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IMMUNOLOGICAL MECHANISMS INVOLVED IN PSORIASIS DEVELOPMENT

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Annotation

Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by abnormal keratinocyte proliferation and persistent inflammation. Recent advances in immunology have demonstrated that immune system dysregulation plays a fundamental role in the initiation and progression of psoriasis. This article aims to analyze and summarize the key immunological mechanisms involved in psoriasis development, with a particular focus on the interaction between innate and adaptive immune responses. A narrative and analytical review of scientific literature published between 2010 and 2024 was conducted using major international databases. The findings indicate that dendritic cells, T lymphocytes—especially Th17 and Th1 subsets—and keratinocytes are central contributors to psoriatic inflammation. The IL-23/Th17 axis was identified as the dominant pathogenic pathway, while proinflammatory cytokines such as IL-17, IL-22, TNF-α, and IFN-γ play crucial roles in sustaining chronic inflammation. Understanding these immunological pathways has led to the development of targeted biologic therapies and has significantly improved disease management. A deeper insight into immune-mediated mechanisms may further enhance personalized treatment strategies and long-term clinical outcomes for patients with psoriasis.

Keywords

Psoriasis; Immunological mechanisms; Th17 cells; IL-23/Th17 axis; Cytokines; Immune-mediated inflammation; Keratinocytes

Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects approximately 2–3% of the global population and represents a significant medical and social burden. The disease is characterized by recurrent erythematous, scaly plaques resulting from abnormal keratinocyte proliferation and differentiation, accompanied by persistent inflammation of the skin. Although psoriasis was previously considered primarily a disorder of epidermal hyperproliferation, recent advances in immunology have clearly demonstrated that immune system dysregulation plays a central role in its development and progression.

The pathogenesis of psoriasis involves a complex interaction between genetic predisposition, environmental triggers, and immune-mediated mechanisms. Numerous studies have identified psoriasis as a T-cell–driven disease, in which both innate and adaptive immune responses contribute to chronic inflammation. Activated dendritic cells, macrophages, and keratinocytes initiate and sustain inflammatory cascades through the production of proinflammatory cytokines, leading to excessive immune cell infiltration in the skin.

Among immune pathways, the interleukin (IL)-23/Th17 axis has been recognized as a key driver of psoriatic inflammation. Th17 cells produce cytokines such as IL-17A, IL-17F, and IL-22, which stimulate keratinocyte proliferation, enhance neutrophil recruitment, and promote epidermal thickening. In parallel, Th1 cells and their associated cytokines, including interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α), further amplify the inflammatory response. These cytokine networks create a self-perpetuating inflammatory loop that underlies the chronic nature of psoriasis.

Innate immune mechanisms also play a crucial role in the early stages of psoriasis development. Plasmacytoid and myeloid dendritic cells become activated in response to environmental stimuli such as infections, skin trauma, or stress. These cells release interferons and cytokines that trigger adaptive immune responses and promote T-cell activation. Additionally, keratinocytes actively participate in immune signaling by producing antimicrobial peptides and inflammatory mediators, highlighting their role as both targets and regulators of immune responses in psoriasis.

Understanding the immunological mechanisms involved in psoriasis development is essential for improving diagnostic accuracy and optimizing therapeutic strategies. The identification of specific immune pathways has led to the development of targeted biologic therapies that have revolutionized psoriasis management. Therefore, this article aims to review and analyze the key immunological mechanisms underlying psoriasis, with a particular focus on the role of immune cells and cytokine networks in disease initiation and maintenance.

