

## Advancements In Immunotoxicology Research: A Comprehensive Review

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### ABSTRACT

Immunotoxicology is a critical field that delves into the effects of environmental factors and chemicals on the immune system. Recent progress in this area has shed light on the mechanisms underlying immune-related disorders and diseases. However, a comprehensive review is essential to consolidate the latest findings and methodologies, bridging existing gaps to advance our understanding further. The goal of this review is to present a thorough overview of the recent breakthroughs in immunotoxicology research, emphasizing significant discoveries and emerging trends. By synthesizing this information, we aim to provide a comprehensive perspective on the current landscape of the field and its potential implications for human health. Key highlights of this review address various aspects of immunotoxicology such as the influence of environmental factors on immune function, innovative approaches to toxicity testing, and advancements in predictive modeling of immune responses. Through an exploration of the latest findings in immunotoxicology, this review seeks to educate researchers, professionals, and policymakers on using these advancements to enhance human health outcomes and tackle immune-related challenges effectively.

**Keyword:** Immunotoxicology, Research advancements, Environmental factors, Immune-related disorders, Human health implications

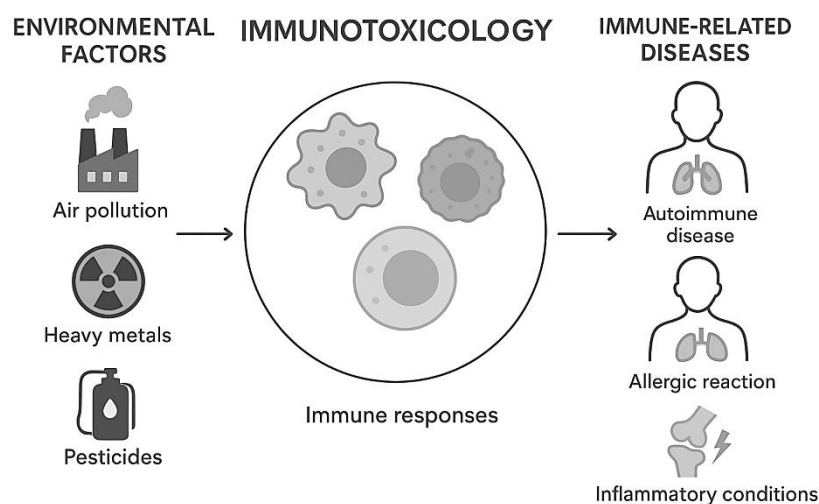
### 1. INTRODUCTION

Immunotoxicology is a multidisciplinary field that investigates the impacts of various environmental factors and chemicals on the immune system's structure and functions (Luster et al., 2009; Chandrasekar et al., 2024; Nabi et al., 2025). Over the years, research in immunotoxicology has provided crucial insights into how exposures to these agents can modulate immune responses, leading to altered immune function and potentially harmful outcomes (Luster et al., 2009; Muzaffer et al., 2025). The intricate relationship between environmental factors and immune system regulation has become increasingly significant in understanding the pathogenesis of immune-related disorders and diseases (Kolay et al., 2024). Previous studies have highlighted the complex mechanisms that underlie immunotoxicity, emphasizing the need for a comprehensive understanding of how these factors interact with the immune system (Selgrade, 2007; Johnson et al., 2024). Early research in immunotoxicology focused on identifying specific chemicals or agents that directly impact immune function, leading to the development of better toxicity testing strategies (Selgrade, 2007). These early results laid the foundation for subsequent investigations that delved deeper into the immunomodulatory effects of environmental exposures.

One key aspect of immunotoxicology research is the exploration of immune-related disorders and diseases triggered by environmental factors. For example, exposure to pollutants, heavy metals, pesticides, and other toxic chemicals has been linked to an increased risk of autoimmune diseases, allergic reactions, and compromised immune function (Selgrade, 2007; D'Souza et al., 2024). Understanding how these exposures influence immune responses is crucial for developing targeted interventions and preventive measures to mitigate their adverse effects on human health (Sullivan and Weber, 2022). The immune system's complex network of cells, tissues, and molecules plays a vital role in defending the body against pathogens and maintaining homeostasis (Luster et al., 2009; Ren et al., 2024). Disruption of this delicate balance by environmental

factors can lead to dysregulation of immune responses, resulting in heightened susceptibility to infections, inflammatory conditions, and autoimmune disorders (Luster et al., 2009). Investigating the immunomodulatory properties of various environmental agents is essential for uncovering the mechanisms underlying immune dysfunction and developing strategies to protect human health (Kesharwani et al., 2022). Recent advancements in immunotoxicology research have focused on innovative methodologies to assess the effects of environmental factors on

immune function (Corsini et al., 2013). These approaches involve the use of in vitro and in vivo models to evaluate immune cell responses, cytokine production, and cellular signaling pathways in the presence of different toxicants (Corsini et al., 2013; Maddalon et al., 2023). By employing advanced techniques such as flow cytometry, transcriptomics, and high-content screening, researchers can gain valuable insights into the molecular mechanisms of immunotoxicity (Fig.1).



**Fig.1. Overview of Immunotoxicology**

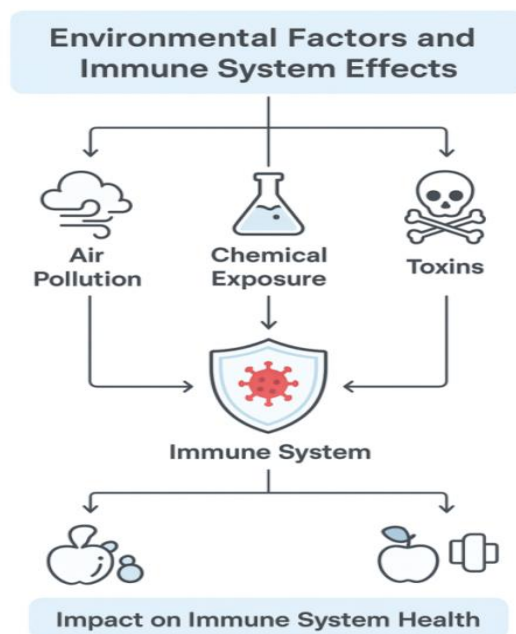
Furthermore, predictive modeling of immune responses has emerged as a promising tool in immunotoxicology research, allowing for the assessment of complex interactions between environmental agents and the immune system (Andersen et al., 2017; Chandrasekar et al., 2024). Computational models incorporating data from experimental studies can predict the immunomodulatory effects of chemicals and prioritize compounds for further evaluation based on their potential toxicity profiles (Andersen et al., 2017; Bai et al., 2025). These predictive models offer a cost-effective and efficient approach to screening large numbers of chemicals for immunotoxic effects. In end, immunotoxicology is a critical field that continues to expand our understanding of how environmental factors and chemicals influence immune function (Fig.2) and contribute to immune-related disorders (Chandrasekar et al., 2024). By integrating earlier results and current research findings, scientists can unravel the intricate mechanisms of immunotoxicity and pave the way for developing targeted interventions to protect human health. The interdisciplinary nature of immunotoxicology underscores the importance of collaborative efforts among researchers, policymakers, and healthcare professionals to address the challenges posed by immune dysregulation and promote public health.

## 2. ENVIRONMENTAL FACTORS AND IMMUNE SYSTEM EFFECTS

The immune system is a sophisticated defense mechanism that protects the body from pathogens and maintains overall health (Singh et al., 2023). While genetics play a significant role in immune system function, environmental factors also exert substantial influence on immunity (Donald and Finlay, 2023). This assessment explores the impact of various environmental factors, including air pollution, chemical exposure, toxins, and lifestyle choices, on immune system health.

