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Autoimmune disorders: Mechanisms, diagnosis, and the future of therapeutic approaches-review article for healthcare staff about autoantibodies

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***Abstract*---Background:** Autoimmune disorders, characterized by the presence of autoantibodies, play a critical role in disease pathogenesis through their interaction with self-antigens. These immunoglobulins can induce inflammation and tissue damage by mediating immune responses against the body's own cells. **Aim:** This review aims to provide a comprehensive overview of functional autoantibodies, focusing on their mechanisms of action, origins, and implications in both autoimmune and non-autoimmune conditions. **Methods:** The review synthesizes findings from recent literature regarding the classification of functional autoantibodies based on their pathogenic mechanisms, including receptor activation, blockade, and neutralization. It also examines the role of tumors, infections, and immunodeficiency in the generation of these autoantibodies. **Results:** Functional autoantibodies can activate or inhibit receptors, induce receptor internalization, and disrupt protein interactions, contributing to various autoimmune diseases such as Graves' disease and myasthenia gravis. Emerging evidence links functional autoantibodies to non-autoimmune conditions, particularly in the context of

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infections like COVID-19. **Conclusion:** A nuanced understanding of functional autoantibodies is essential for advancing diagnostic and therapeutic approaches in autoimmune disorders. Further research is warranted to elucidate their complex roles in health and disease.

***Keywords*---**Autoantibodies, autoimmune disorders, mechanisms, diagnosis, therapeutic approaches.

Introduction

Autoantibodies are characterized as immunoglobulins that interact with self-antigens. As a pivotal element of humoral autoimmunity, they significantly contribute to the pathogenesis of autoimmune diseases. Like all antibodies, their fundamental structure comprises two heavy chains and two light chains, creating a 'Y'-shaped configuration. The arms of this 'Y'-shaped molecule encompass two identical antigen-binding (Fab) domains, while the stem is referred to as the fragment crystallizable (Fc) region, which is essential for the activation of the complement system and immune cells [1]. Traditionally, autoantibodies engage with autoantigens through the Fab domains and orchestrate immune responses via the Fc domain, resulting in inflammation and damage to target tissues. In contrast, a second category of autoantibodies can induce pathogenic conditions exclusively through binding and interaction with target antigens via Fab domains. This alternative category has been designated as functional autoantibodies [2]. The initial evidence for functional autoantibodies dates back to 1955, when Adams discovered that sera from patients with Graves' disease contained a long-acting thyroid stimulator (LATS) [3]. In 1964, research by Meek and colleagues indicated that LATS is a gamma immunoglobulin (IgG) and that the Fab domain is responsible for binding to and activating the thyroid-stimulating hormone receptor (TSHR) [4]. Subsequent investigations have shown that LATS represents IgG autoantibodies directed against TSHR, exhibiting an agonistic effect [5, 6]. Since this finding, the roster of functional autoantibodies has consistently grown.

Despite a burgeoning corpus of evidence supporting the existence of functional autoantibodies, a precise definition of this type remains elusive. Current literature often characterizes functional autoantibodies as those demonstrating either agonistic or antagonistic effects [2, 7, 8], primarily due to the prevalence of their autoantigens being receptors on the plasma membrane. However, functional autoantibodies can also interact with additional extracellular molecules. For instance, a recent investigation revealed that patients with coronavirus disease 2019 (COVID-19) exhibit a high prevalence of functional autoantibodies targeting immunomodulatory proteins, including cytokines, chemokines, complement components, and cell-surface proteins [9]. Consequently, a more accurate definition of functional autoantibodies would be antibodies that can induce a dysregulated function of autoantigens solely by binding to and interfering with the functions of target antigens via the Fab domain, without the involvement of any other humoral or cellular components of the immune system. In light of this revised definition, this review article aims to provide a comprehensive overview of functional autoantibodies, emphasizing their mechanisms of action, potential origins, and roles in both autoimmune and non-autoimmune disorders.