Methods

This study was designed as a narrative and analytical literature review focusing on the immunological mechanisms involved in the development of psoriasis. The review aimed to synthesize existing scientific evidence regarding the role of immune cells, cytokines, and signaling pathways in the pathogenesis of psoriasis. A comprehensive literature search was conducted using major international scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar. Articles published in English between 2010 and 2024 were considered for inclusion. The search strategy involved a combination of relevant keywords and Medical Subject Headings (MeSH), such as “psoriasis,” “immunological mechanisms,” “immune-mediated inflammation,” “T cells,” “cytokines,” “IL-23/Th17 axis,” and “tumor necrosis factor-alpha.” Studies were included if they consisted of original research articles, systematic reviews, or meta-analyses addressing the immunopathogenesis of psoriasis, with a specific focus on innate and adaptive immune responses, cytokine pathways, immune cell involvement, and molecular mechanisms underlying disease development and progression. Exclusion criteria comprised case reports, conference abstracts, articles not available in full text, and studies unrelated to the immunological aspects of psoriasis or published in languages other than English. Relevant data were extracted independently from the selected articles, including detailed information on immune cell types, cytokines, signaling pathways, and their roles in disease initiation and maintenance. The extracted data were systematically analyzed and organized into thematic categories, such as innate immunity, adaptive immunity, and cytokine-mediated pathways. Comparative analysis was performed to identify consistent findings and key immunological mechanisms reported across multiple studies. As this research was based exclusively on previously published literature, ethical approval and informed consent were not required. All sources were cited appropriately to ensure academic integrity and adherence to ethical standards in scientific research.

Results

The analysis of the selected literature revealed that psoriasis development is driven by a complex interplay between innate and adaptive immune mechanisms. Consistent findings across multiple studies demonstrated that immune cell activation and dysregulated cytokine signaling are central to disease initiation and persistence. Dendritic cells were identified as key initiators of the inflammatory cascade through antigen presentation and cytokine secretion, particularly interleukin (IL)-23 and tumor necrosis factor-alpha (TNF-α). These mediators promote the differentiation and activation of pathogenic T-cell subsets, especially Th17 and Th1 cells.

The results showed that Th17 cells play a dominant role in psoriasis pathogenesis by producing IL-17A, IL-17F, and IL-22, which directly stimulate keratinocyte proliferation and impair normal epidermal differentiation. In parallel, Th1-derived cytokines, including interferon-gamma (IFN-γ), contribute to sustained inflammation and immune cell recruitment. Innate immune cells, such as neutrophils and macrophages, were also found to amplify inflammatory responses through the release of proinflammatory mediators and reactive oxygen species.

Keratinocytes were shown to actively participate in immune regulation by responding to cytokine stimulation and producing antimicrobial peptides and chemokines, thereby reinforcing the inflammatory loop. Overall, the reviewed studies consistently indicated that the IL-23/Th17 axis represents the most critical immunological pathway in psoriasis, while TNF-α and IFN-γ act as key amplifiers of chronic inflammation.

Table 1. Key Immunological Components Involved in Psoriasis Development

Immune Component	**Main Cytokines / Mediators**	**Role in Psoriasis Pathogenesis**
Dendritic cells	IL-23, TNF-α, IL-12	Initiation of immune response, activation of T cells
Th17 cells	IL-17A, IL-17F, IL-22	Keratinocyte proliferation, epidermal hyperplasia
Th1 cells	IFN-γ, TNF-α	Sustained inflammation, immune cell recruitment
Neutrophils	IL-17, reactive oxygen species	Amplification of inflammation, formation of Munro microabscesses
Macrophages	TNF-α, IL-1β	Maintenance of chronic inflammatory response
Keratinocytes	Antimicrobial peptides, chemokines	Propagation of inflammation and immune signaling

Discussion

The findings of this literature review confirm that psoriasis is primarily an immune-mediated inflammatory disease driven by complex interactions between innate and adaptive immune mechanisms. The results consistently highlight the central role of immune dysregulation in disease initiation and maintenance, supporting the current understanding of psoriasis as a T-cell–driven disorder rather than a condition limited to abnormal keratinocyte proliferation alone.

