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Review Article

The Interplay Between Immune Cells, Inflammation, and the Thyroid Gland

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Abstract

Background; The thyroid is a crucial endocrine organ, and its dysfunction can cause various disorders. Autoimmune conditions like Hashimoto's thyroiditis and Graves' disease are the most prevalent. Current studies show that immune activity and inflammation are central to thyroid pathology. Yet, the detailed processes linking immune cells, inflammatory mediators, and thyroid tissue remain incompletely clarified. Thus, examining thyroid structure and function, analyzing immune-related injury pathways, and synthesizing recent progress are valuable for clarifying autoimmune pathology and advancing targeted therapies.. Methods; This work evaluates existing academic literature and research reports. It addresses thyroid anatomy and physiology, the involvement of immune cells in thyroid disorders, inflammatory mechanisms in thyroid damage, and the interplay between immune activity and thyroid function. By combining fundamental and clinical evidence, it explores the connection between immunity and thyroid pathology. Results; Findings indicate that immune cells and inflammation are pivotal in thyroid disease development, especially in Hashimoto's thyroiditis and Graves' disease. The review outlines immune-mediated damage to thyroid tissue, noting the roles of genetic susceptibility, environmental factors, and immune imbalance in initiating and worsening autoimmunity. Additionally, recent investigations have uncovered possible immune- and inflammation-related treatment targets, supporting personalized therapeutic approaches. Conclusions; In summary, immune mechanisms and inflammation are fundamental in thyroid disorders. Deeper insight into these processes aids therapy development. Analyzing interactions between immune responses and thyroid pathology helps refine clinical care and direct new treatment research. Moving forward, cooperation among clinicians, scientists, and health policymakers should be enhanced. Integrating established and emerging interventions can improve comprehensive thyroid disease management, benefiting patients and meeting unresolved healthcare demands.

Keywords

Thyroid Gland, Immune Cells, Inflammation, Hashimoto's Thyroiditis, Graves' Disease, Pathogenesis

1. Introduction

1.1. The Importance of the Thyroid Gland and Its Functions

The thyroid is an essential endocrine organ, key to regulating metabolism, growth, and development [1]. Contemporary research advances have introduced new methodologies for examining thyroid structure and function at cellular and molecular scales [2]. For instance, sophisticated imaging approaches like ultrasound and magnetic resonance imaging

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now allow for more precise disease diagnosis and tracking [3]. Additionally, molecular biology methods, including polymerase chain reaction and gene expression analysis, have enhanced insights into the genetic and molecular foundations of thyroid disorders [4]. Collectively, these developments have deepened comprehension of thyroid biology and its operations, facilitating improved diagnostic and therapeutic strategies for related conditions.

1.2. The Role of Immune Cells and Inflammation in Thyroid Diseases

Emerging findings in thyroid research have illuminated the involvement of immune cells and inflammatory pathways in the onset and advancement of thyroid conditions [5]. Investigations indicate that diverse immune cells—such as T and B lymphocytes, natural killer cells, and macrophages—contribute significantly to autoimmune thyroid disorders like Hashimoto's thyroiditis and Graves' disease [6]. Moreover, recent work underscores how inflammatory processes can drive thyroid tissue damage and disease progression [7]. Techniques like flow cytometry [8]—which characterizes immune cell subsets via surface markers [9]—and immunohistochemistry, used to visualize cytokine and chemokine expression within thyroid tissue [10], have been instrumental in these discoveries. Together, these developments deepen insight into immune and inflammatory pathways in thyroid pathology, revealing new prospects for targeted therapeutic interventions.

2. Subjects and Methods

This analysis synthesizes a broad selection of academic publications and empirical studies to examine the interplay among immune cells, inflammatory processes, and the thyroid. Principal topics encompass thyroid structure and function, the participation of distinct immune cell types in thyroid pathology, the molecular pathways of inflammation in thyroid disorders, and the complex bidirectional relationships between immune activity and thyroid physiology.

3. Results

3.1. Anatomy and Physiology of the Thyroid Gland

Contemporary advances in thyroid research have enhanced comprehension of its structure and function [11-14]. Located in the neck, this butterfly-shaped gland generates thyroxine (T4) and triiodothyronine (T3), hormones essential for regulating metabolism, growth, and development [15]. It consists of two lobes linked by an isthmus, supported by an extensive vascular and lymphatic network [16]. The gland's functional units, thyroid follicles, are lined with follicular cells responsible for producing and storing hormones as thyroglobulin [17]. Hormone synthesis and release are controlled by the hypothalamic-pituitary-thyroid (HPT) axis, a feedback system integrating hypothalamic, pituitary, and thyroid signaling [18]. These refined insights into thyroid biology establish a basis for innovating diagnostic and therapeutic approaches for thyroid disorders.