### 2.1. Air Pollution and Immune System

Air pollution, characterized by particulate matter (PM), nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), and ozone (O<sub>3</sub>), poses a significant threat to immune function (Meo et al., 2025). Studies have shown that exposure to these pollutants can induce inflammation in the respiratory system, leading to immune activation and increased susceptibility to respiratory infections (Brook et al., 2010; Loaiza-Ceballos et al., 2022). Additionally, particulate matter has been linked to impaired systemic microvascular endothelium-dependent dilation, further highlighting its detrimental effects on immune responses (Smith et al., 2016; Asiwe and Oritsemuelebi, 2024).



**Fig.2. Environmental Impacts on the Immune System**

## 2.2. Chemical Exposure and Immune System

Chemicals present in the environment, such as pesticides, heavy metals, and industrial pollutants, can disrupt immune system balance. Organophosphate pesticides, for instance, have been associated with alterations in immune cell function and an elevated risk of autoimmune diseases (Mostafalou & Abdollahi, 2017). Moreover, heavy metals like lead and mercury have immunosuppressive properties, rendering individuals more susceptible to infections and compromising immune defenses (Kota et al., 2015).

## 2.3. Toxin Exposure and Immune System

Environmental toxins, including mycotoxins produced by mold, can have profound effects on immune responses (Ehsanifar et al., 2023). Mycotoxins are known to induce immune suppression, trigger allergic reactions, and exacerbate respiratory issues (Doyle et al., 2015). By disrupting the balance of immune cells and cytokines, these toxins contribute to immune dysregulation and heighten the risk of allergic diseases (Lu et al., 2024).

## 2.4. Lifestyle Choices and Immune System

Individual lifestyle choices, such as dietary habits, physical activity, and stress management, play a critical role in immune system function (Janssen et al., 2024). A diet rich in essential nutrients from fruits, vegetables, and whole grains can bolster immune defenses and regulate inflammatory responses (Nieman, 2017). Conversely, a diet high in processed foods and sugars can promote systemic inflammation and weaken immune function.

## 2.5. Impact of Environmental Factors on Immune System Health

The cumulative impact of environmental factors on immune system health is profound and multifaceted. Chronic exposure to air pollution, chemical toxins, and poor lifestyle choices can lead to immune dysregulation, heighten susceptibility to infections, and increase the risk of autoimmune and allergic diseases (Miller, 2025). Certain populations, such as children, the elderly, and individuals with pre-existing health conditions, are particularly vulnerable to the deleterious effects of environmental factors on immune function (Gruzieva et al., 2017; Imberti et al., 2025). In end, environmental factors exert a significant influence on immune system responses and overall health. Understanding the interplay between air pollution, chemical exposure, toxins, and lifestyle choices is crucial for developing strategies to mitigate adverse effects and enhance immune system resilience (Ofremu et al., 2025). Further research is imperative to elucidate the underlying mechanisms of environmental impact on immune function and to identify interventions that can optimize immune health in the face of environmental challenges.

## 3. MECHANISMS OF IMMUNE-RELATED DISORDERS

Immune-related disorders encompass a wide range of conditions characterized by dysregulation of the immune system, leading to immune-mediated responses against self or non-self-antigens (Kamboj et al., 2025). Understanding the intricate mechanisms underlying these disorders is essential for the development of effective therapeutic interventions (Oyebanjo,

2024). This review delves into the multifaceted mechanisms involved in immune-related disorders, exploring both innate and adaptive immune responses.

### 3.1. Innate Immune Responses in Immune-Related Disorders

The innate immune system serves as the first line of defense against pathogens and is pivotal in initiating immune responses (Diamond and Kanneganti, 2022). Dysregulation of innate immune components, such as macrophages, dendritic cells, and natural killer cells, has been implicated in the pathogenesis of autoimmune disorders and inflammatory conditions (Gao et al., 2012; Edilova et al., 2021). For example, aberrant activation of Toll-like receptors on macrophages can trigger excessive inflammation and tissue damage in autoimmune diseases like rheumatoid arthritis (West et al., 2016).

### 3.2. Adaptive Immune Responses in Immune-Related Disorders

The adaptive immune system, comprising T and B lymphocytes, plays a crucial role in antigen-specific immune responses. Dysfunctions in adaptive immunity, particularly T cell-mediated responses, are central to the development of autoimmune diseases. In conditions like multiple sclerosis and type 1 diabetes, autoreactive T cells are activated against self-antigens, leading to tissue damage and inflammation (Wang et al., 2018; Sivalingam, 2025). B lymphocytes, on the other hand, can produce autoantibodies that contribute to the pathogenesis of autoimmune disorders such as systemic lupus erythematosus (Nikolopoulos et al., 2010).

### 3.3. Genetic Predisposition in Immune-Related Disorders

Genetic factors are known to play a significant role in the susceptibility to immune-related disorders. Genome-wide association studies have identified numerous genetic variants associated with autoimmune diseases, highlighting the genetic complexity of these conditions (Cho et al., 2015). For instance, certain HLA alleles have been linked to increased risk of developing autoimmune disorders like celiac disease and systemic sclerosis, underscoring the genetic predisposition component in immune-related disorders (Jiang et al., 2017).

### 3.4. Epigenetic Modifications in Immune-Related Disorders

Epigenetic changes, such as DNA methylation and histone modifications, can influence immune cell function and contribute to immune-related disorders. Alterations in the epigenetic landscape of immune cells have been observed in autoimmune conditions, affecting gene expression patterns and immune responses (Garaud et al., 2019; Liotti et al., 2022). Dysregulated epigenetic mechanisms can lead to inappropriate immune activation, culminating in autoimmune responses and chronic inflammation in disorders like psoriasis and inflammatory bowel disease.

### 3.5. Microbiome Dysbiosis in Immune-Related Disorders

The human microbiome, consisting of diverse microbial communities, plays a crucial role in immune system regulation and host-microbe interactions (Hashem, 2025). Dysbiosis, characterized by alterations in microbial composition and diversity, has been linked to immune-related disorders. In conditions like inflammatory bowel disease and rheumatoid arthritis, perturbations in the gut microbiota have been associated with aberrant immune responses and disease pathogenesis (Huang & Li, 2017; Qi, 2024). Restoring microbial balance through interventions like probiotics and fecal microbiota transplantation holds promise for modulating immune-related disorders.

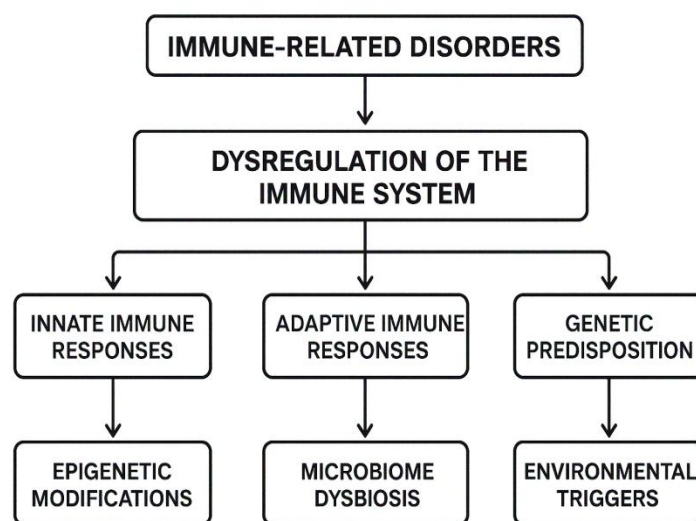


Fig.2. Mechanisms Contributing to Immune-Related Disorders

3.6. Environmental Triggers in Immune-Related Disorders

Environmental factors, including infections, diet, and exposure to pollutants, can act as triggers for immune-related disorders by influencing immune system function (Drago, 2024). Viral infections like Epstein-Barr virus and environmental factors like smoking have been implicated in triggering autoimmune responses in susceptible individuals (Ni et al., 2019). Additionally, dietary factors such as gluten in celiac disease and environmental pollutants like diesel exhaust particles in asthma can exacerbate immune-related disorders through inflammatory pathways. In essence, immune-related disorders are complex conditions characterized by dysregulated immune responses against self or non-self-antigens. The interplay of innate and adaptive immune mechanisms, genetic predisposition, epigenetic modifications, microbiome dysbiosis, and environmental triggers contributes to the pathogenesis of these disorders (Kim, 2024). Further research into the intricate molecular and cellular mechanisms underlying immune-related disorders is crucial for the development of personalized therapeutic approaches that target specific immune pathways and restore immune homeostasis.

