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Comparison of IL-17, IL-33 and MMP-3 gene expression levels between patients with psoriasis and psoriatic arthritis and healthy controls

Hatice Reşorlu[1], Rahime Özlem Öztopuz[2] & Özlem Coşkun[2]*
[1]Department of Physical Medicine and Rehabilitation,
[2]Department of Biophysics, Çanakkale Onsekiz Mart University, Faculty of Medicine, Çanakkale, Turkey

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This study aimed to compare gene expression levels of biomarkers of inflammation, bone damage and cartilage damage (IL-17, IL-33, MMP-3) in psoriasis (PsO) and psoriatic arthritis (PsA) patients with healthy controls and to examine the relationship between changes in expression levels and disease activity. PsO and PsA patients and healthy volunteers were included in the study. Gene expression levels of IL-17, MMP-3 and IL-33 proteins were measured in blood samples. The severity of PsO disease was assessed by PASI, and the severity of PsA disease was assessed by DAS28 CRP and BASDAI. The study included 25 PsO patients (10 women, 15 men), 23 PsA patients (16 women, 7 men) and 26 healthy controls (18 women, 8 men). The disease duration of PsO patients was 12.2±7.9 years and the PASI score was 9.8±6.2. The disease duration of PsA patients was 9.6±9.1 years, 12 patients had axial, and 11 patients had peripheral features. BASDAI score of axial patients was 3.5±1.5 and DAS28 CRP score of peripheral patients was 3.80±1.8. The results revealed that IL-17, IL-33 and MMP-3 gene expression levels were higher in PsO and PsA patients than in healthy controls, but these expression levels were not significantly associated with disease activity. However, a significant correlation was found between IL-33 gene expression level and PASI score in PsO patients ($P < 0.001$).

Keywords: Psoriasis, Psoriatic arthritis, IL-17, MMP-3, IL-33, Gene expression

Psoriasis (PS) is a common and chronic skin disease with a strong genetic background. Although it is a common disease, its exact etiology is still unclear. Genetic, immunological, and environmental factors are suspected in its pathogenesis[1]. Psoriatic Arthritis (PsA) is a chronic inflammatory arthritis affecting one-third of PS patients. It may involve peripheral joints or the axial skeleton. The underlying mechanisms of progression from PS to PsA are not fully elucidated[2,3]. Since patients with PsO are at high risk of developing PsA, early detection is considered at the heart of efforts to prevent the development of PsA. While there is no conclusive evidence on which PsA patients progress to PsA, several factors have been studied, including duration of psoriasis, family history, pain level, nail involvement, and musculoskeletal symptoms. To this end, predictive tools have been developed to determine the likelihood of progression to PsA[4,5]. However, there is still a need to identify early markers to detect high-risk patients and focus on treatment.

Gene expression analysis from peripheral blood is a simple screening method that does not harm the patient and has great potential in this respect. This study aimed to analyze IL (interleukin)-17, IL-33, and MMP (Matrix metalloproteinase) gene expression by comparing the groups and determining the correlation of the changes in expression levels with disease activity.

Materials and Methods

Study group

The study included patients who were admitted to Canakkale Onsekiz Mart University, Faculty of Medicine, Health Practice and Research Hospital, Physical Therapy and Rehabilitation Outpatient Clinic and diagnosed with PsO by a dermatologist and patients who were diagnosed with PsA according to the Classification Criteria for Psoriatic Arthritis (CASPAR)[6]. All patients were on methotrexate treatment. Healthy individuals without any rheumatologic or chronic diseases who had no family history of psoriasis or arthritis were included in the volunteer group. Demographic characteristics of the patients were recorded.

The severity and involvement of psoriasis were assessed using the Psoriasis Area and Severity Index (PASI)[7]. PsA disease activity was assessed using the Disease Activity Score (DAS 28 CRP)[8] in patients

*Correspondence:
Phone: +90 286 2180018
E-mail: ozlemcd38@hotmail.com

with peripheral involvement and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[9] in patients with axial involvement. All genetic parameters were compared using the selected clinical indicators (DAS28 CRP, BASDAI, PASI) for disease activity in patients.