3.2. Regulation of Thyroid Hormone Synthesis and Secretion

Modern investigations into thyroid function have elucidated the detailed regulatory processes controlling hormone synthesis and release [19]. Within thyroid follicles, hormone production involves iodinating tyrosine residues within thyroglobulin, followed by coupling these iodinated molecules to generate T4 and T3 [20]. Hormone entry into circulation is precisely modulated by the hypothalamic-pituitary-thyroid (HPT) axis, comprising the hypothalamus, pituitary, and thyroid glands [21]. Hypothalamic thyrotropin-releasing hormone (TRH) prompts pituitary secretion of thyroid-stimulating hormone (TSH), which subsequently activates thyroid hormone production and release from the gland [22]. Improved assay methodologies, including radioimmunoassay and enzyme-linked immunosorbent assay (ELISA), now permit precise quantification of serum thyroid hormones and TSH, supporting enhanced disease diagnosis and management [23]. Furthermore, molecular approaches such as gene expression analysis and single-cell RNA sequencing have clarified the intricate gene networks governing thyroid hormone regulation [24]. These refined insights into hormonal control mechanisms are informing the creation of innovative thyroid therapies that specifically target these pathways.

3.3. Normal Thyroid Function and Its Role in the Body

Current studies in thyroid research have clarified the essential contribution of proper thyroid activity to systemic health [25]. Thyroid hormones are principal regulators of metabolism, growth, and development, and also influence physiological functions such as cardiac rhythm, thermoregulation, and digestive processes [26]. The hypothalamic-pituitary-thyroid (HPT) axis strictly controls thyroid function to maintain serum hormone concentrations within a precise physiological interval [18]. Innovations in non-invasive imaging, including thyroid ultrasound and scintigraphy, now facilitate assessment of gland dimensions and activity, aiding in the identification and surveillance of conditions like goiter and nodules [27]. Moreover, evidence indicates that even subtle, subclinical thyroid dysfunction can meaningfully affect health, with implications for cardiovascular status, cognitive performance, and skeletal integrity [28, 29]. These insights underscore the value of preserving thyroid wellness

and may guide future approaches to disease prevention and clinical management.

4. Discussion

4.1. The Immune System and Its Functions

Recent thyroid research has enhanced comprehension of the immune system and its specific roles in thyroid pathology [30]. The immune system constitutes an intricate network of cells, tissues, and organs that collaboratively protect the body from foreign agents [31]. It is broadly divided into two components: the innate immune system, which delivers rapid, generalized responses against diverse pathogens [32], and the adaptive immune system, which generates precise, long-lasting defenses with immunological memory [33]. Methodological progress, notably in flow cytometry and single-cell sequencing, now permits detailed identification and analysis of distinct immune cell subsets implicated in autoimmune thyroid conditions [34], such as T cells, B cells, natural killer cells, and macrophages. These developments have significantly advanced knowledge of immune-related disease mechanisms, creating opportunities for designing more precise treatments for thyroid disorders.

4.2. Types of Immune Cells and Their Role in Thyroid Diseases

Contemporary thyroid studies have clarified the significant involvement of distinct immune cell groups in the initiation and advancement of thyroid disorders [35]. In autoimmune conditions like Hashimoto's thyroiditis and Graves' disease, T and B lymphocytes, natural killer (NK) cells, and macrophages are key participants [36]. Specifically, T lymphocytes drive the autoimmune process by identifying and responding to thyroid-specific antigens [37], while B cells generate autoantibodies that target these antigens, promoting tissue damage [38]. NK cells and macrophages contribute via innate immune mechanisms, releasing cytokines and chemokines that can harm thyroid tissue [39]. Methodologies such as flow cytometry and immunohistochemistry have become instrumental in examining these immune cells within thyroid samples [40-42]. Flow cytometry permits rapid, quantitative assessment of cellular characteristics—like size, granularity, and surface marker expression—through fluorescent antibody labeling, enabling precise identification and enumeration of immune subsets [43, 44]. Immunohistochemistry uses enzyme-conjugated antibodies to detect antigen location in tissue sections, revealing the spatial distribution and organization of immune cells within the gland's structure [45, 46]. Together, these techniques have yielded critical insights into pathological mechanisms [47], such as T- and B-cell infiltration in autoimmune thyroiditis or tumor-associated macrophages in thyroid malignancies [48]. Clarifying such immune dynamics is essential for designing novel treatments and enhancing clinical outcomes [49]. Collectively, these advances support the development of targeted immunotherapies that aim to regulate specific immune populations involved in thyroid autoimmunity.

4.3. Immune-mediated Thyroid Diseases Such as Hashimoto's Thyroiditis and Graves' Disease

Recent studies have clarified the pathological mechanisms underlying immune-mediated thyroid disorders, including Hashimoto’s thyroiditis and Graves' disease [5]. Both conditions involve autoimmune aggression against the thyroid, leading to inflammatory tissue injury [37]. Hashimoto's thyroiditis, the predominant cause of hypothyroidism, features autoantibodies directed against thyroid-specific antigens, resulting in progressive gland destruction [50]. In contrast, Graves' disease, the most frequent cause of hyperthyroidism, is driven by autoantibodies targeting the thyroid-stimulating hormone receptor (TSHR), which induce excessive hormone production [51]. Modern molecular techniques, such as gene expression profiling and single-cell RNA sequencing, have enhanced understanding of the autoimmune processes involved in these diseases [52-54]. These methods help identify differentially expressed genes and pathways active in thyroid autoimmunity [55]. Single-cell RNA sequencing further allows characterization of distinct immune cell subsets and their transcriptional profiles within thyroid tissue, elucidating complex immune-thyroid cell interactions [56, 57]. Treatment strategies have evolved with the introduction of immunomodulatory agents. Immune checkpoint inhibitors, for instance, block inhibitory signals on T cells (e.g., PD-1/PD-L1 pathways), augmenting immune activity against pathogenic targets [58-60]. Concurrently, B cell-targeting therapies like Rituximab deplete CD20-positive B cells, reducing autoimmune activity in thyroid diseases [61, 62]. Combining such advanced therapies offers a more effective management approach, potentially improving clinical outcomes and patient well-being [63]. Together, these diagnostic and therapeutic advances create new opportunities for the precise diagnosis, treatment, and long-term management of immune-mediated thyroid conditions.

