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Secukinumab affects the expression levels of LncRNAs MEG3 and MSX2P1 in an in vitro psoriasis model

Secukinumab, in vitro psoriasis modelinde uzun kodlamayan RNA'lar (lncRNA) MEG3 ve MSX2P1'in ekspresyon düzeylerini etkilemesi

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Abstract

Purpose: Psoriasis is a common chronic inflammatory skin disease characterized by recurrent, scaly plaques. IL-17 plays a central role in its pathogenesis, and Secukinumab—an anti-IL-17A monoclonal antibody—is widely used for treatment. Long non-coding RNAs (LncRNAs) regulate keratinocyte proliferation and immune responses, yet their response to IL-17 inhibition remains unclear. This study aimed to investigate the effect of Secukinumab on MEG3 and MSX2P1 lncRNA expression in a psoriasis cell culture model.

Materials and methods: HaCaT cells were stimulated with lipopolysaccharide (LPS) to mimic inflammatory conditions, followed by treatment with various doses of secukinumab. Cell viability was assessed at 24, 48, and 72 hours using CCK-8, with 7.5 mg/ml determined as the LD_{50} concentration. RNA was isolated, and gene expression levels were measured via qRT-PCR.

Results: The results demonstrated an approximately 20-fold reduction in MEG3 expression and an approximately 190-fold reduction in MSX2P1 expression following secukinumab treatment compared to the control group. These findings suggest that IL-17 inhibition may influence keratinocyte function through the modulation of LncRNAs associated with proliferation and inflammation.

Conclusion: Secukinumab appears to alter the expression patterns of key LncRNAs in keratinocytes. Further investigation is warranted to clarify the downstream molecular pathways involved and their relevance in the clinical management of psoriasis.

Keywords: Psoriasis, MEG3, MSX2P1, secukinumab, long non-coding RNA.

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Öz

Amaç: Psoriasis, tekrarlayan ve pullu plaklarla karakterize edilen yaygın bir kronik inflamatuar deri hastalığıdır. IL-17, hastalığın patogenezinde merkezi bir rol oynamakta olup, IL-17A'yı hedefleyen monoklonal bir antikor olan Secukinumab bu amaçla yaygın olarak kullanılmaktadır. Uzun zincirli kodlamayan RNA'lar (lncRNA'lar), keratinosit proliferasyonu ve bağışıklık yanıtlarının düzenlenmesinde rol oynamaktadır; ancak IL-17 blokajına verdikleri yanıt hâlâ net olarak bilinmemektedir. Bu çalışma, bir psoriasis hücre kültürü modelinde IL-17 inhibitörü Secukinumab'ın, keratinosit proliferasyonu ve inhibisyonunda rol oynayan MEG3 ve MSX2P1 adlı iki lncRNA'nın ekspresyonu üzerindeki etkisini araştırmayı amaçlamaktadır.

Gereç ve yöntem: HaCaT hücreleri, inflamatuar koşulları taklit etmek amacıyla lipopolisakkarit (LPS) ile uyarılmış ve ardından çeşitli dozlarda Secukinumab ile tedavi edilmiştir. Hücre canlılığı 24, 48 ve 72 saatlerde CCK-8 yöntemi ile değerlendirilmiş ve 7,5 mg/ml konsantrasyonu LD_{50} olarak belirlenmiştir. RNA izolasyonu yapılmış ve gen ekspresyon seviyeleri qRT-PCR yöntemiyle ölçülmüştür.

Bulgular: Secukinumab tedavisi sonrası, kontrol grubuna kıyasla MEG3 ekspresyonunda yaklaşık 20 kat, MSX2P1 ekspresyonunda ise yaklaşık 190 kat azalma gözlenmiştir. Bu bulgular, IL-17 inhibisyonunun, proliferasyon ve inflamasyonla ilişkili lncRNA'ların modülasyonu yoluyla keratinosit fonksiyonunu etkileyebileceğini düşündürmektedir.