Laboratory measurements

For laboratory measurements, 2 cc of venous blood with EDTA was collected from the patient and control groups. Following blood collection, the samples were centrifuged at 3000 rpm, and the sera and plasma were kept at -80°C until the measurement day. Gene expression levels were assessed by quantitative RT-PCR [Reverse Transcription Polymerase Chain Reaction]. Total mRNA was quantified from blood samples of the patients using the Trizol method. The quality and quantity of mRNA were determined at a 260/280 absorbance ratio using a NanoDrop ND-1000 spectrophotometer. Reverse transcription was performed using a cDNA synthesis kit (High-Capacity cDNA Reverse Transcription Kit). Synthesized cDNA (complementary DNA) samples were used for RT-PCR analysis. Gene expression levels were analyzed by RT-PCR (ABI Step One) using Applied Biosystems™ TaqMan® Gene Expression (Thermo Fisher Scientific, USA). β-actin was used for the normalization of genes. Gene expression was determined using Ct values, and fold changes were evaluated by the $2^{-[\Delta\Delta CT]}$ method. Primary ID numbers for IL-17A, IL-33, MMP-3, and β-actin are respectively Hs00174383_m1, Hs04931857_m1, Hs00968305_m1, and Hs0106-0665_g1.

Statistical analysis

The data obtained were analyzed using SPSS v20.0 for Windows (Armonk, New York, USA: IBM Corp.). All data were evaluated by the Kolmogorov-Smirnov test and the Shapiro-Wilk test to determine normal distribution. Gene expression levels were evaluated by the 2-ΔΔCt method (ΔΔCt= [Ct Target gene-Ct reference gene]). Nonparametric tests were performed for change in expression, and intergroup comparison was performed by the Kruskal-Wallis, the Mann-Whitney U-test, ANOVA, and the Bonferroni correction. $P < 0.05$ value was considered statistically significant.

Results

Comparison of patient and control groups

We included 25 PsO patients (10 Female and 15 Male), 23 PsA patients (16 Female and 7 Male), and 26 healthy controls (18 Femaleand 8 Male) in the study. Demographic characteristics of the patient and control groups were similar (P>0.05). (Table 1)

Comparison of disease activity and gene expression level of the patient group

The mean disease duration of PsA patients was 9.6±9.1 years, and the mean PASI score was 9.8±6.2. The duration of PsO disease was 12.2±7.9 years. Among the patients with PsA, 12 were axially predominant, and 11 were peripherally predominant. The mean BASDAI score of axial patients was 3.5±1.5, and the mean DAS 28 CRP score of peripheral patients was 3.80±1.8. The patient global assessment score was 3.9±1.79. The mean CRP was 1.5±1.51. There was no correlation between the IL-17, IL-33, and MMP-3 levels and the BASDAI score in patients with axial disease (P value 0.3, 0.4, and 0.5, respectively). No correlation was detected between the IL-17, IL-33, and MMP-3 levels and the DAS28 CRP in patients with peripheral disease (P value 0.4, 0.7, 0.8, respectively). No correlation was noted between the IL-17 and MMP-3 levels and the PASI scores in patients with PsO (P value 0.2 and 0.1, respectively). There was a correlation between the IL-33 levels and the PASI scores (P=0.001).

Gene expression measurements in control, PS, and PSA patient groups

No statistically significant difference was detected between control, PsO, and PsA groups gene expression levels. IL-17, IL-33, and MMP-3 levels were higher in

Table 1 — Demographic characteristics of the participants

Variable/Groups	Control Mean ± SD	PsO Mean ± SD	PsA Mean ± SD	χ^2	*P value*
Age	41.2 ± 12.6	45.0 ± 14.7	45.6 ± 11.1	2.115	0.347*
Height	168.6 ± 9.4	170.2 ± 8.3	166.4 ± 8.8	1.916	0.384*
Weight	72.7 ± 11.7	81.2 ± 20.5	73.8 ± 15.9	3.026	0.220*
BMI	25.8 ± 4.6	27.9 ± 6.1	26.6 ± 4.6	1.808	0.405*
Sex – Female/Male	8/18	15/10	7/16	5.932	0.052**
Smoking – Yes/No	15/11	12/13	7/16	3.715	0.156**