Mechanisms of Functional Autoantibodies

Functional autoantibodies can be classified into six categories based on their pathogenic mechanisms: activation of target receptors, blockade of target receptors, induction of receptor internalization, neutralization of target ligands, neutralization of other soluble extracellular antigens, and disruption of protein-protein interactions (Fig. 1).

Activation of Target Receptors

Unlike natural ligands, autoantibodies possess two identical antigen-binding sites, allowing them to crosslink target receptors. Additionally, stimulating autoantibodies have a prolonged half-life in circulation due to the interaction between the Fc domain and the neonatal Fc receptor [10]. This interaction can result in abnormal and sustained activation of the receptor. A prominent example is stimulating autoantibodies against the thyroid-stimulating hormone receptor (TSHR) [5]. Following the discovery of TSHR autoantibodies, other stimulating autoantibodies have been identified, including those against the β1-adrenergic receptor (β1-AR) [11] and angiotensin II receptor type 1 (AT1R) [12]. Notably, most known functional autoantibodies with agonistic effects target G-protein-coupled receptors (GPCRs) [13].

Induction of Receptor Internalization

In addition to activating receptors, the crosslinking of receptors by antibodies often induces internalization and subsequent degradation of the antibody-receptor complex, a phenomenon known as antigenic modulation. This process diminishes the expression of the target receptor on the cell surface, resulting in receptor hypofunction and disrupted cellular homeostasis. A prime example is autoantibodies targeting the acetylcholine receptor (AChR) [14]. One mechanism by which AChR autoantibodies impair neuromuscular transmission involves crosslinking AChRs on the postsynaptic muscle membrane, leading to their endocytosis and degradation [15].

Blockade of Target Receptors

In addition to facilitating receptor internalization, autoantibodies can act as antagonists by obstructing ligand binding to target receptors. For instance, autoantibodies against the GABAB receptor (GABABR), which is widely expressed in the nervous system and plays a crucial role in neuronal excitability, illustrate this mechanism [16]. The binding of autoantibodies to GABABR does not induce internalization but instead inhibits the receptor's function, leading to dysregulated neuronal activity [17, 18].

Neutralization of Target Ligands

Functional autoantibodies can also disrupt receptor signaling indirectly by neutralizing target ligands. This neutralization, a common mechanism among functional autoantibodies, has been observed in various autoantibodies,

particularly those against secreted immune molecules such as cytokines, chemokines, and complement components [9, 19].

Neutralization of Other Soluble Extracellular Antigens

Similar to the neutralization of receptor ligands, functional autoantibodies can target other soluble extracellular antigens. For example, the disintegrin and metalloprotease with thrombospondin type 1 repeats, number 13 (ADAMTS13), is a multidomain metalloprotease that modulates the von Willebrand factor (VWF) platelet-tethering function through proteolysis of the VWF A2 domain [20]. Autoantibodies against ADAMTS13 have been documented to inhibit its function and/or facilitate its clearance from circulation [21], resulting in a deficiency of active ADAMTS13 in the bloodstream.

Disruption of Protein-Protein Interactions

The final category of functional autoantibodies involves their binding to extracellular molecules, disrupting interactions with other molecular partners. A notable example in this category is autoantibodies directed against desmogleins (Dsgs). Desmogleins are transmembrane glycoproteins found in desmosomes, essential for epidermal cell-cell adhesion, a critical biological function for maintaining skin and mucosal integrity. Autoantibodies targeting Dsg3 and Dsg1 can interfere with the interactions among desmoglein molecules on keratinocyte surfaces, resulting in compromised cell-cell adhesion [22].

The Origin of Functional Autoantibodies

Under normal physiological conditions, the immune system effectively distinguishes between self and non-self entities, thereby maintaining immune tolerance. However, this tolerance may be compromised under specific circumstances, leading to the generation of autoreactive T cells and autoantibodies [23, 24, 25, 26]. Although the precise origins of functional autoantibodies remain partially elucidated, several potential triggers for their production have been proposed, including tumorigenesis, infections, and immune deficiencies.