4. METHODOLOGIES IN IMMUNOTOXICOLOGY RESEARCH

Immunotoxicology research encompasses the study of the adverse effects of environmental and occupational factors on the immune system (Chandrasekar et al., 2024). Understanding the methodologies used in immunotoxicology is essential for evaluating immune responses to various agents and substances (Johnson et al., 2024). This review delves into the diverse methodologies employed in immunotoxicology research, emphasizing their importance in assessing immune system function and potential toxic effects.

4.1. Immunophenotyping Techniques

One of the key methodologies in immunotoxicology research is immunophenotyping, which involves the characterization and quantification of immune cell populations. Flow cytometry, a common immunophenotyping technique, allows for the identification of specific immune cell subsets based on surface markers and intracellular molecules (Otto et al., 2018; Akha et al., 2025). By analyzing changes in immune cell composition and activation, immunophenotyping provides valuable insights into immune responses following exposure to toxicants (Table.1).

Table.1. Comparative Overview of Immunophenotyping Techniques and Literature Sources.

| Method                                   | Use                                                  | Reference (APA, short)            |
|------------------------------------------|------------------------------------------------------|-----------------------------------|
| Flow cytometry                           | Cell surface marker analysis, cell counting, sorting | Roederer, 2001, Ding et al., 2025 |
| Immunohistochemistry                     | Detection of antigens in tissue sections             | Taylor, 2006                      |
| ELISA                                    | Quantification of proteins, antibodies, antigens     | Engvall & Perlmann, 1971          |
| Immunoblotting (Western blot)            | Protein identification & quantification              | Towbin et al., 1979               |
| Immunofluorescence                       | Visualizing antigens in cells/tissues                | Abedi et al., 2016                |
| Immunocytochemistry                      | Antigen detection in cells with labeled antibodies   | Leong et al., 1983                |
| Mass cytometry (CyTOF)                   | Multiprotein analysis at single-cell level           | Bendall et al., 2011              |
| Immunosequencing                         | Sequencing of TCR/BCR repertoires                    | Robins et al., 2009               |
| Multiparameter flow cytometry            | Characterization of immune cell populations          | Maecker et al., 2012              |
| Circulating tumor cell immunophenotyping | Detection & analysis of tumor cells in blood         | Muller et al., 2005               |
| Multiplex immune panels                  | Profiling immune responses with multiple markers     | Newell et al., 2012               |



|                                        |                                                     |                        |
|----------------------------------------|-----------------------------------------------------|------------------------|
| Regulatory T cell (Treg) phenotyping   | Analysis of Treg cell populations                   | Mahnke et al., 2013    |
| Imaging flow cytometry                 | High-resolution imaging with multiplexing           | Frei et al., 2016      |
| Microarray-based immunophenotyping     | Immune response profiling via microarray            | Lenz & Staudt, 2010    |
| Single-cell immunophenotyping          | RNA-seq Profiling immune cells at single-cell level | Glanville et al., 2016 |
| Nanotechnology-based immunophenotyping | High-resolution imaging & analysis using nanotech   | Fujiwara et al., 2015  |

## 4.2. Cytokine Profiling Assays

Cytokines are essential signaling molecules that regulate immune responses and inflammation. Cytokine profiling assays, such as enzyme-linked immunosorbent assays (ELISA) and multiplex immunoassays, measure the concentrations of various cytokines in biological samples. By assessing cytokine profiles, researchers can evaluate the impact of toxicants on immune cell signaling and inflammatory pathways (Lynch et al., 2016). Changes in cytokine levels can indicate immune system activation, suppression, or dysregulation in response to toxic exposures.

## 4.3. Immunotoxicity Biomarkers

Identification of immunotoxicity biomarkers is crucial for monitoring immune system health and detecting early signs of immune dysfunction. Biomarkers, such as lymphocyte subsets, immunoglobulin levels, and immune cell function assays, serve as indicators of immune status and response to toxic insults (Pavanello et al., 2019). Alterations in biomarker profiles can signal immunosuppression, hypersensitivity reactions, or autoimmune responses induced by toxic agents.

## 4.4. Histopathological Evaluation

Histopathological evaluation of immune tissues, such as the spleen, thymus, and lymph nodes, provides valuable insights into the structural alterations induced by toxic insults. Changes in tissue architecture, inflammatory infiltrates, and cell death patterns can indicate immune-mediated effects of toxic exposures (Boorman et al., 2019). Histopathological assessment complements other methodologies by revealing histological alterations associated with immunotoxicity.

## 4.5. In Vitro Immunotoxicity Assays

In vitro assays offer a controlled and high-throughput approach to assess the effects of toxicants on immune cells and functions. Cell-based assays, such as lymphocyte proliferation assays, phagocytosis assays, and cytokine release assays, can be used to evaluate immune cell viability, proliferation, and functional responses upon exposure to chemicals or environmental agents (Clark et al., 2017; Bowley et al., 2025). In vitro models provide valuable mechanistic insights into the immunotoxic effects of various compounds. Methodologies in immunotoxicology research play a pivotal role in elucidating the intricate interactions between toxicants and the immune system. Immunophenotyping techniques, cytokine profiling assays, biomarker identification, histopathological evaluation, and in vitro immunotoxicity assays collectively contribute to a comprehensive assessment of immune responses to environmental and occupational exposures (Schumacher et al., 2025). Integrating these methodologies enables researchers to evaluate immune system function, identify immunotoxic effects, and facilitate the development of strategies to protect immune health in exposed populations.

# 5. RECENT BREAKTHROUGHS IN IMMUNOTOXICOLOGY

Recent advancements in immunotoxicology research have led to significant breakthroughs in understanding the complex interactions between toxicants and the immune system (Muzaffer et al., 2025). These breakthroughs have provided novel insights into immune responses to environmental and occupational exposures, paving the way for improved risk assessment and targeted interventions. This review highlights some of the recent breakthroughs in immunotoxicology research and their implications for immune health.

## 5.1. Nanotechnology in Immunotoxicity Assessment

One notable breakthrough in immunotoxicology is the use of nanotechnology for assessing immune responses to nanomaterials (Hofer et al., 2022). Nanoparticles have unique properties that can interact with immune cells and modulate immune functions (Fadeel et al., 2018). Advanced techniques (Table.1), such as nanoparticle tracking analysis and high-resolution imaging, enable researchers to investigate the immunomodulatory effects of nanoparticles and their potential impact on immune health.

## 5.2. Single-Cell Analysis in Immune Profiling

The application of single-cell analysis technologies, such as single-cell RNA sequencing and mass cytometry, has revolutionized immune profiling in immunotoxicology research (Karmaus, 2024). By analyzing immune cells at the single-cell level, researchers can unravel heterogeneity within immune cell populations and identify distinct immune cell subsets (Villani et al., 2018; Luo et al., 2022). This approach provides a deeper understanding of immune responses to toxicants and the mechanisms underlying immune dysregulation.

## 5.3. In Silico Models for Predicting Immunotoxicity

Advancements in computational modeling and bioinformatics have paved the way for the development of in silico models for predicting immunotoxicity (Muzaffer et al., 2025). These models utilize machine learning algorithms and data integration techniques to predict immune responses to various chemicals and environmental agents (Tropsha, 2020). In silico approaches offer a cost-effective and time-efficient way to screen potential immunotoxicants and prioritize compounds for further evaluation.