Sonuç: Secukinumab keratinositlerde önemli lncRNA'ların ekspresyon düzenini değiştirebilmektedir. Psoriasis'in klinik yönetiminde bu değişikliklerin rolünü ve ilişkili moleküler yolları aydınlatmak için ileri çalışmalara ihtiyaç vardır.

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Anahtar kelimeler: Psoriasis, MEG3, MSX2P1, secukinumab, uzun kodlamayan RNA.

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Introduction

Psoriasis is a prevalent, chronic inflammatory dermatological condition defined by well-defined flaky plaques. It exhibits a high incidence rate and a propensity for relapse. The pathogenesis of psoriasis is intricate and not fully understood; it is believed to be related to multiple elements, including atypical keratinocyte proliferation and differentiation and immune disorders [1].

The epidermis is a continuously regenerating epithelial tissue, typically consisting of several layers: at the bottom, the basal layer (stratum basale), and at the top, the stratum corneum. Its primary function is protecting the body from possibly harmful surroundings by providing barriers. The basal layer cells account for the ongoing regeneration of the epidermis; however, only 15% of these cells are actively engaged in this process, while the remainder are in a quiescent state [2].

Nine distinct genomic regions have been identified as susceptible to psoriasis. Only the PSORS1 (Psoriasis susceptibility gene) has been robustly confirmed across all examined organisms [3].

Long noncoding RNAs (LncRNAs) are RNAs more than 200 nucleotides in length that lack protein-coding capacity. LncRNAs play roles in several critical biological functions, such as cellular balance, genomic imprinting, and growth [4].

Secukinumab is a human monoclonal antibody targeting interleukin-17 (IL-17A). In Phase III clinical trials involving moderate to severe plaque psoriasis, secukinumab demonstrated high efficacy and tolerability [5].

Advancements in understanding the critical role of T cells in psoriasis pathogenesis and chronic inflammatory pathways have facilitated the development of various biological agents targeting specific inflammatory processes [6].

LncRNA maternally expressed 3 (*MEG3*) is located at the *DLK1-MEG3* locus on chromosome 14q32.3. Significantly reduced expression of *MEG3* has been observed in various neoplasms, gastric NSLC, and gallbladder cancer. Overexpression of *MEG3* may inhibit proliferation and promote apoptosis in certain tumor cells. *MEG3* influences the growth, apoptosis, and metastasis of gastric and cervical cancer cells by regulating miR-21 expression. Physically, *MEG3* is associated with miR-21 expression. Nonetheless, the effect of *MEG3* on miR-21 on the growth and apoptosis of psoriatic cells remains uncertain [7].

Numerous mechanisms contribute to the reduction of *MEG3* expression in tumors, including deletion, hypermethylation of promoter and intergenic sites. The expression of *MEG3* has been shown to inhibit tumor proliferation and colony formation in vitro. The growth prevention is partially attributed to *MEG3*-induced apoptosis. *MEG3* facilitates the accumulation of p53 protein, stimulates transcription from a p53-dependent promoter, and selectively regulates the expression of p53 target genes. *MEG3* is composed of ten exons. Its transcription results in various *MEG3* transcripts arising from different RNA splicing. 12 *MEG3* RNA isoforms, designated as *MEG3* and *MEG3*a to *MEG3*k, have been identified. The predominant variant is *MEG3*, which includes 1-4 and 8-10 exons. The mature *MEG3* RNA is approximately 1600 nucleotides in length [8]. *MEG3* has been implicated in the elimination of mycobacteria through autophagy, indicating its potential role in regulating psoriasis autophagy and inflammation, a function not previously reported [9].

The lncRNA *Msh* homeobox 2 pseudogene 1 (*MSX2P1*) is associated with the *MSX* gene family, which belongs to the homeobox family. Homeobox genes constitute a ginormous and heterogeneous group of genes that perform a

crucial task in embryonic development across most organisms. The genes are defined with a specific DNA sequence known as a homeobox, which codes a recognizable protein homeodomain. Many homeodomains' proteins function as transcription factors integral to embryonic formation and cell differentiation [10]. *MSX2P1* promotes the proliferation of IL-22-stimulated keratinocytes by inhibiting microRNA (miRNA/miR)-6731-5p and upregulating S100A7 expression [11].

