tumor cells typically encounter a second line of defense consisting of metastatic niche-associated vaccines that utilize these proteinaceous factors to suppress immune cell expansion and function while also promoting tumor stemness. While the immune cells of the primary tumor and metastatic niche are independent, they also communicate and thereby must be considered as, at least partially, dysregulated [22].

In addition to "normal" adult-onset cancer, immunity also participates in the development of autoimmunity-associated cancers. In this instance, an increased frequency of neo-autoantigens in targetable tumor cells together with the increased expression of T cell homing signals attracts immune cells, in particular autoreactive immune effectors, into the tumor stroma [23]. Within the tumor site, potent immune

inhibitors actively dampen the local T cell response. Antigen-bearing dendritic cells, which are usually the primary driver of an adaptive co-stimulatory immune response, are also impacted by dysregulated tumor cells and fail to prime robust helper and effector T cell responses that would otherwise keep tumor development in check. Interestingly, these exhausted immune cells are unable to undergo apoptosis and instead undergo metabolic adaptation while remaining within the tissue, preserving the capability for the rapid proliferation seen in the effector cytotoxic T cells but unable to effectively kill the tumor. At the metastatic niche, where the immune system evolves independently, the process of tumor-elicited immune suppression against as yet undetected anti-oncogenic rejected neoantigens is also typically occurring and summarized in Immune Dysregulation Mechanisms Table 1. [24].

3.1 Inflammation and Tumor Microenvironment

It is well established that inflammation lies at the core of the tumor microenvironment and can critically influence cancer progression. Chronic inflammation results in the recruitment and expansion of myeloid and lymphoid immune cells in the Tumor Microenvironment (TME). The immune cells and their mediators then influence tumor growth, differentiation, angiogenesis, and cancer cell dissemination [25].

Inflammatory cells and the signaling mediators, such as cytokines, chemokines, matrix metalloproteinases, angiopoietins, eicosanoids, and a variety of growth factors lead to a dysregulated immune landscape that nurtures tumor growth, ranging from initial tolerogenic and immunoescape states to immunoediting and development of a precancerous niche, affecting local and distal host responses. Often, it is the dynamic interactions of Tumor Endothelial Cells (TECs), with recruited inflammatory cells that play a role in promoting immune dysregulation as show in **Figure 1**. Inflammatory cells can directly abrogate effector T cells and natural killer cells and can also be induced by the crosstalk with MM cells to produce immunosuppressive factors [26].

Several proinflammatory and immunosuppressive cell markers and chemokines and their receptors, cytokines, and transcriptional filters have been identified which favor progression of TME into cancer, like Transforming Growth Factor-beta (TGF-β), Interleukin-1 (IL-1), Interleukin-2 (IL-2), Interleukin-10 (IL-10), Interleukin-13 (IL-13), Interleukin-17 (IL-17), C-C Motif Chemokine Ligand 5 (CCL5), C-C Motif Chemokine Ligand 7 (CCL7), C-X-C Motif Chemokine Receptor 4 (CXCR4), Tumor Necrosis Factor-alpha (TNF-α), Neural Cell Adhesion Molecule (CD56 or NCAM). Tumor-associated macrophages typically

express factors involved in remodeling extracellular matrix like urokinase plasminogen activator, uPA receptor, and plasminogen activator inhibitor type I and II in addition to Matrix Metalloproteinases (MMPs). Neutrophils secrete Matrix Metalloproteinase (MMP-9) and produce free radicals which in turn affect the membrane choline esterase system and can themselves oxidize and inactivate MMPs leading to Extracellular Matrix (ECM) breakdown. These cells support tumor angiogenesis by secreting potent angiogenic growth factors [27]. In fact, a majority of patients are treated with nti-Vascular Endothelial Growth Factor (anti-VEGF) therapy and Multi-Receptor Tyrosine Kinase inhibitors (multi-RTK) inhibitors for malignant tumors and just now, antibodies against IL-17 are being tested for cancer therapy. Steroidal anti-inflammatory drugs and Cyclooxygenase enzymes (COX) inhibitors are showing promise in clinical trials. However, strategies to therapeutically shift the Cyclooxygenase enzymes (TME) from angiogenesis to immunogenesis still need to be explored further [28].