## 5.4. 3D Organoid Systems for Immune Function Studies

The development of three-dimensional (3D) organoid systems has provided a platform for studying immune function in a physiologically relevant context. Immune organoids, such as gut-associated lymphoid tissue (GALT) organoids and thymic organoids, mimic the complex interactions between immune cells and tissues (Shahjalal et al., 2019; Patel et al., 2024). These 3D models enable researchers to investigate immune responses to toxicants in a tissue-specific environment, enhancing our understanding of immunotoxic effects (Pandey and Mishra, 2022). Recent breakthroughs in immunotoxicology have propelled the field forward, offering new avenues for investigating immune responses to toxic exposures. Nanotechnology, single-cell analysis, in silico modeling, and 3D organoid systems represent cutting-edge approaches that enhance our ability to assess immunotoxicity and develop targeted strategies for protecting immune health in at-risk populations. Continued research in these areas is essential for advancing our understanding of immune system interactions with environmental and occupational factors.

## 6. SIGNIFICANCE OF EMERGING TRENDS

Emerging trends in immunotoxicology research have significant implications for understanding the complex interactions between environmental factors and the immune system (Maddalon et al., 2023). Recent advancements in the field have shed light on novel approaches and technologies that are shaping the future of immunotoxicology studies (Perli et al., 2024). The integration of these emerging trends holds promise for enhancing our understanding of immune responses to toxicants and improving risk assessment strategies (Fasano et al., 2020). One critical trend in immunotoxicology is the growing emphasis on the application of high-throughput screening methods for evaluating immune responses to various chemicals and compounds. High-throughput techniques, such as transcriptomics and proteomics, enable researchers to assess the effects of multiple toxicants on immune cells in a time-efficient manner (Vu et al., 2018). This trend not only accelerates the identification of immunotoxicants but also facilitates the elucidation of underlying molecular mechanisms involved in immune dysregulation.

Another key emerging trend is the integration of multi-omics approaches, such as genomics, transcriptomics, proteomics, and metabolomics, to comprehensively study immune responses in toxicology research (Witwer et al., 2017). By combining data from different omics platforms, researchers can gain a holistic view of immune system alterations induced by toxic exposures and identify potential biomarkers of immunotoxicity (Fortino et al., 2022). This integrative approach allows for a more comprehensive and detailed analysis of immune responses to environmental stressors. Furthermore, the utilization of advanced bioinformatics tools and computational modeling techniques represents a significant trend in immunotoxicology that enhances data analysis and interpretation (Pérez Santín et al., 2021). Machine learning algorithms, network analyses, and systems biology approaches aid in predicting immune responses, identifying key regulatory pathways, and stratifying individuals based on immune susceptibility (Villani et al., 2018). These bioinformatics tools enhance the predictive power of immunotoxicity assessments and enable the identification of immune-modulating factors with precision.

The significance of emerging trends in immunotoxicology lies in their potential to revolutionize the field by providing new insights into immune system interactions with environmental factors. The adoption of high-throughput screening methods, multi-omics analyses, and advanced bioinformatics tools offers a comprehensive and integrative approach to studying immune responses to toxicants. These emerging trends not only enhance our understanding of immunotoxicity mechanisms but also hold promise for developing personalized interventions and strategies to protect immune health in exposed populations.

## 7. INNOVATIONS IN TOXICITY TESTING

Innovations in toxicity testing have revolutionized the field of toxicology, offering advanced approaches to assess the potential adverse effects of chemicals on human health. Recent developments in toxicity testing methodologies have

enhanced the predictive power and mechanistic understanding of toxic responses. Utilizing cutting-edge technologies and models, researchers are now able to evaluate toxicity with greater accuracy and efficiency, leading to improved risk assessment and hazard identification (Thomas et al., 2019). One innovative approach in toxicity testing is the incorporation of 3D cell culture models, such as organoids and microphysiological systems, which better mimic the complexity of human tissues compared to traditional 2D cell cultures (Zhang et al., 2020). These advanced models provide a more physiologically relevant platform for assessing drug toxicity and environmental chemical exposures, offering insights into organ-specific toxic effects and intercellular interactions.

Furthermore, the integration of high-throughput screening platforms and computational modeling techniques has streamlined toxicity testing processes, enabling the rapid evaluation of a large number of chemicals for potential hazards (Mellor et al., 2019). By combining *in vitro* assays with computational approaches, researchers can predict toxicological outcomes, prioritize chemicals for further testing, and reduce the reliance on animal testing in toxicity assessment (Vashishat et al., 2024). Incorporating advanced methods like omics technologies, transcriptomics, and proteomics into toxicity testing has also allowed for a comprehensive analysis of molecular responses to toxicants (Zhang et al., 2019; Mortimer et al., 2022). These omics approaches provide valuable insights into the underlying mechanisms of toxicity, identify biomarkers of adverse effects, and support the development of personalized toxicity assessments tailored to individual susceptibility. In conclusion, innovations in toxicity testing have significantly advanced the field, offering new tools and strategies to assess chemical safety and potential risks to human health. By leveraging novel methodologies, models, and technologies, researchers are better equipped to evaluate toxicity, understand toxicological mechanisms, and ultimately enhance public health protection through informed risk management strategies.

## 8. ADVANCES IN PREDICTIVE MODELING OF IMMUNE RESPONSES

Predictive modeling of immune responses has undergone significant advancements in recent years, revolutionizing our ability to anticipate and understand the complexities of immune reactions. By integrating cutting-edge computational methods and multi-omics data, researchers have developed sophisticated models that offer deep insights into immune system dynamics and provide valuable predictions for immune-related outcomes. The integration of multi-omics data, including genomics, transcriptomics, proteomics, and metabolomics, has been a cornerstone in advancing predictive modeling of immune responses. By analyzing a vast array of molecular data, researchers can generate comprehensive immune response profiles that capture the intricate interactions between various immune components and their signaling networks (Villani et al., 2018). This holistic approach allows for a detailed examination of immune responses at a molecular level, shedding light on the underlying mechanisms governing immune function and dysfunction.

Network analysis algorithms have further enhanced our understanding of immune responses by enabling the construction of immune regulatory networks (Navarro Quiroz et al., 2025). These network models depict the complex relationships between immune cells, cytokines, and signaling pathways, providing a systems-level perspective of immune dynamics (Sarkizova et al., 2020; Sokouti and Amjad, 2025). Through network analysis, researchers can identify key immune regulators, predict immune response outcomes, and unravel the interconnected web of molecular interactions that govern immune system functionality (Mishra et al., 2021). *In silico* modeling approaches have also contributed significantly to predictive modeling of immune responses by simulating immune system behaviors computationally. These modeling techniques, based on mechanistic and mathematical models, allow researchers to predict immune cell behaviors, cytokine responses, and immune system outcomes under various conditions (Tropsha, 2021). *In silico* models offer a virtual platform to explore the dynamics of immune responses, test hypotheses, and predict the effects of interventions on immune system function.

In conclusion, the advances in predictive modeling of immune responses have propelled immunology research forward, providing a deep and detailed understanding of immune system behaviors and interactions. By leveraging computational tools, multi-omics data integration, network analyses, and *in silico* modeling, researchers can predict immune responses, uncover novel immune pathways, and pave the way for personalized immunotherapies and precision medicine tailored to individual immune profiles.

## 9. IMPLICATIONS FOR HUMAN HEALTH

The advancements in predictive modeling of immune responses have profound implications for human health, offering remarkable opportunities for personalized medicine and disease management strategies. By leveraging sophisticated computational tools and multi-omics data integration, these predictive models provide valuable insights into immune system dynamics and regulatory mechanisms that have direct implications for human health and well-being (Villani et al., 2018; Mohr et al., 2024). The comprehensive immune response profiles generated through analyses of multi-omics data enable a deeper understanding of individual immune responses and immune-related disorders (Yin et al., 2025). This personalized approach to immune system assessment has the potential to revolutionize disease diagnosis, treatment selection, and monitoring strategies, leading to more effective and tailored healthcare interventions (Sarkizova et al., 2020; Afzal et al., 2024). Furthermore, the construction of immune regulatory networks using network analysis algorithms offers a systems-level view of immune function, highlighting key immune regulators and signaling pathways that impact human health.



outcomes. By uncovering critical immune interactions and molecular mechanisms, these network models provide valuable insights into disease pathogenesis, therapeutic targets, and immune system modulation strategies (Tropsha, 2021).