This study investigates the impact of keratinocyte proliferation and the inhibition of the IL-17 inhibitor secukinumab, the latest biological agent employed in psoriasis treatment, on the expression levels of *MEG3* and *MSX2P1* in a cell culture psoriasis model.

Materials and methods

HaCaT cell culture

HaCaT human keratinocyte cells were cultured to evaluate the effects of secukinumab (Verxant). Cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM; Sigma) supplemented with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin, and 1% amphotericin B (Capricorn). A total of 2.5×10^5 cells were seeded in 25 cm^2 flasks containing complete medium and incubated at 37°C in a humidified atmosphere with 5% CO_2. Upon reaching approximately 80% confluency, cells were passaged.

For subculturing, cells were washed with phosphate-buffered saline (PBS), treated with trypsin-EDTA, and incubated at 37°C for 5 minutes. After detachment, cells were collected by centrifugation. Cell viability and counts were assessed using a Neubauer chamber following trypan blue staining.

Cell viability test

To establish an in vitro psoriasis-like model, HaCaT cells were pre-treated with 200 ng/mL lipopolysaccharide (LPS; Sigma, L2630) for 24 hours. Following LPS stimulation, cells were exposed to increasing concentrations of secukinumab (Verxant) (0.1, 0.25, 0.5, 1, 2.5, 5, 7.5, and 10 mg/mL) to assess drug cytotoxicity. For this purpose, cells were cultured in 96-well plates and incubated at 37°C with 5% CO_2 for 24 hours. After treatment with LPS and secukinumab, cell viability was evaluated at 24, 48, and 72 hours using the Cell Counting Kit-8 (CCK-8; Dojindo). Briefly, 10 µL of CCK-8 solution was added to each well and incubated for 4 hours. Absorbance at 450nm was measured using a plate reader, and the half-maximal inhibitory concentration (LD_{50}) was calculated based on viability results.

RNA isolation

For total RNA extraction, HaCaT cells were seeded in each well of 6-well plates. After 24 hours of incubation, cells were stimulated with LPS, followed by 7.5 mg/mL secukinumab treatment after an additional 24 hours. Cells were then incubated for 72 hours before RNA isolation using the Hybrid-R Mini Kit (GeneALL), following the manufacturer's protocol.

Shortly, cells were lysed with RiboEx™, mixed with chloroform, and centrifuged at 12,000 × g for phase separation. The aqueous phase was recovered and mixed with RB1 buffer before loading onto Hybrid-R spin columns. Washing steps were sequentially performed with SW1 and RNW buffers. RNA was eluted in nuclease-free water, and concentration and purity were assessed using a NanoDrop spectrophotometer.

cDNA synthesis

cDNA conversion was performed for lncRNA expression analysis using (A.B.T.™ cDNA Synthesis Kit). The reaction mixture was prepared with 1x buffer in a 20 µl reaction volume.

Expression analysis

The expression reaction of *MEG3* and *MSX2P1* was prepared using the original primers and A.B.T. ™ 2X PCR MasterMix in a 20 µl total reaction volume for 40 cycles. The analysis was performed using PCR array data. The primers used in this study and their corresponding base sequences are shown in Table 1.

Table 1. Primers and base sequences

Primers	Base Sequence
MEG3-F	5' TTGAAACTTAACTCTTTTGGGGCA 3'
MEG3-R	5' TGCCGATATTGTTGTTCATCTTGT 3'
MSX2P1-F	5' CGTCACTGATACTCACCTCATA 3'
MSX2P1-R	5' GTACTGGCCTACAGAACTGGTA 3'
GAPDH-F	5' ATGTTCCAATATGATTCACCC 3'
GAPDH-R	5' ATGAGTCCTTCCACGATACC 3'

Potential targets analysis

Potential targets of *MEG3* were determined utilizing Encori (https://rnasysu.com/encori/). Afterwards, hierarchical classification and plot analysis were conducted utilising ShinyGO (https://bioinformatics.sdstate.edu/go/).