Table 1: Immune Dysregulation Mechanisms [24]

Mechanism	Description	Associated Diseases	Key Features
Loss of Immune Tolerance	Breakdown in distinguishing self from non-self-antigens.	Autoimmune diseases (e.g., SLE, RA, T1D).	Central and peripheral tolerance defects.
Hyperactive Responses	Excessive immune activation causing tissue damage.	Allergies, asthma, autoimmunity.	Overproduction of cytokines (cytokine storm), T/B-cell overactivation.
Immunodeficiency	Impaired immune response due to genetic or acquired causes.	SCID, HIV, secondary to chemotherapy.	Increased susceptibility to infections, reduced immune surveillance.
Chronic Inflammation	Persistent immune activation damaging tissues.	IBD, atherosclerosis, COPD.	Dysregulated inflammatory cytokines like TNF-α, IL-1, IL-6.

Misdirected Responses	Immune attacks against harmless antigens or microbiota.	Allergies, food intolerances, eczema.	Hypersensitivity to environmental allergens or microbiota imbalance.
Failure of Checkpoints	Loss of inhibitory signals regulating immune responses.	Cancer (immune evasion), autoimmunity.	Dysfunction of PD-1, CTLA-4 pathways, leading to excessive immune responses.
Molecular Mimicry	Cross-reactivity between microbial and self-antigens.	Rheumatic fever, Guillain-Barré syndrome.	Structural similarity triggers autoimmunity after infections.
Epigenetic/Environmental	Non-genetic factors altering immune gene expression.	MS, psoriasis, autoimmune thyroid diseases.	DNA methylation, histone modification, environmental triggers (diet, infections, pollution).

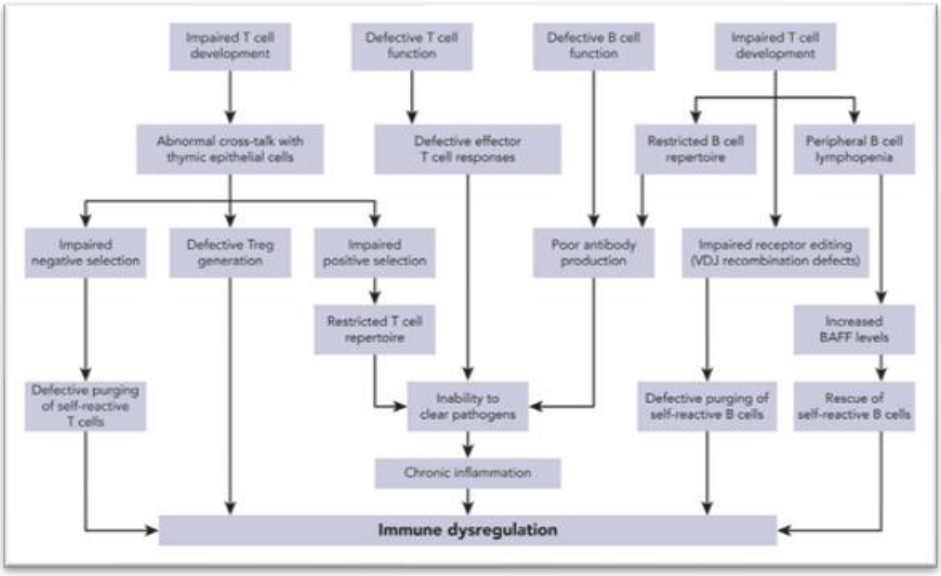

Figure 1: Role in promoting immune dysregulation [26]

3.2. Autoimmunity and Cancer

Immune dysregulation can lead to not only an autoimmune disease but also to cancer. These conditions share chronic inflammation and perturbation of the immune responses. Autoimmune disease leads to significant morbidity by targeting a specific organ, whereas cancer, if untreated, leads to significant mortality and eventually death as shown in figure 1, often with a restricted latency of a few months after diagnosis. a spectrum of immune dysregulation, from over-reaction to no reaction, i.e., immune ignorance, to under-reaction [29]. Importantly, many patients develop both cancer and autoimmunity, implying a link in the pathogenesis of these two diseases. This could occur if the immune system has a fundamental defect in its ability to recognize or clear cell debris, foreign or altered self-proteins, either on the cell surface or in circulation, as a result of a defective innate immune system or an interferon-regulated process, creating an abnormally high inflammatory environment [30].

