

Commentary on “Identification of CD19 as a shared biomarker via PPAR γ / β -catenin/Wnt3a pathway linking psoriasis and major depressive disorder”

Bin Zhou¹, Zhujun Ma², Jiahao Yang³, Lingui Li^{1,4}, Hanying Ma^{2,5,*}

¹Southwest Hospital, Third Military Medical University (Army Medical University), Chongqing, 400038, China

²China Three Gorges University, Yichang, 443000, China

³Department of Physiology, School of Basic Medicine and Tongji Medical College, Huazhong University of Science and Technology, Wuhan 4030030, China

⁴People's Hospital of Yanhe Tujia Autonomous County, Guizhou, 565399, China

⁵School of Life Sciences, Huanggang Normal University, Huanggang, 438000, China

*Author for correspondence:
Email: 1553626530@qq.com

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Abstract

This study presents a comprehensive exploration into the shared molecular mechanisms linking psoriasis and major depressive disorder (MDD), two conditions that are increasingly recognized as having potential comorbidities. It offers new insights into the immune and genetic pathways that may contribute to both disorders, emphasizing the potential of CD19 as a biomarker and therapeutic target through the PPAR γ / β -catenin/Wnt3a signaling pathway. The study's findings underscore the need for further investigation into how inflammation and immune dysregulation may drive both the physical and mental health symptoms observed in patients with psoriasis and MDD. In this commentary, I will analyze the key findings of this study, explore its implications, and discuss areas for future research.

Keywords: Psoriasis, Major depression disease, CD19, Mouse model, PPAR γ / β -catenin/Wnt3a

Understanding the Psoriasis-MDD Link

Psoriasis is traditionally viewed as an immune-mediated skin disorder characterized by hyperproliferative keratinocytes and chronic inflammation [1]. Recent studies, however, show that the impact of psoriasis extends beyond the skin, affecting cardiovascular health, metabolism, and mental well-being. Patients with psoriasis frequently report higher rates of depression, a finding consistent across multiple studies [2]. This comorbidity is particularly notable in severe cases of psoriasis and among those with psoriatic arthritis. Similarly, individuals with MDD show a higher risk of developing inflammatory diseases, including psoriasis, suggesting a bidirectional relationship between these conditions [3].

The shared pathways between psoriasis and MDD have long been hypothesized but remain underexplored at the molecular level. The present study bridges this gap by employing bioinformatics tools to identify differentially expressed genes (DEGs) common to both conditions, leveraging datasets from the GEO database, and performing functional enrichment analyses to elucidate the biological pathways involved. This data-driven approach led to the identification of CD19 as a central hub gene potentially driving both psoriasis and MDD through immune-related pathways.

Identification of CD19 as a Shared Biomarker

The study's central finding is the identification of CD19 as a hub gene through machine learning models, specifically the LASSO and random forest algorithms, suggesting its critical role

in both psoriasis and MDD pathophysiology. CD19 is known as a B cell marker involved in B cell activation and immune response [4]. Elevated levels of CD19 were validated in clinical samples from psoriasis and MDD patients, as well as in animal models for both conditions. The upregulation of CD19 in both diseases suggests that B cell activation may be a critical immunological overlap, highlighting the potential of CD19 as a biomarker for identifying individuals at risk of both conditions.

Additionally, the study's immune infiltration analysis using CIBERSORT revealed distinct immune cell changes in psoriasis and MDD. In psoriasis, there was an increase in naive B cells, follicular T helper cells, and resting NK cells, all of which were positively correlated with CD19 expression. In MDD, naive B cells and neutrophils were notably elevated. These findings reinforce the role of immune dysregulation and the unique involvement of B cells in both diseases.