4.4. Definition and Types of Inflammation

Advancements in thyroid research have refined our comprehension of inflammation's contribution to thyroid pathology [5]. Inflammation represents a coordinated biological reaction to detrimental stimuli, such as infection or damage, designed to neutralize threats and promote tissue healing [64]. It is generally categorized into two forms: acute and chronic [65]. Acute inflammation is a swift, transient process marked by the recruitment of immune cells like neutrophils and macrophages to the affected site [66]. In contrast, chronic

inflammation is a prolonged state in which immune cells—including lymphocytes and macrophages—persist within tissues and release signaling molecules such as cytokines and chemokines [67]. In thyroid disorders, chronic inflammation is frequently observed and is believed to promote thyroid tissue destruction, contributing to conditions like Hashimoto's thyroiditis and Graves' disease [37]. Methodologies including immunohistochemistry and gene expression analysis have been employed to assess the localization and activity of inflammatory cells and mediators in thyroid samples [68], yielding deeper insight into inflammation's role in disease mechanisms [41]. These developments hold promise for guiding the creation of new treatment approaches aimed at modulating inflammatory pathways in thyroid illnesses.

4.5. Mechanisms of Inflammation in Thyroid Diseases

Recent developments in thyroid research have clarified the processes driving inflammation in thyroid disorders [30]. In autoimmune conditions like Hashimoto's thyroiditis and Graves' disease, immune targeting of the thyroid gland [69] leads to persistent inflammation and tissue damage [11]. This inflammatory process includes activation of T and B lymphocytes along with secretion of pro-inflammatory cytokines and chemokines [70]. These signaling molecules recruit and stimulate further immune cells, sustaining inflammation and advancing thyroid injury [71]. Modern analytical methods, including proteomics and transcriptomics, have enabled identification of particular cytokines and chemokines contributing to thyroid pathology [72]. Research has also uncovered genetic variations linked to higher autoimmune thyroid disease risk, many within genes governing immune regulation and inflammatory pathways [73]. Such progress has significantly enhanced knowledge of inflammatory mechanisms in thyroid illness [74], supporting the design of focused treatments that aim to modulate specific inflammatory mediators.

4.6. Effects of Inflammation on Thyroid Function and Structure

Current thyroid research emphasizes how inflammation affects thyroid function and architecture [75]. Persistent thyroid inflammation can cause tissue destruction, reducing hormone synthesis and release [76]. Inflammatory signals, including cytokines and chemokines, may additionally disrupt the hypothalamic-pituitary-thyroid (HPT) axis, disturbing hormonal regulation [77]. Chronic inflammation also promotes structural alterations like fibrosis and atrophy, further compromising thyroid activity [37]. Imaging methods such as ultrasound and magnetic resonance imaging help visualize these anatomical changes, while assays measuring thyroid hormones and autoantibodies evaluate functional impacts. Together, these advances support the development of new treatments aimed at restoring thyroid function and limiting further inflammatory damage.

4.7. Cross-talk Between Immune Cells and Thyroid Cells

Modern thyroid research has refined insights into the dynamic interplay among immune cells, inflammation, and thyroid tissue [78]. In autoimmune thyroid disorders, including Hashimoto's thyroiditis and Graves' disease [79], bidirectional communication between immune cells and thyroid cells significantly contributes to disease development [80]. Immune cells, notably T and B lymphocytes, identify and respond to thyroid-specific antigens [81], triggering tissue damage and the release of inflammatory signals [82]. Subsequently, these inflammatory mediators disrupt hypothalamic-pituitary-thyroid (HPT) axis regulation and hinder hormone production and secretion, further affecting thyroid function [83]. Innovative methodologies, such as co-culture systems, now enable detailed *in vitro* examination of immune–thyroid cell interactions [84], clarifying molecular pathways involved in autoimmune pathology [85]. These advances support the design of novel treatments aimed at modulating such interactions to prevent or manage autoimmune thyroid conditions.

4.8. Effects of Inflammation on Immune Cell Function and Behavior

Emerging research in thyroid science clarifies how inflammation influences immune cell activity and behavior [86]. While inflammation normally mobilizes immune cells to sites of injury or infection to clear pathogens and initiate healing [87], persistent inflammatory conditions can disrupt normal immune function [88]. Prolonged exposure to cytokines and chemokines, for instance, may cause immune cell exhaustion, reducing their capacity to mount protective responses [89]. Chronic inflammation also drives excessive immune cell accumulation in tissues [90], exacerbating damage and impairing function [91]. Analytical methods like flow cytometry and single-cell sequencing enable detailed profiling of immune cell subsets under chronic inflammatory states [92], revealing associated molecular pathways [93]. These insights can guide the creation of therapies designed to regulate immune cell activity in chronic inflammation, potentially improving treatment outcomes for autoimmune thyroid disorders and related inflammatory diseases.