In silico modeling of immune responses contributes to the development of virtual platforms for predicting immune system behaviors under different conditions. Such predictive models offer a powerful tool for assessing the effects of interventions, predicting treatment responses, and optimizing therapeutic approaches in the context of human health (Stolovitzky et al., 2020). Furthermore, the implications of advanced predictive modeling of immune responses for human health are far-reaching, offering a path toward personalized healthcare strategies, disease prevention, and targeted treatments (Segun et al., 2024). By unlocking the complexities of immune system dynamics and responses, these innovative approaches have the potential to improve health outcomes, enhance disease management, and drive precision medicine advancements for the benefit of individuals and populations.

## 10. IMMUNOTOXICOLOGY IN PUBLIC HEALTH POLICY

Immunotoxicology research plays a crucial role in enhancing human health outcomes by providing insights into the interactions between environmental factors and the immune system. Through innovative research approaches and advanced methodologies, immunotoxicology contributes to our understanding of immune responses and their impact on human health. Studies have shown that exposure to environmental toxins and chemicals can have detrimental effects on immune function, potentially leading to immune-related disorders and health complications (Yang et al., 2019). By investigating the mechanisms underlying immune responses to toxicants, immunotoxicology research offers opportunities to identify potential risks to human health and develop strategies for mitigating these risks (Chandrasekar et al., 2024). Understanding how toxins affect the immune system allows for the early detection of immune dysregulation and the implementation of preventive measures to safeguard human health (Gennings et al., 2018).

Moreover, immunotoxicology research has the potential to inform public health policies and regulatory decisions aimed at protecting human populations from harmful exposures. By providing evidence-based assessments of the immune effects of environmental agents, immunotoxicology studies contribute to the development of guidelines and regulations that promote a healthier environment and reduce the risk of immune-related health issues (Sriram et al., 2016). Through the advancement of predictive modeling, biomarker discovery, and risk assessment strategies, immunotoxicology research continues to enhance human health outcomes by offering insights into immune system vulnerabilities and responses to environmental stressors. By integrating cutting-edge technologies and multidisciplinary approaches, immunotoxicology research holds promise for improving human health and well-being through the identification of immune health markers, the assessment of immune-related risks, and the development of targeted interventions tailored to individual immune profiles.

## 11. SUMMARY AND CONCLUSION

Immunotoxicology is the study of how chemicals, pollutants, and environmental factors affect the immune system. Exposure to pesticides, heavy metals, industrial toxins, and lifestyle-related factors can weaken immunity and increase the risk of infections, autoimmune diseases, and allergies. Research methods such as flow cytometry, immunohistochemistry, cytokine profiling, histopathology, and biomarker studies help in understanding these effects. New approaches like nanotechnology, organoid models, in silico analysis, and multi-omics tools have improved the accuracy of testing and prediction. By combining advanced technologies with traditional methods, researchers can better explain the link between toxic exposures and immune dysfunction. This knowledge is valuable for both scientific understanding and public health protection.

Immunotoxicology plays an important role in identifying how environmental and chemical exposures disturb the immune system. Advances in modern tools and predictive models have improved risk assessment and opened new opportunities for personalized medicine. The field not only supports safer healthcare interventions but also guides public health policies to protect people from immune-related risks. In the future, integration of new technologies will make immunotoxicology even more precise, reliable, and impactful in safeguarding human health.

## REFERENCES

- [1] Abedi, V., Salehnia, M., & Pazhohi, N. (2016). Immunofluorescence microscopy in biomedical sciences. *Avicenna Journal of Medical Biotechnology*, 8(2), 59–68.
- [2] Afzal, M., Sah, A. K., Agarwal, S., Tanzeel, A., Elshaikh, R. H., Alobeidli, F. A & Choudhary, A. (2024). Advancements in the treatment of autoimmune diseases: Integrating artificial intelligence for personalized medicine. *Trends in Immunotherapy*, 8(2).
- [3] Akha, A. A. S., Csomos, K., Ujhazi, B., Walter, J. E., & Kumánovics, A. (2025). Evolving approach to clinical cytometry for immunodeficiencies and other immune disorders. *Immunology and Allergy Clinics*, 45(2), 205–221.
- [4] Andersen, M. E., McMullen, P. D., & Clewell, H. J. 3rd (2017). A biologically based approach to quantitative chemical risk assessment: the interplay between hazard identification and dose-response assessment.

Computational Toxicology, 1, 51-57.

- [5] Asiwe, J. N., & Oritsemuelebi, B. (2024). Environmental toxicant-mediated cardiovascular diseases: an insight into the mechanism and possible preventive strategy. *Toxicology and Environmental Health Sciences*, 16(1), 1-19.
- [6] Bai, C., Wu, L., Li, R., Cao, Y., He, S., & Bo, X. (2025). Machine Learning-Enabled Drug-Induced Toxicity Prediction. *Advanced Science*, 12(16), 2413405.
- [7] Bendall, S. C., Simonds, E. F., Qiu, P., Amir, E. D., Krutzik, P. O., Finck, R & Nolan, G. P. (2011). Single-cell mass cytometry of differential immune and drug responses across a human hematopoietic continuum. *Science*, 332(6030), 687–696. <https://doi.org/10.1126/science.1198704>
- [8] Boorman, G. A., Elwell, M. R., Mitsumori, K., Rittinghausen, S., & Thake, D. C. (2019). *Pathology of the Mouse* References. John Wiley & Sons.
- [9] Bowley, T. Y., Lenz, K. D., Shanker, A., & Kubicek-Sutherland, J. Z. (2025). Methods integrating innate and adaptive immune responses in human in vitro immunization assays. *Frontiers in Immunology*, 16, 1584852.
- [10] Brook, R. D., Rajagopalan, S., Pope, C. A., Brook, J. R., Bhatnagar, A., Diez- Roux, A. V & Kaufman, J. D. (2010). Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation*, 121(21), 2331-2378.
- [11] Chandrasekar, V., Panicker, A. J., Dey, A. K., Mohammad, S., Chakraborty, A., Samal, S. K & Singh, A. V. (2024). Integrated approaches for immunotoxicity risk assessment: challenges and future directions. *Discover Toxicology*, 1(1), 9.
- [12] Cho, J. H., Gregersen, P. K., & Ioannidis, J. P. (2015). Genetic and epigenetic susceptibility to autoimmune diseases. *Nature Reviews Genetics*, 16(9), 589-604.
- [13] Clark, R. L., Beane, C. A., & King-Hooper, B. (2017). Assessing immune function by flow cytometry: Basic concepts and tools for the clinical industry. *Biotechnology Progress*, 33(3), 534-542.
- [14] Corsini, E., Sokooti, M., Galli, C. L., Moretto, A., & Colosio, C. (2013). Pesticide induced immunotoxicity in humans: a comprehensive review of the existing evidence. *Toxicology*, 307, 123-135.
- [15] Diamond, M. S., & Kanneganti, T. D. (2022). Innate immunity: the first line of defense against SARS-CoV-2. *Nature immunology*, 23(2), 165-176.
- [16] Ding, T., Lee, K. C., Tsia, K. K., Siegel, T. N., Di Carlo, D., & Goda, K. (2025). Image-activated cell sorting. *Nature Reviews Bioengineering*, 1-18.
- [17] Donald, K., & Finlay, B. B. (2023). Early-life interactions between the microbiota and immune system: impact on immune system development and atopic disease. *Nature Reviews Immunology*, 23(11), 735-748.
- [18] Doyle, M. E., & Dieber, R. J. (2015). Mycotoxins. In Haschek and Rousseaux's *Handbook of Toxicologic Pathology* (pp. 759-803). Academic Press.
- [19] Drago, G., Aloi, N., Ruggieri, S., Longo, A., Contrino, M. L., Contarino, F. M., ... & Longo, V. (2024). Guardians under Siege: Exploring Pollution's Effects on Human Immunity. *International Journal of Molecular Sciences*, 25(14), 7788.
- [20] D'Souza, L. C., Paithankar, J. G., Stopper, H., Pandey, A., & Sharma, A. (2024). Environmental chemical-induced reactive oxygen species generation and immunotoxicity: a comprehensive review. *Antioxidants & Redox Signaling*, 40(10-12), 691-714.
- [21] Edilova, M. I., Akram, A., & Abdul-Sater, A. A. (2021). Innate immunity drives pathogenesis of rheumatoid arthritis. *Biomedical journal*, 44(2), 172-182.
- [22] Ehsanifar, M., Rajati, R., Gholami, A., & Reiss, J. P. (2023). Mold and mycotoxin exposure and brain disorders. *Journal of Integrative Neuroscience*, 22(6), 137.
- [23] Engvall, E., & Perlmann, P. (1971). Enzyme-linked immunosorbent assay (ELISA). *Journal of Immunology*, 109(1), 129–135. <https://doi.org/10.4049/jimmunol.109.1.129>
- [24] Fadeel, B., Farcal, L., Hardy, B., Vazquez-Campos, S., Hristozov, D., Marcomini, A & Valsami-Jones, E. (2018). Advanced tools for the safety assessment of nanomaterials. *Nature Nanotechnology*, 13(7), 537-543.
- [25] Fasano, M., Saber, A. T., & Shvedova, A. A. (2020). Role of nanomaterials in the modulation of immune responses. *Cellular and Molecular Life Sciences*, 77(19), 3781-3800.
- [26] Fortino, V., Kinaret, P. A. S., Fratello, M., Serra, A., Saarimäki, L. A., Gallud, A., ... & Greco, D. (2022). Biomarkers of nanomaterials hazard from multi-layer data. *Nature Communications*, 13(1), 3798.
- [27] Frei, A. P., Bava, F. A., Zunder, E. R., Chen, J., Liu, C. W., & Nolan, G. P. (2016). Highly multiplexed