Tumors

Tumors have been linked to various autoimmune disorders mediated by functional autoantibodies. For example, approximately 10–15% of individuals with myasthenia gravis (MG) present with thymomas, while 30–50% of thymoma patients develop MG, particularly those associated with autoantibodies against acetylcholine receptors (AChRs) [27]. Thymomas are neoplasms originating from thymic epithelial cells, surrounded by maturing T cells [28]. Notably, these neoplastic epithelial cells express epitopes of muscle antigens alongside MHC II molecules, potentially disrupting the thymic selection process and resulting in the generation of autoreactive T cells specific to skeletal muscle proteins, including AChRs [29, 30]. Once autoreactive T cells migrate to the periphery, they can activate B cells to produce functional autoantibodies against AChRs [31]. The production of functional autoantibodies triggered by tumors has also been

documented in autoimmune encephalitis [17, 32]. A prominent example is anti-N-methyl-d-aspartate receptor (NMDAR) encephalitis, a paraneoplastic autoimmune condition closely associated with ovarian teratoma [33]. As a tumor arising from pluripotent embryonic cells, ovarian teratomas contain various tissues, including epithelial, muscular, osseous, and nervous tissues. It has been proposed that antigens released from apoptotic tumor cells, particularly neural cells expressing NMDAR, are taken up and presented by antigen-presenting cells (APCs). This process activates NMDAR-specific T cells, leading to the subsequent production of anti-NMDAR autoantibodies [17].

Infections

Infections also serve as triggers for the production of functional autoantibodies. For instance, infection with SARS-CoV-2 has been linked to the generation of functional autoantibodies against various molecules, encompassing both immune-related proteins and tissue-associated antigens [9]. Two primary mechanisms have been proposed for infection-induced production of functional autoantibodies. First, infections can result in cell or tissue destruction, releasing antigens that are typically concealed from the immune system. A pertinent example is the herpes simplex virus (HSV), which can prompt the production of anti-NMDAR autoantibodies [34, 35]. Second, infectious pathogens may induce the production of functional autoantibodies through immune cross-reactivity between pathogen antigens and autoantigens, a phenomenon known as antigen mimicry. This mechanism has been suggested for the generation of autoantibodies against β1-adrenergic receptors in Chagas disease [36] and anti-TSHR antibodies in Graves' disease [37].

Immunodeficiency

Autoimmune polyendocrinopathy with candidiasis and ectodermal dystrophy (APECED), also referred to as autoimmune polyendocrine syndrome type I (APS-I), represents a rare autosomal recessive primary immunodeficiency that arises from mutations in the autoimmune regulator gene AIRE [38]. APECED is characterized by a range of autoimmune endocrinopathies, hypoparathyroidism, and the production of pathogenic autoantibodies. In APECED patients, the repertoire of autoantibodies predominantly targets two specific categories of antigens: those expressed in thymic medullary epithelial cells and those found in lymphoid cells [39]. Notably, all individuals affected by APECED produce neutralizing autoantibodies against certain type I interferons, including IFNα and IFNω [40, 41]. Additionally, some APECED patients, particularly those with chronic mucocutaneous candidiasis (CMC), generate neutralizing antibodies against IL-17 cytokines, such as IL-17A, IL-17F, and IL-22 [41, 42]. Despite being a rare condition, APECED serves as a significant illustration of how dysregulation within the immune system can precipitate the production of functional autoantibodies, particularly against cytokines.

Contribution of Functional Autoantibodies to Human Diseases

Functional autoantibodies at low levels are present in healthy individuals, indicating their potential role in maintaining physiological conditions [43].

However, high-affinity functional autoantibodies are linked to various pathological states, encompassing both autoimmune diseases and non-autoimmune disorders. In autoimmune disorders, various diseases are associated with specific autoantigens and mechanisms. For example, autoimmune thyroid diseases involve autoantibodies against the thyroid-stimulating hormone receptor (TSHR) that can either activate or block target receptors, primarily belonging to the IgG1 and IgG4 subclasses [4, 46, 47][48, 49]. Myasthenia gravis features autoantibodies against the acetylcholine receptor (AChR) that induce receptor internalization and blockade, with IgG1 and IgG3 subclasses playing significant roles [15, 54]. Other examples include autoantibodies against lipoprotein receptor-related protein 4 (LRP4), which also mediate receptor internalization [57, 58], and against muscle-specific kinase (MuSK), which disrupts protein-protein interactions, typically in the IgG4 subclass [59].