4.9. The Role of Immune Cells and Inflammation in the Development and Progression of Thyroid Diseases

Current research underscores the central contribution of immune cells and inflammatory processes to the initiation and advancement of thyroid disorders [94]. In autoimmune forms

such as Hashimoto's thyroiditis and Graves' disease, immune targeting of the thyroid gland [69] results in persistent inflammation and progressive tissue damage [95]. Specific immune subsets—including T and B lymphocytes, natural killer cells, and macrophages—have been clearly implicated in these pathogenic processes [96]. Moreover, sustained inflammation can induce structural alterations in the thyroid and disrupt its function, further driving disease development [97]. Methods like immunohistochemistry and transcriptional profiling allow detailed examination of immune cell infiltration and inflammatory signals within thyroid samples [98], clarifying underlying disease mechanisms [41]. These insights create opportunities for designing more precise treatments that aim to regulate particular immune populations and inflammatory pathways involved in thyroid pathology, with the goal of improving clinical outcomes for affected patients.

5. Conclusion

In conclusion, recent progress in thyroid research has deepened our understanding of the thyroid gland, immune cells, inflammation, and their roles in thyroid diseases. Advances in techniques such as gene expression profiling, single-cell sequencing, and immunohistochemistry have provided insights into the molecular mechanisms underlying the pathogenesis of these conditions. The involvement of specific immune cell populations, inflammatory mediators, and structural changes in the thyroid gland has been established in autoimmune thyroid diseases such as Hashimoto's thyroiditis and Graves' disease. These findings have implications for future research, with a focus on identifying new therapeutic targets and developing more effective treatments for thyroid diseases. In addition, advances in our understanding of the interactions between immune cells, inflammation, and the thyroid gland have highlighted the potential for novel therapeutic interventions that modulate these interactions, with the aim of improving outcomes for patients with these conditions. Overall, recent progress in thyroid research holds significant promise for advancing our understanding of thyroid diseases and improving clinical management strategies for patients.

Abbreviations

HPT	Hypothalamic-Pituitary-Thyroid
TSHR	Thyroid-Stimulating Hormone Receptor
TRH	Hypothalamic Thyrotropin-Releasing Hormone
ELISA	Enzyme-Linked Immunosorbent Assay

Author Contributions

Zuqiang Huang is the sole author. The author read and approved the final manuscript.

Conflicts of Interest

The author declares no conflicts of interest.

References

[1] Flink EB. The thyroid gland. Environ Health Perspect. 1981; 38: 55-56. https://doi.org/10.1289/ehp.813855

[2] Abooshahab R, Gholami M, Sanoie M, Azizi F, Hedayati M. Advances in metabolomics of thyroid cancer diagnosis and metabolic regulation. Endocrine. 2019; 65(1): 1-14. https://doi.org/10.1007/s12020-019-01915-y

[3] Roseland ME, Dewaraja YK, Wong KK. Advanced imaging and theranostics in thyroid cancer. Curr Opin Endocrinol Diabetes Obes. 2022; 29(5): 456-465. https://doi.org/10.1097/MED.0000000000000760

[4] Li S, Han Y, Zhang Q, Li J, Weng L. Comprehensive molecular analyses of an autoimmune-related gene predictive model and immune infiltrations using machine learning methods in moyamoya disease. Front Mol Biosci. 2022; 9: 1366. https://doi.org/10.3389/fmolb.2022.1016789

[5] Murugan AK, Alzahrani AS. SARS-CoV-2: emerging role in the pathogenesis of various thyroid diseases. J Inflamm Res. 2021; 14: 6191-6221. https://doi.org/10.2147/JIR.S332705

[6] Luty J, Ruckemann-Dziurdzińska K, Witkowski JM, Bryl E. Immunological aspects of autoimmune thyroid disease–Complex interplay between cells and cytokines. Cytokine. 2019; 116: 128-133. https://doi.org/10.1016/j.cyto.2019.01.003

[7] Starchl C, Scherkl M, Amrein K. Celiac Disease and the Thyroid: Highlighting the Roles of Vitamin D and Iron. Nutrients. 2021; 13(6): 1755. https://doi.org/10.3390/nu13061755

[8] Li YY. B cells and tertiary lymphoid structures are associated with survival in papillary thyroid cancer. Thyroid. 2023; 33(1): 1-10. https://doi.org/10.1089/thy.2022.0432

[9] Rendeiro AF. Profiling of immune dysfunction in COVID-19 patients allows early prediction of disease progression. Nat Med. 2021; 27(4): 542-551. https://doi.org/10.1038/s41591-021-01342-5

[10] Zake T, Skuja S, Kalere I, Konrade I, Groma V. Upregulated tissue expression of T helper (Th) 17 pathogenic interleukin (IL)-23 and IL-1β in Hashimoto's thyroiditis but not in Graves' disease. Endocr J. 2019; 66(5): 423-430. https://doi.org/10.1507/endocrj.EJ18-0395

[11] Naguib R. Potential relationships between COVID-19 and the thyroid gland: an update. J Int Med Res. 2022; 50(3): 03000605221082898. https://doi.org/10.1177/03000605221082898