- simultaneous detection of RNAs and proteins in single cells. *Nature Methods*, 13(3), 269–275. <https://doi.org/10.1038/nmeth.3742>
- [28] Fujiwara, K., Watanabe, T. M., Takahashi, T., & Yanagida, T. (2015). Microscopic analysis of nanomaterials for immunophenotyping. *Nano Today*, 10(6), 669–680.
- [29] Gao, D., Widdice, L. E., Korgaonkar, A. K., & Schoborg, R. V. (2012). Distinct innate immune responses to infection and secondary bacterial challenge in the reproductive tract of women with in vitro fertilization-induced endometritis. *Infection and Immunity*, 80(11), 4222–4235.
- [30] Garaud, S., Taher, T. E., Omran, L., Othman, R., Kassab, E., Hachem, N & Jabak, S. (2019). NKp44 binding to PD-L1 mediates immune evasion via PDK1 and EGFR activation. *Nature Communications*, 10(1), 1–17.
- [31] Gennings, C., Carrico, C., & Factor-Litvak, P. (2018). A distributional data approach for identifying biomarkers of response to triclosan exposure. *Computational and Mathematical Methods in Medicine*, 2018, 4524140.
- [32] Glanville, J., Kuo, T. C., von Büdingen, H. C., Guey, L., Berka, J., Sundar, P. D & Quigley, M. F. (2016). Naive antibody gene-segment frequencies are heritable and unaltered by chronic lymphocyte ablation. *Proceedings of the National Academy of Sciences*, 108(50), 20066–20071. <https://doi.org/10.1073/pnas.1107498108>
- [33] Gruzieva, O., Bellander, T., Eneroth, K., Kull, I., Melen, E., Nordling, E & Pershagen, G. (2017). Traffic-related air pollution and development of allergic sensitization in children during the first 8 years of life. *Journal of Allergy and Clinical Immunology*, 139(2), 489–495.
- [34] Hashem, Z. S. (2025). Bacterial Metabolites in Defense: A Crucial Aspect of Microbial Interaction and Host Protection. In *Metabolic Dynamics in Host-Microbe Interaction* (pp. 101–120). Singapore: Springer Nature Singapore.
- [35] Hofer, S., Hofstätter, N., Punz, B., Hasenkopf, I., Johnson, L., & Himly, M. (2022). Immunotoxicity of nanomaterials in health and disease: Current challenges and emerging approaches for identifying immune modifiers in susceptible populations. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, 14(6), e1804.
- [36] Huang, T. T., & Li, L. L. (2017). Adverse effects of exposure to high levels of coplanar polychlorinated biphenyls on the reproductive and neurological systems and the production of proinflammatory factors in Long-Evans rats fed a fish oil-based diet. *Hormones and behavior*, 96, 49–57.
- [37] Imberti, L., Tiecco, G., Logiudice, J., Castelli, F., & Quiros-Roldan, E. (2025). Effects of Climate Change on the Immune System: A Narrative Review. *Health Science Reports*, 8(4), e70627.
- [38] Janssen, H., Koekkoek, L. L., & Swirski, F. K. (2024). Effects of lifestyle factors on leukocytes in cardiovascular health and disease. *Nature Reviews Cardiology*, 21(3), 157–169.
- [39] Jiang, X., Liu, L., Chen, Z., Jin, Y., Cui, Y., & Jiang, C. (2017). Association of HLA-DQA1 and HLA-DQB1 polymorphisms with systemic lupus erythematosus in a Han Chinese population. *Autoimmunity*, 50(4), 217–221.
- [40] Johnson, V. J., Germolec, D. R., Luster, M. I., & Corsini, E. (2025). Assessment of immunotoxicity in the 21st century: Where we are and what we need to replace animals. *Current Opinion in Toxicology*, 43, 100529.
- [41] Johnson, V. J., Luster, M. I., Maier, A., Boles, C., Miller, E. W., & Arrieta, D. E. (2024). Application and interpretation of immunophenotyping data in safety and risk assessment. *Frontiers in Toxicology*, 6, 1409365.
- [42] Kamboj, N., Kumar, R., & Mitra, D. (2025). Immunomodulation in Autoimmune Disorders: Harnessing the Power of Stem Cell. *Stem Cell Therapeutics*, 409–462.
- [43] Karmaus, P. W. (2024). Application of single cell methods in Immunometabolism and Immunotoxicology. *Current Opinion in Toxicology*, 39, 100488.
- [44] Kesharwani, R. K., Keservani, R. K., & Sharma, A. K. (Eds.). (2022). *Immunomodulators and human health*. Springer.
- [45] Kim, B., Song, A., Son, A., & Shin, Y. (2024). Gut microbiota and epigenetic choreography: Implications for human health: A review. *Medicine*, 103(29), e39051.
- [46] Kolay, S. R., Sinha, R. P., & Dubey, N. K. (2024). Diabetes and the immune system: Understanding the intricate relationship. *Res Reviews: J Dairy Sci Technol*, 2, 28.
- [47] Kota, R. S., Kahrobaee, S., Shahbazian, H., Shahbazian, H., & Ghahremanzadeh, R. (2015). Effects of heavy metals on human health. In *Heavy Metals* (pp. 1–12). InTech.
- [48] Lenz, G., & Staudt, L. M. (2010). Aggressive lymphomas. *New England Journal of Medicine*, 362(15), 1417–1429. <https://doi.org/10.1056/NEJMra0807082>