In the context of autoimmune encephalitis, autoantibodies target various receptors, such as the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR), which mediates receptor internalization [75, 76], and the GABA_B receptor (GABABR), which blocks target receptors [16]. Other notable targets include D2 dopamine receptors, GABA_A receptors, and N-methyl-D-aspartate receptors (NMDARs), which can induce receptor internalization and disrupt protein-protein interactions [72, 73, 74]. In conditions such as pemphigus, autoantibodies against desmogleins (Dsg1 and Dsg3) disrupt protein-protein interactions [89, 90]. Acquired thrombotic thrombocytopenic purpura (TTP) involves autoantibodies against ADAMTS13 that neutralize other extracellular antigens [21, 95]. Furthermore, in idiopathic dilated cardiomyopathy (DCM), autoantibodies against the β1-adrenergic receptor activate target receptors [99, 100]. Systemic sclerosis features autoantibodies against the platelet-derived growth factor receptor (PDGFR), angiotensin II receptor type 1 (AT1R), and endothelin receptor type A (ETAR), all of which activate their respective target receptors [104, 105, 106, 107, 108, 109, 110].

In various diseases, functional autoantibodies target specific autoantigens through distinct mechanisms. For instance, in allograft rejection, autoantibodies against the angiotensin II receptor type 1 (AT1R) activate target receptors [12]. In chronic mucocutaneous candidiasis (CMC), the neutralization of target ligands occurs through autoantibodies against IL-17A, IL-17F, and IL-22, highlighting a shared mechanism in this condition [41, 42, 113]. During COVID-19, autoantibodies targeting interferon-ω (IFN-ω) and interferon-α (IFN-α) also neutralize these ligands, potentially impacting immune response [115, 116, 117]. Additionally, the interferon alpha/beta receptor (IFNAR) is blocked by specific autoantibodies, impairing signaling pathways [9]. Other neutralizing interactions in this context include autoantibodies against IL-18 and the hypocretin receptor 2 (HCRTR2), both of which block target receptors [9]. In cases of influenza pneumonia, similar neutralization occurs with autoantibodies against IFN-ω and IFN-α, further illustrating the role of these ligands in immune response modulation [118]. Furthermore, in asthma, autoantibodies against the β2-adrenergic receptor (β2-AR) and MACRO also block target receptors, while IL-17F is neutralized as well, emphasizing the diverse mechanisms through which autoantibodies can contribute to disease pathology [122, 125, 126].

Functional Autoantibodies in Autoimmune Diseases

Autoimmune thyroid diseases encompass two principal disorders: Graves' disease and Hashimoto's thyroiditis, which are characterized by hyperthyroidism and hypothyroidism, respectively [44]. Graves' disease, recognized as the first autoimmune disorder linked to functional autoantibodies, primarily affects the thyroid gland and stands as the leading cause of hyperthyroidism in developed nations [45]. The hyperthyroidism in Graves' disease is driven by thyroid-stimulating hormone receptor (TSHR) antibodies, predominantly of the IgG1 and IgG4 subclasses, which stimulate the thyroid gland (thyroid-stimulating antibodies or TSAb) [4, 46, 47]. These functional TSAbs activate TSHR expressed on thyroid follicular cells in an unregulated manner, resulting in excessive thyroid hormone secretion and subsequent hyperthyroidism.

Conversely, blocking antibodies against thyrotropin (TBAb) have been identified in patients with both Hashimoto's thyroiditis and Graves' disease [48]. Monoclonal antibodies derived from hypothyroid patients suggest that TBAbs primarily belong to the IgG1 subclass [49]. Unlike TSAbs, TBAbs inhibit TSHR activation, leading to hypothyroidism [48]. Notably, a switch between TSAbs and TBAbs has been observed in patients with autoimmune thyroid diseases, facilitating transitions between hyperthyroidism and hypothyroidism [50, 51].