[*Kruskal Wallis Test, **Chi-Square Test, χ^2; Chi-Square test value]

Table 2 — Differences in gene expression levels of participants

Variable/Groups	Control Mean ± SD	PsO Mean ± SD	PsA Mean ± SD	*P value*
IL-17A	1.79±0.41 (0.01-7.84)	2.01±0.49 (0.01-5.82)	3.23±0.91 (0.04-9.78)	0.688
IL-33	1.72±0.37 (0.03-8.73)	2.43±0.71 (0.14-12.18)	3.51±1.01 (0.20-15.91)	0.755
MMP-3	1.55±0.40 (0.18-15.34)	2.87±0.88 (0.12-18.86)	2.49±0.67 (0.16-11.08)	0.476

the PsO and PsA patient groups compared to the control group (P>0.05) (Table 2 & Fig. 1).

Discussion

In our study, no significant difference was observed between the expression levels of IL-17A, IL-33, and MMP3 genes in the PsO, PSA, and control groups. Although IL-17A, IL-33, and MMP-3 expression levels did not reach statistically significant levels in PsO and PsA patients, they were higher than that in the control group. IL-17 is a common element in various inflammatory diseases. It has six known isoforms (IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F). IL-17A is the most prominent form in the development of psoriasis. IL-17A is a proinflammatory cytokine that plays a crucial role in the pathogenesis of PsA and PsO diseases. IL-17A, released by Th17 cells induced by IL-23, is overexpressed in skin lesions and leads to the induction of inflammatory mediators and the abnormal proliferation of keratinocytes. Moreover, it also contributes to chronic inflammation and synovium damage by inducing the transcription of genes for several inflammatory cytokines, including IL-1β, IL-6, IL-8, and TNF-α[10-12]. In general, it is suggested that increased IL-17 increases both the proliferation of keratinocytes and neo-angiogenesis and decreases the expression of adhesion molecules, thereby facilitating the breakdown of the skin barrier[13,14]. Considering its pathogenic role, IL-17 has become a therapeutic target for treating PsO. The three biologic treatments targeting the IL-17 pathway are ixekizumab, secukinumab, and brodalumab. These treatments are FDA-approved. In addition, ongoing studies evaluate the efficacy of two new biologic therapies, i.e., bimekizumab, an IL-17A and IL-17-F inhibitor, and netakimab, an IL-17A inhibitor[15,16].

Gene expression studies revealed that PsA synovium is more similar to psoriatic skin than synovium in inflammatory arthritis. However, IL-17 expression was found to be more potent in the skin compared to the synovium. It is also observed that IL-17 mRNA expression in skin samples collected from the lesions in PsO patients varies even within clinical subtypes [more in pustular psoriasis][17,18]. In our