Statistical analysis

Expression changes were discovered using the 2-ΔΔCT method and web-based RT2 lncRNA PCR data analysis. The web-based analysis was performed based on Student's t-tests. All experiments were performed in triplicate. A *p*-value of <0.05 was considered statistically significant.

In this study, cell line experiments do not require ethical approval.

Results

Cell viability test

Based on the CCK-8 assay results, treatment with Secukinumab at a concentration of 7.5 mg/ml corresponded to the LD_{50} value, indicating that this dose induced approximately 50% cell death under the experimental conditions.

Expression analysis

Upon the induction of the psoriasis model in HaCaT cell culture, the expression levels of the lncRNA *MEG3* and the *MSX2P1* gene were assessed using quantitative real-time PCR, with GAPDH serving as the internal control. Relative to the control group, *MEG3* expression increased approximately 20.68-fold, while *MSX2P1* expression exhibited a substantial upregulation of approximately 190.02-fold. These results indicate that psoriasis-like inflammatory conditions in HaCaT cells may lead to significant dysregulation of *MEG3* and *MSX2P1*, suggesting a potential role for these genes in the molecular pathology of psoriasis.

To investigate the potential therapeutic effect of Secukinumab, induced HaCaT cells were subsequently analyzed. Secukinumab treatment resulted in a 0.27-fold change in *MEG3* expression and a 1.77-fold change in *MSX2P1* expression. These findings suggest that Secukinumab partially reversed the psoriasis-associated dysregulation of *MEG3* and *MSX2P1* expression (Table 2).

Table 2. Fold change in *MEG3* and *MSX2P1* expression in HaCaT cells after LPS-induced psoriasis model and subsequent secukinumab treatment

		Control Fold Change	Secukinumab Fold Change
1	**GAPDH**	1	1
2	**MEG3**	20.68	0.27
3	**MSX2P1**	190.02	1.77

MEG3 targets and signaling pathway analysis

The possible targets of lncRNA *MEG3* were identified using the ENCORI platform. These targets were then organized into a hierarchical structure using ShinyGO software, followed by chart analyses. The analysis indicated that *MEG3* target genes are primarily involved in signaling cascades pertinent to keratinocyte biology, including the IL-17, mTOR, PI3K-Akt, Hippo, Wnt, cell cycle, ErbB, and EGFR tyrosine kinase inhibitor resistance pathways, as well as metabolic processes such as cysteine and methionine metabolism and purine metabolism (Figure 1).