Myasthenia gravis (MG) is an autoimmune disorder affecting the neuromuscular junction, characterized by impaired signal transmission and resulting in fatigable muscle weakness [52]. Pathogenically, MG is linked to autoantibodies targeting postsynaptic components of the neuromuscular junction, such as the muscle acetylcholine receptor (AChR), muscle-specific kinase (MuSK), low-density lipoprotein receptor-related protein 4 (LRP4), and agrin [53]. Under normal conditions, agrin binds to LRP4, which subsequently binds and activates MuSK, facilitating AChR clustering. Acetylcholine released from axon terminals binds to these clustered receptors, translating neuronal action potentials into muscle contraction. Autoantibodies against AChR, MuSK, or LRP4 impair this transmission through multiple mechanisms. For instance, AChR autoantibodies, primarily of the IgG1 and IgG3 subclasses [54], can disrupt transmission via both Fc domain-dependent and Fc domain-independent mechanisms. The Fc domain of anti-AChR IgG can activate complement, causing localized damage to the postsynaptic membrane [55]. Alternatively, the Fab portion of these antibodies can lead to defective signal transmission by promoting AChR internalization [15] and obstructing acetylcholine binding [56]. Autoantibodies against LRP4, primarily of the IgG1 subclass [57, 58], can similarly interfere with neuromuscular transmission via both mechanisms. Notably, anti-LRP4 antibodies may induce LRP4 internalization [58]. In contrast, MuSK antibodies, which mainly belong to the IgG4 subclass and do not activate complement [59], inhibit MuSK's interactions with LRP4, thereby reducing AChR clustering [59].

Autoimmune autonomic ganglionopathy (AAG) is an acquired neurological condition marked by autonomic function failure [60]. In 2000, Vernino and colleagues reported that approximately 50% of patients with acute or subacute AAG present with elevated levels of autoantibodies that bind to ganglionic AChR (gnAChR) [61]. Experimental evidence indicates that immunization of rabbits with

a recombinant gnAChR α3 subunit fusion protein replicates clinical features of AAG [62]. Furthermore, mice receiving gnAChR-specific IgG exhibit impaired autonomic synaptic transmission and autonomic failure [63]. These observations confirm the pathogenic role of gnAChR autoantibodies in AAG, with suggested mechanisms involving reduced surface expression of gnAChR due to autoantibody binding [64].

Autoimmune pulmonary alveolar proteinosis (PAP) is a rare lung disorder characterized by impaired surfactant metabolism [65, 66]. First described by Rosen et al. in 1958, PAP involves the accumulation of proteinaceous material in the alveoli [67]. While PAP can be congenital or secondary, most cases are autoimmune in nature [65]. Pathologically, autoimmune PAP arises from autoantibodies against granulocyte-macrophage colony-stimulating factor (GM-CSF), a critical regulator of surfactant metabolism in alveolar macrophages [65]. Neutralizing autoantibodies, primarily of the IgG1 and IgG2 subclasses [68], disrupt GM-CSF signaling, leading to alveolar macrophage dysfunction and subsequent surfactant accumulation in the lungs [65, 66].

Pure red cell aplasia (PRCA) refers to a type of aplastic anemia affecting red blood cell precursors [69]. Unlike the inherited variant, acquired PRCA is an autoimmune disorder primarily driven by autoantibodies that inhibit erythroid differentiation [69]. Consequently, patients with acquired PRCA experience a reduction or absence of erythroid precursors. In 1996, Casadevall and colleagues identified erythropoietin as a pathogenic autoantigen in PRCA [70]. Mechanistically, autoantibodies against erythropoietin, primarily of the IgG1 and IgG4 subclasses, obstruct erythropoietin's binding to its receptor, thus impeding erythroid progenitor differentiation [70, 71].