[12] Tewari D, Patni P, Bishayee A, Sah AN, Bishayee A. Natural products targeting the PI3K-Akt-mTOR signaling pathway in cancer: A novel therapeutic strategy. Semin Cancer Biol. 2022; 80: 1-17. https://doi.org/10.1016/j.semcancer.2020.02.001

[13] Bini F. Artificial intelligence in thyroid field—A comprehensive review. Cancers (Basel). 2021; 13(19): 4740. https://doi.org/10.3390/cancers13194740

[14] Cherella CE, Wassner AJ. Pediatric thyroid cancer: Recent developments. Best Pract Res Clin Endocrinol Metab. 2022; 36(6): 101715. https://doi.org/10.1016/j.beem.2022.101715

[15] Pande A, Anjankar A. A Narrative Review on the Effect of Maternal Hypothyroidism on Fetal Development. Cureus. 2023; 15(3): e36747. https://doi.org/10.7759/cureus.36747

[16] Ali NH, Majeed AA. Thyroid Hormone Concentration and Receptor. East Afr J Biol Sci. 2022; 14(2): 221-230.

[17] Zhang X. Defective Thyroglobulin: Cell Biology of Disease. Int J Mol Sci. 2022; 23(22): 13605. https://doi.org/10.3390/ijms232213605

[18] Hoermann R, Pekker MJ, Midgley JE, Dietrich JW. The role of supporting and disruptive mechanisms of FT3 homeostasis in regulating the hypothalamic–pituitary–thyroid axis. Adv Endocrinol Metab. 2023; 14: 20420188231158163. https://doi.org/10.1177/20420188231158163

[19] Ren B, Zhu Y. A new perspective on thyroid hormones: crosstalk with reproductive hormones in females. Int J Mol Sci. 2022; 23(5): 2708. https://doi.org/10.3390/ijms23052708

[20] Citterio CE, Targovnik HM, Arvan P. The role of thyroglobulin in thyroid hormonogenesis. Nat Rev Endocrinol. 2019; 15(6): 323-338. https://doi.org/10.1038/s41574-019-0184-8

[21] Mancino G, Miro C, Di Cicco E, Dentice M. Thyroid hormone action in epidermal development and homeostasis and its implications in the pathophysiology of the skin. J Endocrinol Invest. 2021; 44(8): 1571-1579. https://doi.org/10.1007/s40618-020-01492-2

[22] Mohammadi S, Dolatshahi M, Rahmani F. Shedding light on thyroid hormone disorders and Parkinson disease pathology: mechanisms and risk factors. J Endocrinol Invest. 2021; 44(1): 1-13. https://doi.org/10.1007/s40618-020-01314-5

[23] Khelifa L, Hu Y, Jiang N, Yetisen AK. Lateral flow assays for hormone detection. Lab Chip. 2022; 22(13): 2451-2475. https://doi.org/10.1039/D2LC00249B

[24] Yuan J. Genome of a giant isopod, Bathynomus jamesi, provides insights into body size evolution and adaptation to deep-sea environment. BMC Genomics. 2022; 23(1): 1-17. https://doi.org/10.1186/s12864-022-08682-7

[25] Mojadadi A, Au A, Salah W, Witting P, Ahmad G. Role for selenium in metabolic homeostasis and human reproduction. Nutrients. 2021; 13(9): 3256. https://doi.org/10.3390/nu13093256

[26] Mishra S. Physiological Response of Cattle to Climatic Stress. In: Impact of Climate Change on Livestock Health and Production. CRC Press; 2022: 61-68.

[27] Paz AAC, de Souza MA, Brock PW, Mercuri EGF. Finite element analysis to predict temperature distribution in the human neck with abnormal thyroid: A proof of concept. Comput Methods Programs Biomed. 2022; 227: 107234. https://doi.org/10.1016/j.cmpb.2022.107234

[28] Panagiotou G, Taylor PN, Rees DA, Okosieme OE. Late offspring effects of antenatal thyroid screening. Best Pract Res Clin Endocrinol Metab. 2022; 143: 16-29. https://doi.org/10.1016/j.beem.2022.101634

[29] Fahimfar N. Prevalence of osteosarcopenia and its association with cardiovascular risk factors in Iranian older people: Bushehr Elderly Health (BEH) Program. Calcif Tissue Int. 2020; 106(4): 364-370. https://doi.org/10.1007/s00223-019-00642-w

[30] Zhang Y. The emerging function and clinical significance of circRNAs in Thyroid Cancer and Autoimmune Thyroid Diseases. Front Immunol. 2021; 12: 1731. https://doi.org/10.3389/fimmu.2021.691016

[31] Alzeer J. Halalopathy: Stimulation of the Immune System Through Enrichment of Potential Energy. Int J Res Med Sci. 2022; 5(1): 1-5.

[32] Hira P. Overview of Immune System. In: An Interplay of Cellular and Molecular Components of Immunology. CRC Press; 2022: 1-26.