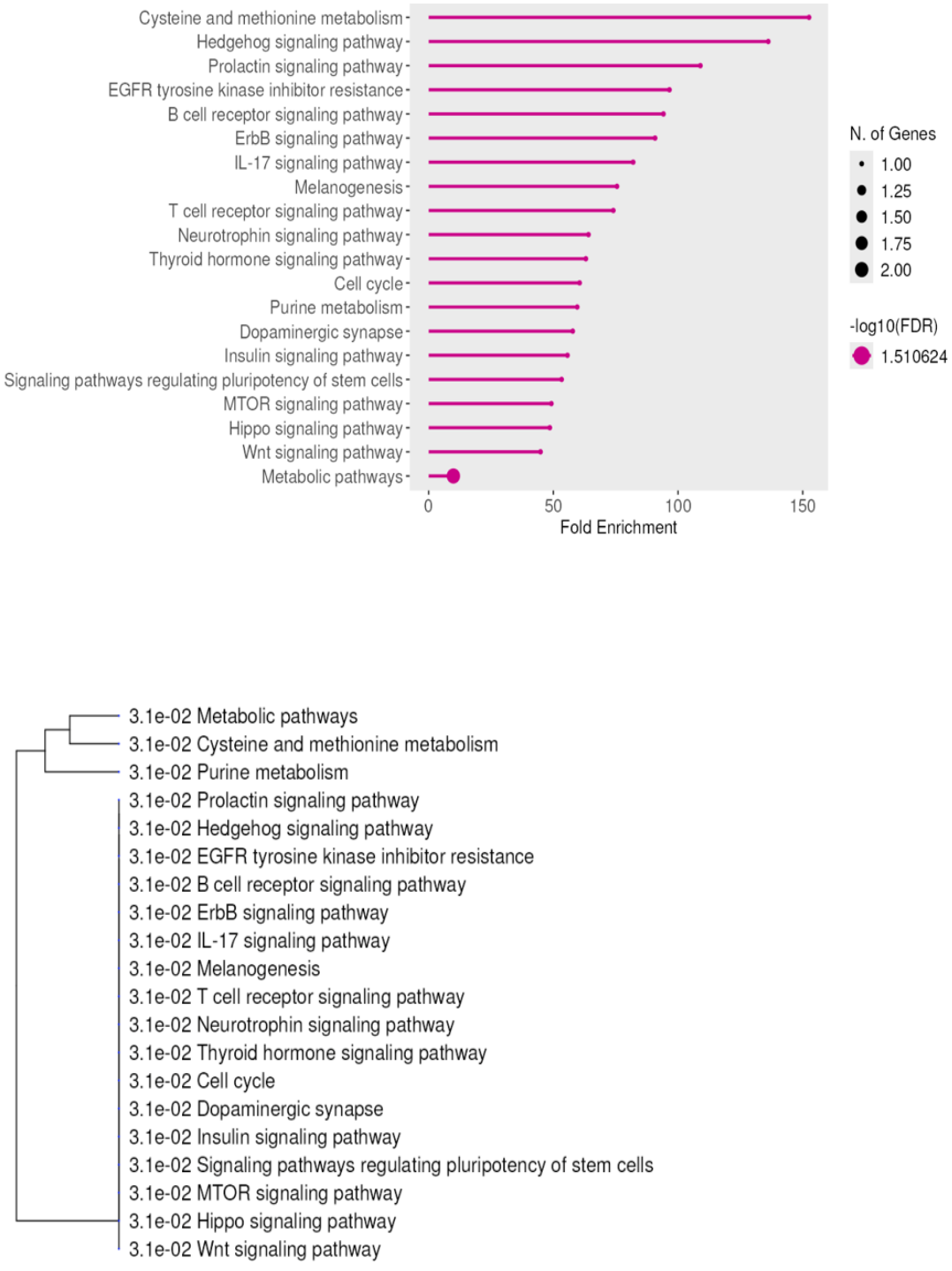

Figure 1. Hierarchical Classification and Chart analysis of MEG3 keratinocyte-related target genes

A separate pathway analysis concentrating on psoriasis-related targets of *MEG3* demonstrated enrichment in a similar array of pathways, including mTOR, PI3K-Akt, ErbB, cell cycle, and EGFR tyrosine kinase inhibitor resistance, alongside metabolic pathways such as cysteine and methionine metabolism (Figure 2). The overlap between keratinocyte-associated and psoriasis-associated pathway profiles suggests that *MEG3* may regulate common molecular mechanisms underlying both epidermal cell function and triggering psoriatic disease processes.