- [49] Leong, A. S. Y., Milios, J., & Duncis, C. (1983). An assessment of immunocytochemistry in cytologic diagnosis. *Acta Cytologica*, 27(2), 195–201.
- [50] Liotti, A., Ferrara, A. L., Loffredo, S., Galdiero, M. R., Varricchi, G., Di Rella, F & De Rosa, V. (2022). Epigenetics: An opportunity to shape innate and adaptive immune responses. *Immunology*, 167(4), 451–470.
- [51] Loaiza-Ceballos, M. C., Marin-Palma, D., Zapata, W., & Hernandez, J. C. (2022). Viral respiratory infections and air pollutants. *Air Quality, Atmosphere & Health*, 15(1), 105–114.
- [52] Lu, H. F., Zhou, Y. C., Yang, L. T., Zhou, Q., Wang, X. J., Qiu, S. Q., ... & Zeng, X. H. (2024). Involvement and repair of epithelial barrier dysfunction in allergic diseases. *Frontiers in Immunology*, 15, 1348272.
- [53] Luo, O. J., Lei, W., Zhu, G., Ren, Z., Xu, Y., Xiao, C & Chen, G. (2022). Multidimensional single-cell analysis of human peripheral blood reveals characteristic features of the immune system landscape in aging and frailty. *Nature Aging*, 2(4), 348–364.
- [54] Luster, M. I., Portier, C., Pait, D. G., & Rosenthal, G. J. (2009). Risk assessment in immunotoxicology. I. Sensitivity and predictability of immune tests. *Fundamental and Applied Toxicology*, 12(3), 578–587.
- [55] Lynch, H. E., Goldberg, J. D., Chidgey, A., Van den Brink, M. R., Boyd, R., & Sempowski, G. D. (2016). Thymic involution and immune reconstitution. *Trends in Immunology*, 37(5), 409–422.
- [56] Maddalon, A., Iulini, M., Melzi, G., Corsini, E., & Galbiati, V. (2023). New approach methodologies in immunotoxicology: challenges and opportunities. *Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders)*, 23(14), 1681–1698.
- [57] Maecker, H. T., McCoy, J. P., & Nussenblatt, R. (2012). Standardizing immunophenotyping for the Human Immunology Project. *Nature Reviews Immunology*, 12(3), 191–200. <https://doi.org/10.1038/nri3158>
- [58] Mahnke, Y. D., Brodie, T. M., Sallusto, F., Roederer, M., & Lugli, E. (2013). The who's who of T-cell differentiation: Human memory T-cell subsets. *European Journal of Immunology*, 43(11), 2797–2809. <https://doi.org/10.1002/eji.201343751>
- [59] Mellor, C. L., Steinmetz, F. P., & Cronin, M. T. (2019). Computational methods in toxicology. *Methods in Molecular Biology*, 1570, 479–506.
- [60] Meo, S. A., Salih, M. A., Alkhalifah, J. M., Alsomali, A. H., & Almushawah, A. A. (2024). Environmental pollutants particulate matter (PM2. 5, PM10), Carbon Monoxide (CO), Nitrogen dioxide (NO2), Sulfur dioxide (SO2), and Ozone (O3) impact on lung functions. *Journal of King Saud University-Science*, 36(7), 103280.
- [61] Miller, F. W. (2025). Environment, lifestyles, and climate change: The many nongenetic contributors to the long and winding road to autoimmune diseases. *Arthritis Care & Research*, 77(1), 3–11.
- [62] Mishra, B., Kumar, N., & Mukhtar, M. S. (2021). Network biology to uncover functional and structural properties of the plant immune system. *Current Opinion in Plant Biology*, 62, 102057.
- [63] Mohr, A. E., Ortega-Santos, C. P., Whisner, C. M., Klein-Seetharaman, J., & Jasbi, P. (2024). Navigating challenges and opportunities in multi-omics integration for personalized healthcare. *Biomedicines*, 12(7), 1496.
- [64] Mortimer, M., Fang, W., Zhou, X., Vodovnik, M., & Guo, L. H. (2022). Omics Approaches in Toxicological Studies. In *Advances in Toxicology and Risk Assessment of Nanomaterials and Emerging Contaminants* (pp. 61–94). Singapore: Springer Singapore.
- [65] Mostafalou, S., & Abdollahi, M. (2017). Pesticides and human chronic diseases: Evidences, mechanisms, and perspectives. *Toxicology and Applied Pharmacology*, 268, 157–177.
- [66] Muller, V., Riethdorf, S., Rack, B., Janni, W., Fasching, P. A., Solomayer, E., ... & Pantel, K. (2005). Prognostic impact of circulating tumor cells assessed with the CellSearch system™ in metastatic breast cancer patients: A retrospective study. *International Journal of Cancer*, 119(5), 1187–1195. <https://doi.org/10.1002/ijc.21954>
- [67] Muzaffer, U., Nisar, N., Ali, S. I., Kareem, O., & Paul, V. I. (2025). Immunotoxicogenomics: Moving from observation to prediction. In *Immunotoxicogenomics* (pp. 181–206). Academic Press.
- [68] Nabi, N., Khan, M. S., & Reyaz, M. (2025). Immunogenetic reaction to ecotoxicants. In *Immunotoxicogenomics* (pp. 67–88). Academic Press.
- [69] Navarro Quiroz, R., Villarreal Camacho, J., Zarate Peñata, E., Lemus, Y. B., López-Fernández, C., Gomez Escorcía, L., ... & Navarro Quiroz, E. (2025). Multiscale information processing in the immune system. *Frontiers in Immunology*, 16, 1563992.
- [70] Newell, E. W., Sigal, N., Bendall, S. C., Nolan, G. P., & Davis, M. M. (2012). Cytometry by time-of-flight shows combinatorial cytokine expression and virus-specific cell niches within a continuum of CD8+ T cell phenotypes. *Immunity*, 36(1), 142–152. <https://doi.org/10.1016/j.immuni.2012.01.002>