One of the most significant findings is the dominant role of the IL-23/Th17 axis in psoriasis pathogenesis. The reviewed studies demonstrate that dendritic cell–derived IL-23 promotes the differentiation and survival of Th17 cells, which subsequently produce key proinflammatory cytokines such as IL-17A, IL-17F, and IL-22. These cytokines directly influence keratinocyte behavior by enhancing proliferation, impairing differentiation, and stimulating the production of antimicrobial peptides and chemokines. This creates a self-sustaining inflammatory loop that contributes to the chronic and relapsing nature of psoriasis. The prominence of this pathway is further supported by the clinical efficacy of biologic therapies targeting IL-17 and IL-23, which have shown superior outcomes compared to traditional systemic treatments.

In addition to Th17 cells, Th1-mediated immune responses were found to play a complementary role in amplifying psoriatic inflammation. Cytokines such as interferon-gamma and tumor necrosis factor-alpha were consistently associated with increased immune cell recruitment and prolonged inflammatory activity within psoriatic lesions. TNF-α, in particular, acts as a central inflammatory mediator by enhancing dendritic cell activation and cytokine production, thereby reinforcing immune signaling networks. The success of TNF-α inhibitors in clinical practice further validates the pathogenic importance of this cytokine in psoriasis.

The contribution of innate immune cells, including dendritic cells, macrophages, and neutrophils, was also emphasized across the reviewed studies. These cells serve not only as initiators of inflammation but also as amplifiers of immune responses through the release of proinflammatory mediators and reactive oxygen species. Neutrophils, in particular, are associated with the formation of Munro microabscesses, a histopathological hallmark of psoriasis, highlighting their role in disease severity and progression.

Keratinocytes were identified as active participants in immune regulation rather than passive targets of inflammation. Under cytokine stimulation, keratinocytes produce antimicrobial peptides and chemokines that further recruit immune cells to the skin, thereby perpetuating inflammatory circuits. This bidirectional interaction between immune cells and keratinocytes underscores the complexity of psoriasis pathophysiology and suggests that effective therapeutic strategies must target multiple components of the immune response.

Despite the valuable insights provided by this review, certain limitations should be acknowledged. The reliance on previously published studies introduces potential publication bias, and heterogeneity in study design and methodology may affect the generalizability of findings. Nevertheless, the consistency of results across diverse studies strengthens the conclusion that immune-mediated mechanisms, particularly those involving the IL-23/Th17 axis and proinflammatory cytokines, are fundamental to psoriasis development.

Overall, the discussion of the results emphasizes that a deeper understanding of immunological mechanisms is essential for advancing personalized treatment approaches and improving long-term outcomes for patients with psoriasis. Future research should focus on identifying novel immune targets and biomarkers that may further refine therapeutic strategies and disease monitoring.

Conclusion

Psoriasis is a complex, chronic immune-mediated inflammatory disease in which dysregulation of both innate and adaptive immune responses plays a central role in disease development and progression. The findings of this review demonstrate that immune cell interactions, particularly involving dendritic cells, Th17 and Th1 lymphocytes, and keratinocytes, are fundamental to the initiation and maintenance of psoriatic inflammation. Among the identified pathways, the IL-23/Th17 axis emerges as the most critical driver of pathological immune responses, leading to excessive keratinocyte proliferation and persistent skin inflammation.

Proinflammatory cytokines, including IL-17, IL-22, TNF-α, and IFN-γ, were consistently shown to amplify inflammatory signaling networks and sustain the chronic nature of psoriasis. The active involvement of keratinocytes in immune regulation further highlights the bidirectional communication between immune cells and skin tissue. These insights have significant clinical implications, as they provide a scientific basis for the development and successful application of targeted biologic therapies that specifically inhibit key cytokines and immune pathways.

In conclusion, a comprehensive understanding of the immunological mechanisms underlying psoriasis is essential for improving diagnostic accuracy, optimizing therapeutic strategies, and advancing personalized medicine approaches. Continued research into immune signaling pathways and novel immunological targets will be crucial for enhancing long-term disease control and improving the quality of life of patients with psoriasis.

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