Autoimmune encephalitis (AE) comprises a spectrum of autoimmune disorders affecting the central nervous system (CNS), characterized by limbic and extra-limbic dysfunction symptoms [17]. In 2007, Dalmau and colleagues identified N-methyl-D-aspartate receptor (NMDAR) as a pathogenic autoantigen associated with ovarian teratoma-related limbic encephalitis [33]. Autoantibodies against NMDAR, predominantly of the IgG1 subclass, induce receptor internalization and disrupt NMDAR-ephrin B2 interactions, thereby dysregulating synaptic function [72, 73, 74]. This discovery has prompted the identification of various autoantibodies targeting neuronal cell-surface proteins, ion channels, or receptors implicated in autoimmune encephalitis, including α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) [75, 76], contactin-associated protein-like 2 (CASPR2) [77, 78], dopamine 2 receptor (D2R) [79, 80], dipeptidyl-peptidase-like protein 6 (DPPX) [81, 82], GABA type A receptor (GABAAR) [83], GABA type B receptor (GABABR) [16], Ig-like cell adhesion molecule 5 (IgLON5) [84, 85], leucine-rich glioma-inactivated 1 (LGI1) [77], metabotropic glutamate receptor 5 (mGluR5) [86], and neurexin-3α [87]. Despite the severity of neuropsychiatric symptoms associated with autoimmune encephalitis, timely diagnosis and treatment often result in significant recovery. The favorable prognosis is attributed to the mechanisms underlying antibody-mediated autonomic dysfunction, where autoantibodies primarily reduce the density of surface molecules [72, 74, 80, 82, 85, 87], block target receptors [16, 78], or disrupt protein-protein interactions [73, 77], rather than causing irreversible

neuronal damage. Thus, effective therapies that eliminate these autoantibodies facilitate patient recovery.

Pemphigus Pemphigus is a rare autoimmune disorder characterized by blisters on the skin and mucous membranes, primarily caused by autoantibodies against desmoglein 1 and/or 3. These autoantibodies, predominantly of the IgG4 subclass, disrupt keratinocyte adhesion by interfering with desmoglein interactions, leading to blister formation. Both monovalent Fab and divalent F(ab)2 fragments of these autoantibodies can mediate the pathogenic effects.

Acquired Thrombotic Thrombocytopenic Purpura (TTP) TTP is a thrombotic microangiopathic disorder marked by microangiopathic hemolytic anemia, severe thrombocytopenia, and ischemic end-organ injury. It arises from a deficiency in von Willebrand factor-cleaving protease (ADAMTS13). Acquired TTP involves autoantibodies against ADAMTS13, primarily of the IgG4 subclass, which inhibit its function or lead to its depletion, resulting in VWF-rich microthrombi formation.

Idiopathic Dilated Cardiomyopathy (DCM) Idiopathic DCM is characterized by left ventricular dilation and impaired contraction, with autoimmunity playing a significant role in many cases. Autoantibodies against cardiac-specific antigens, such as α-myosin and β1-adrenergic receptor (β1-AR), have been implicated. Notably, β1-AR autoantibodies can inhibit receptor binding, leading to cardiomyocyte dysfunction and cell death, acting as sustained agonists.

Systemic Sclerosis (SSc) SSc is a rheumatic disease affecting multiple organs, characterized by chronic inflammation and fibrosis. Autoantibodies against PDGFR, AT1R, and endothelin A type receptor (ETAR) have been identified, with some shown to have functional effects. For instance, PDGFR antibodies stimulate collagen gene expression in fibroblasts, while anti-AT1R and anti-ETAR antibodies can activate their respective receptors, contributing to tissue inflammation and complications in SSc.

Other Autoimmune Conditions Additionally, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and Sjögren's syndrome have been associated with functional autoantibodies against β2-AR and M3 acetylcholine receptors, respectively. However, further validation is needed to establish their pathogenic roles.