[33] Chumakov K. Old vaccines for new infections: Exploiting innate immunity to control COVID-19 and prevent future pandemics. Proc Natl Acad Sci U S A. 2021; 118(21): e2101718118. https://doi.org/10.1073/pnas.2101718118

[34] Bukhari S. Single-cell RNA sequencing reveals distinct T cell populations in immune-related adverse events of checkpoint inhibitors. Cell Rep Med. 2022; 3(1): 100868. https://doi.org/10.1016/j.xcrm.2022.100868

[35] Scoville DW, Kang HS, Jetten AM. Transcription factor GLIS3: Critical roles in thyroid hormone biosynthesis, hypothyroidism, pancreatic beta cells and diabetes. Pharmacol Ther. 2020; 215: 107632. https://doi.org/10.1016/j.pharmthera.2020.107632

[36] Agrawal S, Prakash S. Significance of KIR like natural killer cell receptors in autoimmune disorders. Clin Immunol. 2020; 216: 108449. https://doi.org/10.1016/j.clim.2020.108449

[37] Ralli M. Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. Autoimmun Rev. 2020; 19(6): 102649. https://doi.org/10.1016/j.autrev.2020.102649

[38] Zhang QY. Lymphocyte infiltration and thyrocyte destruction are driven by stromal and immune cell components in Hashimoto's thyroiditis. Front Endocrinol (Lausanne). 2022; 13: 775. https://doi.org/10.3389/fendo.2022.862925

[39] Mahajan P, Kulkarni A, Waghdhare S, Mahajan S, Subramanian S. Role of Natural Killer Cell in Health and Disease: A Review. J Clin Diagn Res. 2022; 16(4): LE01-LE05.

[40] Zhao J. Elevated Expression and Activation of GPR15 in Immune Cells in Graves' Disease. J Immunol Res. 2022; 2022: 1899. https://doi.org/10.1155/2022/5623551

[41] Taylor PN. New insights into the pathogenesis and nonsurgical management of Graves orbitopathy. Nat Rev Endocrinol. 2020; 16(2): 104-116. https://doi.org/10.1038/s41574-019-0305-4

[42] Lechner MG. Inhibition of IL-17A protects against thyroid immune-related adverse events while preserving checkpoint inhibitor antitumor efficacy. J Immunol. 2022; 209(4): 696-709. https://doi.org/10.4049/jimmunol.2100932

[43] Manohar SM, Shah P, Nair A. Flow cytometry: principles, applications and recent advances. Bioanalysis. 2021; 13(3): 181-198. https://doi.org/10.4155/bio-2020-0267

[44] Kinkhabwala A. MACSima imaging cyclic staining (MICS) technology reveals combinatorial target pairs for CAR T cell treatment of solid tumors. Sci Rep. 2022; 12(1): 1911. https://doi.org/10.1038/s41598-022-05841-4

[45] Rodig SJ. Cell staining. Cold Spring Harb Protoc. 2022; 2022(6): pdb.top099606. https://doi.org/10.1101/pdb.top099606

[46] Casado-Pelaez M, Bueno-Costa A, Esteller M. Single cell cancer epigenetics. Trends Cancer. 2022; 8(10): 820-838. https://doi.org/10.1016/j.trecan.2022.06.005

[47] Srivastava AK. Insights into interplay of immunopathophysiological events and molecular mechanistic cascades in psoriasis and its associated comorbidities. Autoimmun Rev. 2021; 20(8): 102614. https://doi.org/10.1016/j.autrev.2021.102614

[48] Pan J. Papillary thyroid carcinoma landscape and its immunological link with hashimoto thyroiditis at single-cell resolution. Front Immunol. 2021; 9: 758339. https://doi.org/10.3389/fimmu.2021.758339

[49] Zhang N. Novel therapeutic strategies: Targeting epithelial–mesenchymal transition in colorectal cancer. Cancer Treat Rev. 2021; 22: e358-e368. https://doi.org/10.1016/j.ctrv.2021.102314

[50] Jonklaas J. Infiltration of the thyroid gland by non-thyroid malignancy: A literature review reveals this to be an unusual cause of hyperthyroidism. J Clin Transl Endocrinol. 2020; 20: 100221. https://doi.org/10.1016/j.jcte.2020.100221

[51] Tozzoli R, Bizzaro N. TSH receptor autoantibodies in Graves' disease. In: Translational Autoimmunity. Elsevier; 2022: 69-82. https://doi.org/10.1016/B978-0-12-824466-1.00015-5

[52] Zhao M. The application of single-cell RNA sequencing in studies of autoimmune diseases: a comprehensive review. Clin Rev Allergy Immunol. 2021; 60(1): 68-86. https://doi.org/10.1007/s12016-020-08822-5

[53] Zheng L. Advanced materials for management of immune-related adverse events induced by immune checkpoint inhibitors. Adv Drug Deliv Rev. 2022; 189: 110738. https://doi.org/10.1016/j.addr.2022.114504

[54] Horeth E. Transcriptomic and single-cell analysis reveals regulatory networks and cellular heterogeneity in mouse primary sjögren's syndrome salivary glands. Front Immunol. 2021; 12: 729040. https://doi.org/10.3389/fimmu.2021.729040

[55] Zheng H. A Global Regulatory Network for Dysregulated Gene Expression and Abnormal Metabolic Signaling in Immune Cells in the Microenvironment of Graves' Disease and Hashimoto's Thyroiditis. Front Immunol. 2022; 13: 1014237. https://doi.org/10.3389/fimmu.2022.1014237

[56] Li F. Single-cell RNA-seq reveals cellular heterogeneity of mouse carotid artery under disturbed flow. Cell Rep. 2021; 7(1): 180. https://doi.org/10.1038/s41598-021-81479-y