Another mechanism is that the tumor-associated autoantigens, expressed de novo by the tumor cell, induce cell debris that becomes available to the immune system against which a cryptic T-cell response is boosted since the T-cells are tolerized to the neoantigen along with other antigens. This would result in an autoimmune response against normal tissue expressing the same antigen [31], This aspect has been called "molecular mimicry." The autoimmune response is then evolutionarily

harnessed by the cancer to promote cell growth, activation, and proliferation. Thus, one does not exclude the other, resulting in a so-called integrated model. A robust and growing literature shows that patients with autoimmune disease have an increased risk of developing cancer. This relationship has been seen with many common autoimmune diseases. Autoimmune diseases have also been detected in lung cancer as an immune-related adverse event: in particular, patients with high lung cancer treated were noted to have cryptogenic organizing pneumonia and hepatitis, and more generally, transaminase increases leading to treatment cessation with steroids, and development of myasthenia gravis, hypophysitis, and aplastic anemia [32]. Taken together, these data support the concept of the immune system being dysregulated and promoting autoimmunity at the same time as failing to fully control the growth and dissemination of the cancer. During sepsis, there is a condition similar to the development of some bacterial infections; this is frequently associated with a marked increase in bacteria in portal circulation of the gut leading to granulomatous hepatitis. The relationship between inflammation, cancer, and autoimmunity is intertwined, and the regulation of immune function integrates these complex relationships. It is likely that the same immune cells are involved in both conditions [33].

4. Clinical Implications

Under this aspect, immune dysregulation at the single tissue level, such as lung, liver, or skin, is diagnostically useful for the assessment of a series of diseases ranging from cancer to chronic infections and autoimmunity. The tissue imprint is unique and holds a wealth of information on immune cells and inflammation. Biomarkers can be used to predict risk or disease fate. A combination of biomarkers in an organ may improve the assessment of the complex associated changes, thus offering a real-life blood biopsy. Among the main diagnostic blood markers related largely to immune dysregulation, thereby permitted in use in the clinic, one can list ceramides, IL-6, TNFα, and probably also tissue enzyme outlets [34].

The new methods to localize active immune cells in organs provide the possibility of testing for tissue immune reactivity. Hence, the combination of tissue immune dysregulation, such as transcriptomics and related fields for cancer, with blood-based tests and imaging technologies provides the possibility not of a classical personalized medicine approach but the selection of a specific therapy or approach and its individualized optimization [35]. Importantly, treatment with cortisone and related agents can reverse the changes in IFN and immunometabolism, such as lipid synthesis. Overall, therapy of tissue immune imbalances is at an early stage. Many non-pharmacological and so-called lifestyle and diet-related factors can lead to

tissue immune imbalance, such as stem cell implantation, functional foods, performing therapies, or environmental and life exposures [36].
The degree to which tissue immune imbalance can be reversed is poorly assessed. The immune-directed drugs are not only used in indications such as cancer to increase immunity or replace functional T cells. Drugs used for the opposite indication include anti-cytokine agents, immune regulatory antibodies, and cortisone. Their use is still partly empirical, and much remains to be discovered concerning exactly when and how to intervene in humans with systemic therapies to reverse the effect of tissue inflammation, resulting in predictive approaches beyond the trial. An integration into current medical practice remains to be developed, as well as the technique to reverse immune imbalance at the systemic level [37].

4.1 Diagnostic Markers

4.1.1 Biomarkers of Tissue

Immune RNA Response Recently, accumulating evidence has shown RNA signatures characterizing the immune response in tissue. These RNA signatures associate with immune response alterations occurring in several pathological conditions, like cancer or systemic diseases. Some of these 'diagnostic markers' or 'biomarkers' are used in clinical practice to improve patient assessment, drug-based therapy, surgical decisions, monitor response to chemotherapy, and study the evolution of a clinical disease. Some RNA markers have great value as neoantigens that can be harnessed for personalized cancer vaccines. Most immune biomarkers can be used in multiplex, and specific RNA signatures can lead to changes in therapy [38].
Other tissue markers will also be worth further exploration in the future. Some characteristics of these immune diagnostic markers are summarized below. In this review, several RNA signatures are provided that deal with tissue microenvironment immune biomarkers and their implications in the setting of cancer and systemic diseases. Most of the tissue biomarkers are organ-specific for cancer and infection and disease-specific in autoimmune diseases and share common immune-related alterations in the tissue. It is noteworthy that some components of the peripheral blood, like the myeloid compartment, have a tissue expression counterpart [39].
Most of the available markers can be used to prioritize the inclusion of a patient in a trial, as well as to figure out general prognosis, but they are still being evaluated for other clinical aspects. Finally, To offer basic scientific insights into this field, we also gathered evidence that supports the fundamental research of the main technical approaches to biomarker discovery in whole tissue sections [40].

4.2. Therapeutic Strategies

As immune dysregulation takes center stage in both cancer and systemic diseases, the principal therapeutic strategies share a common platform: the restoration of immune physiology. In these strategies, the retargeting of immunologic components to favor a full immune restoration is required, functioning as suppressors and modulators of pathological translations [41].