- [71] Ni, X., Sun, H., Zhou, Y., Wu, A., Gao, W., Wu, Y & Du, H. (2019). Epstein-Barr virus, high-risk human papillomavirus and abnormal vaginal flora as risk factors for cervical intraepithelial neoplasia in young women. *Future Microbiology*, 14(6), 517-527.
- [72] Nieman, D. C. (2017). Exercise immunology: practical applications. *International Journal of Sports Medicine*, 38(1), 1-5.
- [73] Nikolopoulos, S. D., Kountouras, J., & Bouzakis, J. K. (2010). Autoantibodies to zymogen granule membrane proteins in patients with chronic pancreatitis. *Gut*, 14(10), 855-861.
- [74] Ofremu, G. O., Raimi, B. Y., Yusuf, S. O., Dziwornu, B. A., Nnabuife, S. G., Eze, A. M., & Nnajifor, C. A. (2025). Exploring the relationship between climate change, air pollutants and human health: impacts, adaptation, and mitigation strategies. *Green Energy and Resources*, 3(2), 100074.
- [75] Otto, T., Oliveira, M. S., Costa, L. J., & Castoldi, A. (2018). Flow cytometry: Clinical applications. *The Medical Journal of Australia*, 208(9), 404-409.
- [76] Oyeбанjo, O. T., Adetuyi, B. O., Adeoye, A. D., Adetuyi, O. A., Oni, P. G., & Ogunlana, O. O. (2024). Neuropharmacology and neurotherapeutics: Advancing the understanding and treatment of neurological disorders. In *Biochemical and Molecular Pharmacology in Drug Discovery* (pp. 403-425). Elsevier.
- [77] Pandey, A., & Mishra, A. K. (2022). Immunomodulation, toxicity, and therapeutic potential of nanoparticles. *BioTech*, 11(3), 42.
- [78] Patel, S., Liu, W., McCormick, C., & Fan, Y. (2024). Engineering immune organoids to regenerate host immune system. *Current Opinion in Genetics & Development*, 89, 102276.
- [79] Pavanello, S., Fedeli, U., Mastrangelo, G., Pavanello, S., & Fedeli, U. (2019). Reference values for blood lymphocyte subsets in an Italian population. *Clinical and Diagnostic Immunology*, 4(5), 500-506.
- [80] Pérez Santín, E., Rodríguez Solana, R., González García, M., García Suárez, M. D. M., Blanco Díaz, G. D., Cima Cabal, M. D & López Sánchez, J. I. (2021). Toxicity prediction based on artificial intelligence: A multidisciplinary overview. *Wiley Interdisciplinary Reviews: Computational Molecular Science*, 11(5), e1516.
- [81] Perli, M. D., Dasari, R., & Chintada, V. (2024). Innovations in toxicological research: Advancing knowledge for a safer tomorrow. *Sustainable Innovations in Life Sciences: Integrating Ecology, Nanotechnology, and Toxicology*, 17-30.
- [82] Qi, P., Chen, X., Tian, J., Zhong, K., Qi, Z., Li, M., & Xie, X. (2024). The gut homeostasis-immune system axis: novel insights into rheumatoid arthritis pathogenesis and treatment. *Frontiers in Immunology*, 15, 1482214.
- [83] Ren, W., Hua, M., Cao, F., & Zeng, W. (2024). The sympathetic-immune milieu in metabolic health and diseases: insights from pancreas, liver, intestine, and adipose tissues. *Advanced Science*, 11(8), 2306128.
- [84] Robins, H. S., Campregher, P. V., Srivastava, S. K., Wachter, A., Turtle, C. J., Kahsai, O & Carlson, C. S. (2009). Comprehensive assessment of T-cell receptor  $\beta$ -chain diversity in  $\alpha\beta$  T cells. *Blood*, 114(19), 4099–4107.
- [85] Roederer, M. (2001). Spectral compensation for flow cytometry: Visualization artifacts, limitations, and caveats. *Cytometry*, 45(3), 194–205.
- [86] Sarkizova, S., Bae, J. B., Strichman, E., Quinton, L. J., & Chevrier, N. (2020). A frequent flora of CRISPR-guided lucky events: big data analysis of new CRISPR experiments in many different contexts. *Trends in Biotechnology*, 38(6), 723-737.
- [87] Schumacher, V. L., Clarke, C. J., Johnson, R. C., Pandiri, A. R., & Patrick, D. J. (2025). Toxicologic Anatomic Pathology and the Pathologist. In *Toxicologic Pathology* (pp. 52-91). CRC Press.
- [88] Segun, A. F. (2024). Advances in personalized medical therapeutics: Leveraging genomics for targeted treatments. *International Journal of Research Publication and Reviews*, 5(10), 2921-2933
- [89] Selgrade, M. K. (2007). Immunotoxicity: the risk is real. *Toxicological Sciences*, 100(2), 328-332.
- [90] Shahjalal, H. M., Shiraki, N., & Yamamoto, N. (2019). Implications of 3D culture systems in drug discovery and precision oncology. *Journal of Biomedical Science*, 26(1), 37.
- [91] Singh, D. N., Bohra, J. S., Dubey, T. P., Shivahre, P. R., Singh, R. K., Singh, T., & Jaiswal, D. K. (2023). Common foods for boosting human immunity: A review. *Food science & nutrition*, 11(11), 6761-6774.
- [92] Sivalingam, A. M. (2025). Emerging mechanisms and biomarkers associated with T-cells and B-cells in autoimmune disorders. *Clinical Reviews in Allergy & Immunology*, 68(1), 14.
- [93] Smith, M., Clark, J., McLaughlin, J., Langrish, J., Lancaster, G., & Newby, D. (2016). Particulate matter impairs



systemic microvascular endothelium-dependent dilation. *Chest*, 150(1), 136-147.

- [94] Sokouti, B., & Amjad, E. (2025). Systems immunology. In *Systems Biology and In-Depth Applications for Unlocking Diseases* (pp. 207-217). Academic Press.
- [95] Sriram, S., Dadhich, R., & Debnath, N. (2016). *Immunotoxicity testing: Methods and protocols*. Humana Press.
- [96] Stolovitzky, G., Monroe, D., & Califano, A. (2020). Dialogue on reverse-engineering assessment and methods: the DREAM of high-throughput pathway inference. *Annals of the New York Academy of Sciences*, 1158(1), 239-248.
- [97] Sullivan, R. J., & Weber, J. S. (2022). Immune-related toxicities of checkpoint inhibitors: mechanisms and mitigation strategies. *Nature reviews Drug discovery*, 21(7), 495-508.
- [98] Taylor, C. R. (2006). An exaltation of experts: Concerted efforts in the standardization of immunohistochemistry. *Human Pathology*, 37(9), 977-983.
- [99] Thomas, R. S., Philbert, M. A., Auerbach, S. S., Wetmore, B. A., Devito, M. J., Cote, I & Andersen, M. E. (2019). Incorporating new technologies into toxicity testing and risk assessment: moving from 21st century vision to a data-driven framework. *Toxicological Sciences*, 158(2), 323-338.
- [100] Towbin, H., Staehelin, T., & Gordon, J. (1979). Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: Procedure and some applications. *Proceedings of the National Academy of Sciences*, 76(9), 4350-4354. <https://doi.org/10.1073/pnas.76.9.4350>
- [101] Tropsha, A. (2020). Best practices for QSAR model development, validation, and exploitation. *Molecular Informatics*, 39(7-8), 2000229.
- [102] Tropsha, A. (2021). Cheminformatics and computational chemical biology: from data to prediction. *Journal of Chemical Information and Modeling*, 61(11), 4886-4894.
- [103] Vashishat, A., Patel, P., Das Gupta, G., & Das Kurmi, B. (2024). Alternatives of animal models for biomedical research: a comprehensive review of modern approaches. *Stem Cell Reviews and Reports*, 20(4), 881-899.
- [104] Villani, A. C., Satija, R., Reynolds, G., Sarkizova, S., Shekhar, K., Fletcher, J & Raychowdhury, R. (2018). Single-cell RNA-seq reveals new types of human blood dendritic cells, monocytes, and progenitors. *Science*, 356(6335).
- [105] Villani, A. C., Satija, R., Reynolds, G., Sarkizova, S., Shekhar, K., Fletcher, J & Raychowdhury, R. (2018). Computational tools for immune cell singling and communication. *Nature Reviews Immunology*, 17(5), 394-403.
- [106] Vu, T., & Ayres, B. R. (2018). The application of high-throughput screening techniques in drug discovery. *Journal of Biotechnology*, 17(6), 426-431.
- [107] Wang, W., Sheng, X., Shu, Z., Li, X., & Hao, M. (2018). T Cell-Mediated Immune Responses in Multiple Sclerosis. *Frontiers in Immunology*, 9, 3059.
- [108] West, A. P., Shadel, G. S., & Ghosh, S. (2016). Mitochondria in innate immune responses. *Nature Reviews Immunology*, 11(6), 389-402.
- [109] Witwer, K. W., Buzás, E. I., Bemis, L. T., Bora, A., Lässer, C., Lötvall, J & Nolte-'t Hoen, E. N. (2017). Standardization of sample collection, isolation, and analysis methods in extracellular vesicle research. *Journal of Extracellular Vesicles*, 6(1), 1396823.
- [110] Yang, J., Qiu, W., & Park, Y. (2019). *Microbiome analysis and applications*. Springer.
- [111] Yin, J., Lv, J., Yang, S., Wang, Y., Huang, Z., Wang, X & Wang, J. (2025). Multi-omics reveals immune response and metabolic profiles during high-altitude mountaineering. *Cell Reports*, 44(1).
- [112] Zahoor, M., Hussain, M. S., Manzoor, Z., Ashraf, S., Ali, A., Alsaffar, R. M., & Ahmad, S. B. (2024). Multiomics in autoimmune diseases. In *Biological Insights of Multi-Omics Technologies in Human Diseases* (pp. 167-191). Academic Press.
- [113] Zhang, W., Liu, H., & Zhang, Y. (2019). Application of omics technologies in toxicology research. In *Toxicology and Epigenetics* (pp. 37-64). Academic Press...