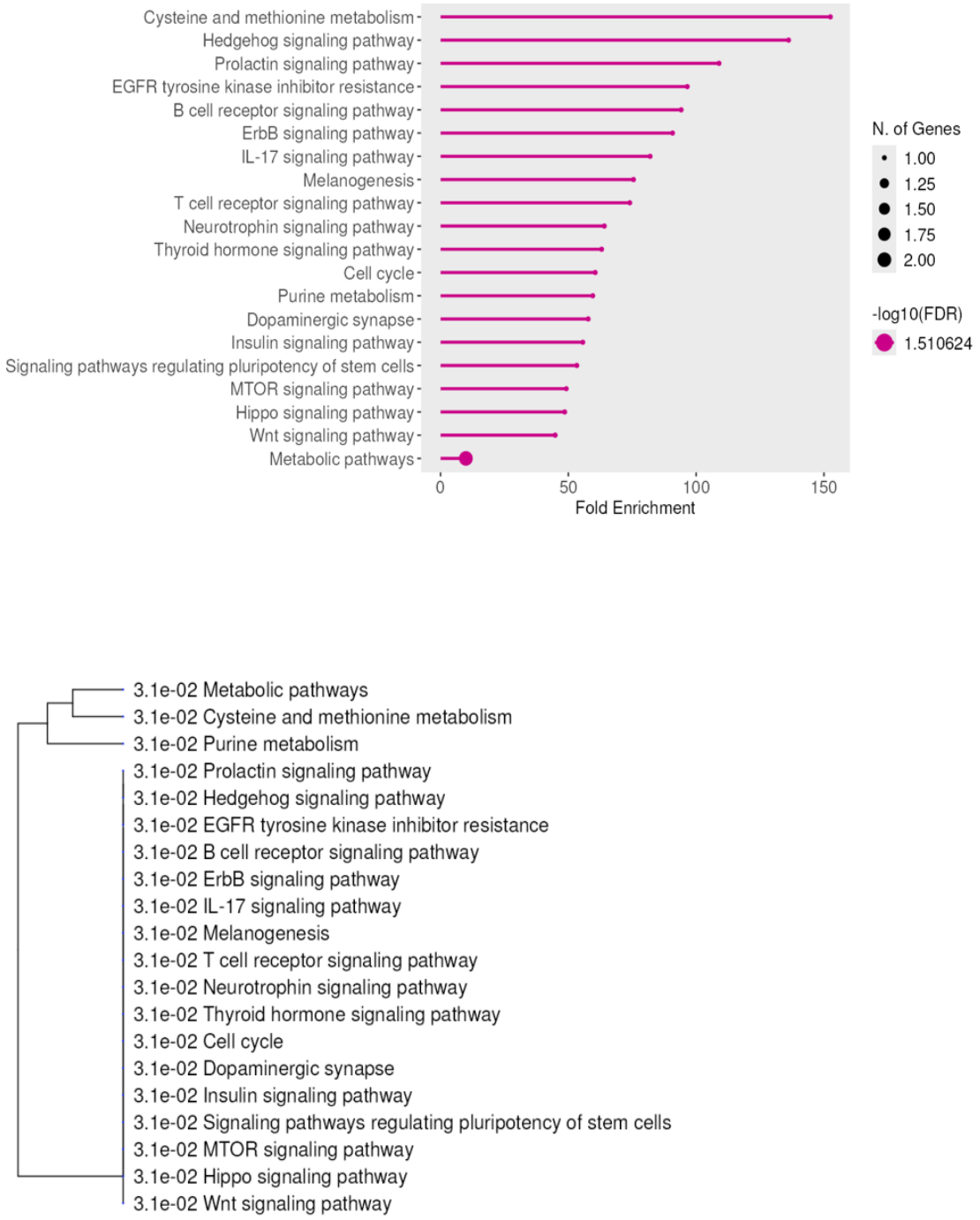

Figure 2. Hierarchical Classification and Chart analysis of MEG3 psoriasis-related target genes

Discussion

Psoriasis, recognized by the WHO as one of the major non-infectious disorders, impacts around 2-3% of the world's people. Mechanistically, immunological mediators of the IL-23 and IL-17 route cause the hyperproliferation and disrupted epidermal keratinocyte differentiation, leading to psoriatic lesions. Therapies that specifically aim at IL-23, IL-17, and IL-17RA are licensed for clinical usage and have excellent performance; in fact, psoriasis is the foremost illness to be effectively cured with therapies that directly inhibit the function of the cytokines of this pathway [12].

Secukinumab is a new-generation biologic drug that specifically targets IL-17, a key molecule in the disease course. Clinical trials have shown that secukinumab is effective in treating plaque psoriasis, in addition to psoriatic arthritis and ankylosing spondylitis. It targets IL-17 and prevents binding to the IL-17 receptor found in various cell types, including keratinocytes, thereby reducing IL-17-mediated effects [13, 14].

Chen et al. [15] reported that reduced expression of *MEG3* led to decreased expression of caspase-8 and Bax, while increasing the expression of Bcl-2, which acts as an inhibitor of apoptosis. Overexpression of *MEG3* significantly diminished miR-21 expression. In HaCaT and NKEK cells, overexpression of miR-21 counteracted the reduction in cell proliferation, elevated apoptosis, increased expression of caspase-8 and Bax, and decreased Bcl-2 expression induced via *MEG3* overexpression. In summary, *MEG3* can mitigate abundant proliferation and poor apoptosis of psoriatic keratinocytes by controlling the expression of miR-21 and caspase-8.