In present day, the arsenal of immune system targets is quite broad as immunomodulatory agents have emerged for implementation. There are immuno-specific antibodies already available for use as immune enhancers with low multi-organ toxicities and as cellular therapies, focused on immune system reconstitution through the provision of engineered immune cells. The innate need for restoration of immune signaling in both cancer and systemic diseases, with immune antiviral and antibacterial protection, means that these therapeutic approaches are, or may emerge as, pan-immune physiology engagers [42].

The administration of targets for immune tolerance is an important advancement in cancer therapy. Although not astounding, the therapeutic results obtained through inhibition of immune checkpoint targets with monoclonal antibodies in tumors are quite relevant. This therapeutic strategy has registered noteworthy efficacy in melanoma, renal cancer, non-small cell prostate cancer, and Hodgkin lymphoma, giving rise to a new series of immune-oncological drug [43].

Of particular interest are molecules responsible for fine-tuning the immune response, as the invasion of immune-competent cells into brain parenchyma, especially in brain cancer, is a challenging goal to accomplish. The development of customized immunotherapeutic strategies for individuals or specific groups is relevant because both systemic diseases and tumors require these therapeutic interventions to be adaptive to a given functionality of immune dysregulation, in situ, and also during the sub-phases of the disease. In addition, the execution of immune physiology signal interference in tissues affected by unbalanced immunity is a challenge taken into consideration when one tries to design physiological restoration [44, 45].

5. Conclusion and Future Directions

We included many examples of immune dysregulation causing cancer and systemic diseases in this review. Many of the known manifestations of tissue immune dysregulation, from inhibitory molecule expression to cytokine production, have been found in tumors and surrounding tissues. Some mechanisms of immune dysregulation affect immune function pleiotropically, but many others are organ- or tissue-specific and may require individual interventions. These processes' basic

biology and key players' interconnected relationships need further study. Redundancy and multifactorial causation add complexity.

We have identified several critical research gaps or understudied phenomena that should be investigated as field priorities. Finally, and most excitingly, many of the immune dysregulation features discussed here are targets of successful therapeutic modalities or promising targets for novel drug discovery. In conclusion, tissue immune dysregulation is only beginning to be appreciated, but there is a strong rationale for its cohesive exploration on all fronts and even for prioritizing immune dysregulation over specific biological details on a case-by-case basis. By conducting truly multidisciplinary and collaborative research, we envision dramatically improved patient outcomes, a drastically reduced global burden of such diseases, and a remarkable step toward understanding human systems-level immunobiology.

6. Acknowledgments

The authors would like to thank Mustansiriyah university (www.uomustansiriyah.edu. iq) Baghdad -Iraq for support in the present work.

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دور الخلل المناعي للأنسجة في السرطان والأمراض الجهازية

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المستخلص: يُعدّ التوازن المناعي للأنسجة ضروريًا للوقاية من الالتهابات المرضية والحفاظ على سلامة الأعضاء. ومع ذلك، عندما يتعطل التنظيم المناعي على مستوى الأنسجة، فقد يُحفّز ذلك أو يُفاقم مجموعة واسعة من الأمراض، بما في ذلك السرطان والاضطرابات الالتهابية الجهازية. تتناول هذه المراجعة الفيزيولوجيا المرضية لاضطرابات المناعة الذاتية والاضطرابات الجهازية المزمنة، بالإضافة إلى الفهم الناشئ لكيفية مساهمة اختلال التنظيم المناعي الخاص بالأنسجة في تكوّن الأورام، وتطور الورم، والنقائل. تُشكّل التفاعلات غير الوظيفية بين الخلايا المناعية المقيمة في الأنسجة، ومكونات النسيج الضام، وشبكات السيتوكين، والبيئة المحلية المحيطة، جوهر هذا الاختلال. ويُعدّ فشل التحمّل المناعي، والالتهاب المزمن منخفض الدرجة، والتنشيط الشاذ لنقاط التفتيش المناعية آلياتٍ حاسمة. بالإضافة إلى ذلك، يُؤكد دور المنافذ المناعية الخاصة بالأنسجة في تشكيل نتائج المرض على الحاجة إلى مناهج علاجية موضعية. إن فهم الأساس الجزيئي والخلوي لاضطراب المناعة في الأنسجة يفتح آفاقًا جديدة في العلاجات المناعية المستهدفة والطب الدقيق للأمراض الخبيثة وغير الخبيثة.

الكلمات المفتاحية: الأنسجة، الخلل المناعي، السرطان، الأمراض الجهازية.

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