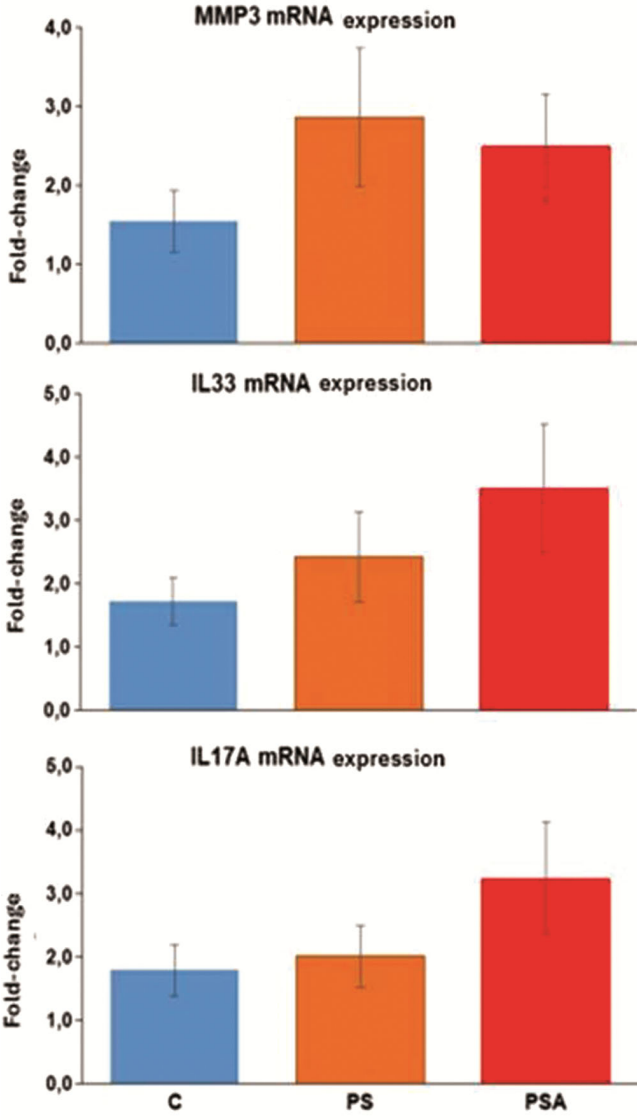

Fig 1 — Changes in IL-17A, IL-33 and MMP-3 expression of the groups are given as mean and standard error. P>0.05 was found in all groups based on the statistical comparison.

patient group, IL-17 mRNA expression was higher in PsA patients (P > 0.05). However, the difference in IL-17 mRNA expression did not reach a statistically significant level because our patient group's disease activity was low.

MMPs are enzymes involved in physiological mechanisms such as cell migration, angiogenesis,

apoptosis, and tissue remodeling[19]. MMPs are classified into 9 subgroups based on structure and function, and many of them are involved in the pathogenesis of psoriasis. MMP-3, which is located in the extracellular matrix, is increased in lesioned skin, basal keratinocytes, and serum and is expressed by immune cells such as macrophages[20,21]. MMP-3 is an enzyme believed to play a role in bone destruction in the course of inflammatory rheumatic diseases. Studies have reported that increased serum MMP-3 levels in PsO patients are associated with PsA. Grohmann *et al*. found that increased levels, compared to the control group, of RANKL, tumor necrosis factor superfamily member 14 (TNFSF14), cartilage oligomeric matrix protein (COMP), and MMP-3 were independently associated with PsO and PsA**.** Cretu *et al*. proposed MMP-3 as a biomarker in PsA[2]. In a recent study, MMP-3 levels were similar between PsO and PsA patients. In the same study, MMP-3 levels were found to be correlated with various inflammatory cytokines (IL-12P/70, IL-17A, and TNF-α) in PsO patients[22]. However, Wirth *et al*. suggested that MMP-3 is a biomarker for the presence of arthritis in psoriatic disease and could be used to screen for PsA in psoriasis patients[23]. In our study, no statistically significant difference was observed between MMP-3 expressions of the groups.

IL-33, also known as Alarmin and a member of the IL-1 family, is a nuclear cytokine expressed on epithelial cells, endothelial cells, fibroblast-like cell surfaces, and in many tissues[24]. It is expressed following structural mechanical or inflammatory damages[25]. By binding to IL-1 receptor-like 1(1RL1 or ST2), it has functions such as regulating the immune response, especially in mast cells, producing T helper 2 (Th2) response and Th2 cytokine, supporting CD8 cytotoxic T cells and activated Th1 cells, activating Treg cells by expressing ST2 receptor, inducing inflammatory cell activation in inflamed skin, increasing IL-17 and TNF-α production, and suppressing proinflammatory gene transcription[26,27]. Therefore, it has been studied in many acute and chronic inflammatory as well as autoimmune diseases. It was shown that IL-33 expression increased in skin lesions of PsO patients due to physiologic stress caused by PsO disease[28]. PsO is a disease of the immune system, both innate and acquired, where the innate is predominant. Activation of Th1/Th17 cells by the innate immune response induces the release of IL-17, IFN-γ, and TNF-α, which triggers inflammation. On the other hand, cytokines such as TNF-α, IL-1β, and IFN-γ cause the release of IL-33 from mast cells[29]. Dong *et al*. found that serum IL-33 levels were increased in PsO patients compared to healthy subjects[30.]