Recently, increasing evidence has elucidated the significant regulatory function of lncRNA *MEG3* in keratinocyte biology and the pathogenesis of psoriasis. Tang et al. [9] pointed out that *MEG3* expression is downregulated in keratinocytes and psoriatic mouse skin with TNF-α–treated, and that its overexpression suppresses inflammation while promoting autophagy by inhibiting the PI3K/AKT/mTOR signaling pathway. This is consistent with our bioinformatic findings, where *MEG3*-associated pathways were enriched in the control of inflammation, keratinocyte proliferation, and autophagy, suggesting a convergent mechanism in disease modulation. Furthermore, several psoriasis-related studies have emphasized the role of *MEG3* in broader regulatory networks involving immune–epidermal interactions. Shi et al. [16] reviewed that multiple psoriasis-associated LncRNAs, including *MEG3*, can regulate keratinocyte proliferation, differentiation, and inflammatory signaling, often through crosstalk with cytokine pathways such as IL-17 and TNF-α. This supports our pathway analysis, which identified cytokine–receptor interactions and NF-κB–mediated inflammation as downstream targets of *MEG3*. Collectively, our bioinformatic mapping of *MEG3* target genes in keratinocytes and psoriasis aligns closely with experimental studies showing its role in suppressing *PI3K/AKT/mTOR*–mediated inflammation, influencing IL-17–related immune pathways, and modulating keratinocyte function. These connections reinforce the notion that *MEG3* may serve as a therapeutic target bridging the epidermal and immune components of psoriasis.

In addition, immune-related literature connects these *MEG3*-modulated pathways to T cell–mediated psoriasis pathogenesis. Chen et al. [15] highlighted that IL-17–producing γδ T cells play a dominant role in sustaining psoriatic inflammation and driving keratinocyte hyperproliferation, linking our *MEG3* target map to IL-17–driven epidermal changes. Shi et al. [17] further reported that IL-17 enhances keratinocyte proliferation and inflammatory mediator production, while regulatory T cell dysfunction exacerbates this effect, underlining the significance of *MEG3*-related cytokine signaling modulation.

In 2018, Qiao et al. [11], reported that following IL-22 treatment, there was a notable rise in *MSX2P1* mRNA levels in both HaCaT and HNEK cells. lncRNA-*MSX2P1* acts as an endogenous sponge RNA by binding directly to miR-6731-5p, resulting in increased S100A7 and other pro-inflammatory cytokines by suppressing miR-6731-5p expression and activating *S100A7* in IL-22-stimulated keratinocytes, thereby contributing to the development of psoriasis.

In this study, which explores the impact of the interleukin-17 inhibitor Secukinumab on the expression levels of two LncRNAs associated with keratinocyte proliferation and inhibition, notable findings emerged from the cell culture psoriasis model. Specifically, *MEG3* expression was decreased by 20 times following the addition of secukinumab treatment, while *MSX2P1* expression decreased by 190 times. Given these data, the observed changes indicate that Secukinumab is associated with the *MEG3* and *MSX2P1* pathways.

It is still necessary to investigate the impact of treatments that target the IL-23 and IL-17 pathways on the long-term fate of the disease.

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Author contributions: I.A. have constructed the main idea and hypothesis of the study, I.A., O.S.K., have done the method and I.A., O.S.K., A.B.E., C.D. collected the data. I.A. and Z.A. have done bioinformatic analysis. I.A., Z.A., A.B.E. have written the manuscript. In addition, all authors approved the final version.