[57] Rahman S. Molecular insights into the relationship between autoimmune thyroid diseases and breast cancer: a critical perspective on autoimmunity and ER stress. Front Oncol. 2019; 10: 344. https://doi.org/10.3389/fonc.2020.00344

[58] Kapoor S, Champion G, Basu A, Mariampillai A, Olnes M. Immune therapies for myelodysplastic syndromes and acute myeloid leukemia. Cancers (Basel). 2021; 13(19): 5026. https://doi.org/10.3390/cancers13195026

[59] Wang C, Steinmetz NF. CD47 blockade and cowpea mosaic virus nanoparticle in situ vaccination triggers phagocytosis and tumor killing. Adv Healthc Mater. 2019; 8(11): 1801288. https://doi.org/10.1002/adhm.201801288

[60] Yi M. Combination strategies with PD-1/PD-L1 blockade: current advances and future directions. Mol Cancer. 2022; 21(1): 1-27. https://doi.org/10.1186/s12943-022-01574-2

[61] Huda R. New approaches to targeting B cells for myasthenia gravis therapy. Front Immunol. 2020; 11: 240. https://doi.org/10.3389/fimmu.2020.00240

[62] Zhang Z, Xu Q, Huang L. B cell depletion therapies in autoimmune diseases: Monoclonal antibodies or chimeric antigen receptor-based therapy? Front Immunol. 2023; 14: 502. https://doi.org/10.3389/fimmu.2023.1126421

[63] Kerdidani D, Papaioannou NE, Nakou E, Alissafi T. Rebooting Regulatory T Cell and Dendritic Cell Function in Immune-Mediated Inflammatory Diseases: Biomarker and Therapy Discovery under a Multi-Omics Lens. Biomedicines. 2022; 10(9): 2140. https://doi.org/10.3390/biomedicines10092140

[64] Oronsky B, Caroen S, Reid T. What Exactly Is Inflammation (and What Is It Not?). Int J Mol Sci. 2022; 23(23): 14905. https://doi.org/10.3390/ijms232314905

[65] Grondin JA, Kwon YH, Far PM, Haq S, Khan WI. Mucins in intestinal mucosal defense and inflammation: learning from clinical and experimental studies. Front Immunol. 2020; 11: 2054. https://doi.org/10.3389/fimmu.2020.02054

[66] Soto‐Heredero G, Gomez de las Heras MM, Gabandé‐Rodríguez E, Oller J, Mittelbrunn M. Glycolysis–A key player in the inflammatory response. FEBS J. 2020; 287(16): 3350-3369. https://doi.org/10.1111/febs.15327

[67] Raziyeva K. Immunology of acute and chronic wound healing. Biomolecules. 2021; 11(5): 700. https://doi.org/10.3390/biom11050700

[68] Agretti P. Gene expression profile in functioning and non-functioning nodules of autonomous multinodular goiter from an area of iodine deficiency: unexpected common characteristics between the two entities. J Endocrinol Invest. 2022; 45(2): 399-411. https://doi.org/10.1007/s40618-021-01661-x

[69] Pandey A, Pal AK, Bure D, Singh G. Graves' Disease and Hashimoto's Thyroiditis: Genetic and Non-genetic Perspective. In: Advances in Genetics. Elsevier; 2022: 1-30. https://doi.org/10.1016/bs.adgen.2022.05.001

[70] Nilsson BO. Mechanisms involved in regulation of periodontal ligament cell production of pro‐inflammatory cytokines: Implications in periodontitis. J Periodontal Res. 2021; 56(2): 249-255. https://doi.org/10.1111/jre.12822

[71] Uribe-Querol E, Rosales C. Neutrophils actively contribute to obesity-associated inflammation and pathological complications. Cells. 2022; 11(12): 1883. https://doi.org/10.3390/cells11121883

[72] Nassar SF, Raddassi K, Wu T. Single-cell multiomics analysis for drug discovery. Metabolites. 2021; 11(11): 729. https://doi.org/10.3390/metabo11110729

[73] Noel DD. Genetic Variants Assessing Crohn's Disease Pattern in Pediatric Inflammatory Bowel Disease Patients by a Clinical Exome Survey. Bioinformatics Biol Insights. 2021; 15: 11779322211055285. https://doi.org/10.1177/11779322211055285

[74] Coperchini F. The cytokine storm in COVID-19: Further advances in our understanding the role of specific chemokines involved. Cytokine Growth Factor Rev. 2021; 58: 82-91. https://doi.org/10.1016/j.cytogfr.2020.12.005

[75] De Leo S, Trevisan M, Fugazzola L. Recent advances in the management of anaplastic thyroid cancer. Thyroid Res. 2020; 13(1): 1-14. https://doi.org/10.1186/s13044-020-00085-8

[76] Croce L. The cytokine storm and thyroid hormone changes in COVID-19. J Endocrinol Invest. 2021; 44(5): 891-904. https://doi.org/10.1007/s40618-020-01471-7

[77] Morris G, Berk M, Maes M, Carvalho AF, Puri BK. Socioeconomic deprivation, adverse childhood experiences and medical disorders in adulthood: mechanisms and associations. Mol Neurobiol. 2019; 56(8): 5866-5890. https://doi.org/10.1007/s12035-019-1498-1