Functional Pathways: PPAR γ / β -Catenin/Wnt3a

The study also explored the downstream pathways of CD19, specifically focusing on the PPAR γ / β -catenin/Wnt3a axis. PPAR γ , a nuclear receptor known for its role in lipid metabolism, is also a critical modulator of inflammation [5]. It has been associated with neuroprotective effects in MDD and the regulation of keratinocyte differentiation in psoriasis. β -catenin and Wnt3a are key components of the Wnt signaling pathway, which has been implicated in cellular proliferation, inflammation, and neurogenesis. In this study, lentiviral suppression of CD19 in mouse models was shown to alleviate the symptoms of psoriasisform dermatitis and depressive-like behaviors, an effect linked to increased expression of PPAR γ , β -catenin, and Wnt3a.

This mechanistic insight is significant because it suggests that the PPAR γ / β -catenin/Wnt3a axis could be targeted for therapeutic purposes in both diseases. By modulating this pathway, it may be possible to address the underlying immune dysregulation that drives both skin inflammation and depressive symptoms.

Implications for Treatment

The discovery of CD19 as a shared biomarker for psoriasis and MDD opens up new avenues for potential treatments targeting B cells. In recent years, B cell-depleting therapies, such as rituximab, have been explored in autoimmune diseases with varying success. Given the role of B cell activation in psoriasis and the immune alterations observed in MDD, therapies targeting CD19 or related pathways may offer relief for both conditions, particularly in patients suffering from the mental health impacts of chronic inflammatory diseases. The modulation of the PPAR γ pathway also presents an appealing option, as PPAR γ agonists are known for their anti-inflammatory properties.

Furthermore, this study's results may have implications for clinical practice, where patients with psoriasis could be screened for depressive symptoms and vice versa. Identifying at-risk patients could lead to earlier intervention and holistic treatment strategies that address both physical and psychological aspects of these conditions.

Strengths and Limitations

A key strength of this study lies in its integrative approach, combining bioinformatics, machine learning, and experimental validation in animal models. This robust methodological framework

allowed for the identification of biologically relevant genes and pathways, enhancing the reliability of the findings. Additionally, the use of both clinical samples and mouse models strengthens the study's translational relevance.

However, the study does have some limitations. First, the analysis relies heavily on data from public gene expression databases, which may lack the granularity required to capture the full complexity of psoriasis and MDD at the cellular level. Differences in sample characteristics, such as demographic variations or disease severity, could also impact the generalizability of the findings. Another limitation is that while the study establishes CD19 as a biomarker, the direct causal mechanisms through which CD19 influences both diseases remain to be fully elucidated. Future studies involving in-depth mechanistic analyses and clinical trials are necessary to validate CD19's role as a therapeutic target.

Future Directions

This study paves the way for several potential research directions. First, additional research into the PPAR γ / β -catenin/Wnt3a pathway could clarify its specific contribution to psoriasis and MDD and potentially identify other modifiable targets within the pathway. Investigating how other immune cells and cytokines interact with CD19 in these conditions could offer a more comprehensive understanding of immune dysregulation in psoriasis and MDD.

Furthermore, future studies should examine the impact of existing immunomodulatory treatments for psoriasis on depressive symptoms and vice versa. It would be valuable to determine if treating one condition could indirectly benefit the other, potentially reducing the need for multiple medications. Additionally, longitudinal studies following psoriasis patients could provide insights into the onset of depressive symptoms and identify early biomarkers for mental health risk.

Finally, clinical trials are needed to explore the safety and efficacy of targeting CD19 in patients with both psoriasis and MDD. This would represent a significant step forward in personalized medicine, potentially enabling a treatment approach that addresses the comorbidities of these complex disorders.

Conclusion

In conclusion, this study contributes to a growing body of evidence supporting the interconnectedness of inflammatory and psychological conditions. By identifying CD19 as a shared biomarker for psoriasis and MDD and elucidating its role within the PPAR γ / β -catenin/Wnt3a pathway, the study highlights potential therapeutic targets that may benefit both conditions. Given the high prevalence of comorbid MDD in psoriasis patients and the rising burden of these diseases, the findings underscore the importance of integrated treatment strategies that address both physical and mental health needs. Continued research on the immunological linkages between psoriasis and MDD promises to advance our understanding and treatment of these comorbid conditions, ultimately improving quality of life for affected individuals.

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