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Refrences

1. Jiang WW, Wang YM, Wang XY, Zhang Q, Zhu SM, Zhang CL. Role and mechanism of matrine alone and combined with acitretin for HaCaT cells and psoriasis-like murine models. *Chin Med J (Engl)*. 2019;132(17):2079-2088. doi:10.1097/CM9.0000000000000412
2. Baroni A, Buommino E, De Gregorio V, Ruocco E, Ruocco V, Wolf R. Structure and function of the epidermis related to barrier properties. *Clin Dermatol*. 2012;30(3):257-262. doi:10.1016/j.clindermatol.2011.08.007
3. Capon F. The genetic basis of psoriasis. *Int J Mol Sci*. 2017;18(12):2526. doi:10.3390/IJMS18122526
4. Zhou Q, Yu Q, Gong Y. Construction of a lncRNAmiRNAmRNA network to determine the regulatory roles of lncRNAs in psoriasis. *Experimental and Therapeutic Medicine*. 2019;18:4011-4021. doi:10.3892/etm.2019.8035
5. Yang EJ, Beck KM, Liao W. Secukinumab in the treatment of psoriasis: patient selection and perspectives. *Psoriasis (Auckl)*. 2018;8:75-82. doi:10.2147/PTT.S146004
6. Catia de Felice C, Marulli GC, Ardigò M, Berardesca E. Biological markers in the etiology of psoriasis: Targeted treatment options. *Biologics.* 2007;1(1):11-18.
7. Jia HY, Zhang K, Lu WJ, Xu GW, Zhang JF, Tang ZL. LncRNA *MEG3* influences the proliferation and apoptosis of psoriasis epidermal cells by targeting miR-21/caspase-8. *BMC Mol Cell Biol*. 2019;20(1):1-13. doi:10.1186/S12860-019-0229-9/TABLES/1
8. Zhou Y, Zhang X, Klibanski A. *MEG3* noncoding RNA: a tumor suppressor. *J Mol Endocrinol*. 2012;48(3):R45-R53. doi:10.1530/JME-12-0008
9. Tang ZL, Zhang K, Lv SC, Xu GW, Zhang JF, Jia HY. LncRNA *MEG3* suppresses PI3K/AKT/mTOR signalling pathway to enhance autophagy and inhibit inflammation in TNF-α-treated keratinocytes and psoriatic mice. *Cytokine*. 2021;148:155657. doi:10.1016/j.cyto.2021.155657
10. Holland PWH, Booth HAF, Bruford EA. Classification and nomenclature of all human homeobox genes. *BMC Biol*. 2007;5(1):1-28. doi:10.1186/1741-7007-5-47/TABLES/1
11. Qiao M, Li R, Zhao X, Yan J, Sun Q. Up-regulated lncRNA-*MSX2P1* promotes the growth of IL-22-stimulated keratinocytes by inhibiting miR-6731-5p and activating S100A7. *Exp Cell Res*. 2018;363(2):243-254. doi:10.1016/J.YEXCR.2018.01.014
12. Ghoreschi K, Balato A, Enerbäck C, Sabat R. Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. *The Lancet*. 2021;397(10275):754-766. doi:10.1016/S0140-6736(21)00184-7
13. Atakan N. Secukinumab. *Turkderm Turk Arch Dermatol Venereol* 2025;56(1):52-54. doi:10.4274/turkderm.galenos.2022.37929
14. Costache DO, Feroiu O, Ghilencea A, et al. Skin Inflammation Modulation via TNF-α, IL-17, and IL-12 Family Inhibitors Therapy and Cancer Control in Patients with Psoriasis. *Int J Mol Sci*. 2022;23(9):5198. doi:10.3390/IJMS23095198
15. Chen Y, Hu Y, Zhou X, et al. Human umbilical cord-derived mesenchymal stem cells ameliorate psoriasis-like dermatitis by suppressing IL-17-producing γδ T cells. *Cell Tissue Res*. 2022;388(3):549-563. doi:10.1007/S00441-022-03616-X
16. Shi R, Ma R, Jiang X, et al. Implications of LncRNAs and CircRNAs in psoriasis: a review. *RNA Biol*. 2023;20(1):334-337. doi:10.1080/15476286.2023.2223486
17. Shi Y, Chen Z, Zhao Z, et al. IL-21 induces an imbalance of Th17/treg cells in moderate-to-severe plaque psoriasis patients. *Front Immunol*. 2019;10:1865. doi:10.3389/FIMMU.2019.01865