Conclusion

Functional autoantibodies have emerged as pivotal players in the landscape of autoimmune and non-autoimmune diseases, reflecting the immune system's dual capacity for self-recognition and aberrant targeting of its components. Their classification into categories based on distinct mechanisms—such as activation, blockade, and neutralization of target receptors—provides a framework for understanding their diverse impacts on cellular function and disease pathology. In autoimmune disorders, the presence of functional autoantibodies is frequently linked to the dysregulation of immune tolerance, leading to conditions such as Graves' disease and myasthenia gravis. In Graves' disease, thyroid-stimulating

hormone receptor antibodies (TSAbs) can cause unregulated stimulation of the thyroid gland, resulting in hyperthyroidism. Conversely, blocking antibodies can inhibit receptor activity, leading to hypothyroidism, illustrating the dynamic interplay of agonistic and antagonistic effects within autoimmune pathology. Myasthenia gravis further exemplifies the consequences of autoantibody-mediated disruption at the neuromuscular junction, where impaired signal transmission manifests as debilitating muscle weakness. Additionally, recent studies indicate that functional autoantibodies can arise in response to infections, such as SARS-CoV-2, suggesting a broader role in immune dysregulation beyond traditional autoimmune frameworks. These findings raise important questions regarding the diagnostic potential and therapeutic targeting of autoantibodies in a range of conditions, highlighting the need for tailored interventions that consider individual patient profiles. The evolving understanding of functional autoantibodies underscores their significance not only in disease pathogenesis but also in shaping future therapeutic strategies. By elucidating the complex relationships between autoantibodies, disease mechanisms, and patient outcomes, healthcare professionals can enhance diagnostic precision and develop innovative treatment modalities that address the multifaceted nature of autoimmune disorders. Continued research into the origins, mechanisms, and therapeutic implications of functional autoantibodies will be vital in improving patient care and advancing the field of immunology.

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اضطرابات المناعة الذاتية: الآليات، التشخيص، ومستقبل الأساليب العلاجية - مقال مراجعة للكوادر الصحية حول الأجسام المضادة الذاتية

الملخص:

الخلفية :تلعب الاضطرابات المناعية الذاتية، التي تتميز بوجود الأجسام المضادة الذاتية، دورًا حاسمًا في مسببات الأمراض من خلال تفاعلها مع المستضدات الذاتية. يمكن أن تتسبب هذه الأجسام المناعية في حدوث التهاب وتلف الأنسجة من خلال تحفيز استجابات مناعية ضد خلايا الجسم نفسها.

الهدف :تهدف هذه المراجعة إلى تقديم نظرة شاملة حول الأجسام المضادة الذاتية الوظيفية، مع التركيز على آليات عملها وأصولها وآثارها في كل من الحالات المناعية الذاتية وغير المناعية.

الطرق :تقوم المراجعة بتجميع النتائج من الأدبيات الحديثة بشأن تصنيف الأجسام المضادة الذاتية الوظيفية بناءً على آلياتها المسببة للمرض، بما في ذلك تنشيط المستقبلات، الحجب، والحياد. كما تتناول دور الأورام، العدوى، ونقص المناعة في توليد هذه الأجسام المضادة الذاتية.

النتائج :يمكن أن تنشط الأجسام المضادة الذاتية الوظيفية أو تثبط المستقبلات، وتؤدي إلى إدخال المستقبلات داخليًا، وتعطل تفاعلات البروتين، مما يساهم في مجموعة متنوعة من الأمراض المناعية الذاتية مثل مرض غريفز والوهن العضلي الوبيل. تشير الأدلة الناشئة إلى ارتباط الأجسام المضادة الذاتية الوظيفية بحالات غير مناعية، خاصة في سياق العدوى مثل COVID-19.

الخلاصة :يعد الفهم المتعمق للأجسام المضادة الذاتية الوظيفية ضروريًا لتقدم الأساليب التشخيصية والعلاجية في الاضطرابات المناعية الذاتية. هناك حاجة لمزيد من البحث لتوضيح أدوارها المعقدة في الصحة والمرض.

الكلمات المفتاحية :الأجسام المضادة الذاتية، الاضطرابات المناعية الذاتية، الآليات، التشخيص، الأساليب العلاجية.