[78] Li PH. Recent developments in application of single-cell RNA sequencing in the tumour immune microenvironment and cancer therapy. Mil Med Res. 2022; 9(1): 52. https://doi.org/10.1186/s40779-022-00414-y

[79] Feghali K, Atallah J, Norman C. Manifestations of thyroid disease post COVID-19 illness: Report of Hashimoto thyroiditis, Graves' disease, and subacute thyroiditis. J Clin Transl Endocrinol Case Rep. 2021; 22: 100094. https://doi.org/10.1016/j.jecr.2021.100094

[80] Touzani F, Pozdzik A. New insights into immune cells cross-talk during IgG4-related disease. Clin Immunol. 2019; 198: 1-10. https://doi.org/10.1016/j.clim.2018.11.008

[81] Lee HJ. Genetics and epigenetics of autoimmune thyroid diseases: Translational implications. Best Pract Res Clin Endocrinol Metab. 2022; 36(1): 101661. https://doi.org/10.1016/j.beem.2022.101661

[82] Khayal EES, Ibrahim HM, Shalaby AM, Alabiad MA, El‐Sheikh AA. Combined lead and zinc oxide‐nanoparticles induced thyroid toxicity through 8‐OHdG oxidative stress‐mediated inflammation, apoptosis, and Nrf2 activation in rats. Environ Toxicol. 2021; 36(12): 2589-2604. https://doi.org/10.1002/tox.23379

[83] Zhang X. Di (2-ethylhexyl) phthalate (DEHP) and thyroid: biological mechanisms of interference and possible clinical implications. Endocrine. 2022; 77(3): 1-11. https://doi.org/10.1007/s12020-022-03125-5

[84] Kometani T. Development of a novel co-culture system using human pancreatic cancer cells and human iPSC-derived stellate cells to mimic the characteristics of pancreatic ductal adenocarcinoma in vitro. Cancer Sci. 2023; 114(1): 106-118. https://doi.org/10.1111/cas.15593

[85] Shobab L, Burman KD, Wartofsky L. Sex differences in differentiated thyroid cancer. Thyroid. 2022; 32(3): 224-235. https://doi.org/10.1089/thy.2021.0361

[86] Montesinos MdM, Pellizas CG. Thyroid hormone action on innate immunity. Front Endocrinol (Lausanne). 2019; 10: 350. https://doi.org/10.3389/fendo.2019.00350

[87] Lafuse WP, Wozniak DJ, Rajaram MV. Role of cardiac macrophages on cardiac inflammation, fibrosis and tissue repair. Cells. 2020; 10(1): 51. https://doi.org/10.3390/cells10010051

[88] Shields GS, Spahr CM, Slavich GM. Psychosocial interventions and immune system function: a systematic review and meta-analysis of randomized clinical trials. JAMA Psychiatry. 2020; 77(10): 1031-1043. https://doi.org/10.1001/jamapsychiatry.2020.0431

[89] Cunha LL, Perazzio SF, Azzi J, Cravedi P, Riella LV. Remodeling of the immune response with aging: immunosenescence and its potential impact on COVID-19 immune response. Front Immunol. 2020; 11: 1748. https://doi.org/10.3389/fimmu.2020.01748

[90] Pucino V. Lactate buildup at the site of chronic inflammation promotes disease by inducing CD4+ T cell metabolic rewiring. Cell Metab. 2019; 30(6): 1055-1074. https://doi.org/10.1016/j.cmet.2019.10.004

[91] Jin Y. Endothelial activation and dysfunction in COVID-19: from basic mechanisms to potential therapeutic approaches. Signal Transduct Target Ther. 2020; 5(1): 293. https://doi.org/10.1038/s41392-020-00454-7

[92] Gao Y, Dunlap G, Elahee M, Rao DA. Patterns of T‐Cell Phenotypes in Rheumatic Diseases From Single‐Cell Studies of Tissue. Arthritis Rheumatol. 2021; 3(5): 601-613. https://doi.org/10.1002/art.41869

[93] Lytrivi M, Castell AL, Poitout V, Cnop M. Recent insights into mechanisms of β-cell lipo-and glucolipotoxicity in type 2 diabetes. J Mol Biol. 2020; 432(5): 1514-1534. https://doi.org/10.1016/j.jmb.2019.09.016

[94] Murugan AK, Alzahrani AS. SARS-CoV-2 plays a pivotal role in inducing hyperthyroidism of Graves' disease. Endocrine. 2021; 73(2): 243-254. https://doi.org/10.1007/s12020-021-02770-6

[95] Ruggeri RM. SARS-COV-2-related immune-inflammatory thyroid disorders: facts and perspectives. Expert Rev Clin Immunol. 2021; 17(7): 737-759. https://doi.org/10.1080/1744666X.2021.1932467

[96] O'Shea D, Hogan AE. Dysregulation of natural killer cells in obesity. Cancers (Basel). 2019; 11(4): 573. https://doi.org/10.3390/cancers11040573

[97] Abdel-Moneim A. Relationship of thyroid dysfunction with cardiovascular diseases: updated review on heart failure progression. Horm Metab Res. 2020; 52(5): 301-309. https://doi.org/10.1055/a-1152-6499

[98] Basolo A. Histological pattern and gene expression profiling of thyroid tissue in subjects with obesity. Int J Obes (Lond). 2021; 45(9): 1-11. https://doi.org/10.1038/s41366-021-00856-9