Studies in mice with imiquimod-induced psoriasis inflammation revealed an increase in IL-33/ST2 in the skin. It has also been emphasized that IL-33 is an important cytokine because it decreases CD4 and CD8 cells, inhibits autophagy in the skin, stimulates tyrosyl phosphorylation of STAT3, and exacerbates disease severity in mice[31]. Cannavò *et al*. similarly found higher levels of IL-33 in patients with PsO and PsA as compared to healthy controls; however, they were unable to show any correlation between IL-33 and disease activity score[32]. It was found that IL-33 expression decreased in sera and lesions after methotrexate treatment, while it increased in those receiving NB-UVB[33].

It was discovered that TNF-α, INF-gamma, and IL-17, cytokines of the Th1/Th17 response involved in the pathogenesis of psoriasis, stimulate the release of IL-33[34,35]. Moreover, the decrease in IL-33 levels by anti-TNF therapies confirms this finding[36]. When all studies are reviewed, the data on the role of IL-33 in the development of PsO is inconsistent. While many studies provided data on increased levels of IL-33[29-31], some studies showed that the levels were similar in PsO patients and healthy subjects[37]. One study found that IL-33 expression levels were lower in PsO patients as compared to healthy subjects. The same study reported a significant correlation between PASI scores and IL-33 levels[38,39]. In a recent meta-analysis, it was concluded that there is no significant difference between the serum IL-33 levels of healthy controls and PsO patients and that the IL-33 level cannot be used as a diagnostic marker[40,41].

In our study, we observed that IL-33 levels increased in both PsO and PsA patients, although not to a significant level. This result was consistent with literature. The above-mentioned differences and inconsistencies in literature may be due to the different kits used to analyze patient samples. Disease activation or treatments used at the time of sample collection might have influenced the results.

The most important limitations of our study are the relatively small number of participants and the fact that the patient population consists of patients with established diseases. Therefore, the study is not representative of the outcomes for patients in the early stages of the disease. The second most important

limitation is the lack of detailed microarray analysis of gene expression. Low disease activity levels and systemic methotrexate use may have affected the results. There is a critical need to identify new biomarkers that can shed light on the molecular mechanisms driving the progression of PsA in PsO patients. Despite the limited sample size, our study provides promising insights into evaluating the transition to arthritis.

In the future, systematic gene expression analyses at the genetic microarray and transcriptome levels, particularly focusing on PsO patients at the onset of arthritis during the progression to PsA, hold significant potential. Such studies could offer valuable contributions to understanding disease mechanisms and developing targeted interventions.

Conclusion

We were not able to detect any statistical difference in gene expression levels in the PsO and PsA patient groups and the control groups based on the results obtained in this study. In terms of disease activation and gene expression levels, only IL-33 gene expression and PASI score were found to be correlated. It is known from the literature that IL-17, IL-33, and MMP-3 are involved in the disease pathogenesis of PsA and PsO. For gene expression levels to be used as a biomarker in routine screening, studies that include a larger number of patients and detailed microarray analysis should be conducted. Future research should focus on larger study populations to further evaluate the relationship between serum cytokine levels and the pathogenesis of psoriasis and psoriatic arthritis. Prospective studies analyzing the interactions between various biomarkers in PsO and PsA pathogenesis hold significant promise for advancing our understanding of these diseases.

Ethical statement

All procedures for experimental protocols of the present study involving animals were performed by the ethical standards of the institutions of practice at which the studies were conducted. This study was approved by the Clinical Research Ethics Committee of Çanakkale Onsekiz Mart University, Faculty of Medicine (Ethical Committee Decision No :2019-13).

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Author contribution

HR, ÖÖ, ÖC: planned the study, planned the experiments. Collected the experimental materials, supervised the study, ÖÖ, ÖC: Performed the experiments, HR, ÖÖ, ÖC: analyzed the data, prepared the draft manuscript, HR, ÖÖ, ÖC: read the draft and made necessary corrections HR, ÖC: read the entire article and approved it.

Conflict of interest

The authors declare no conflict of interest.

References

1 Kamiya K, Kishimoto M, Sugai J, Komine M, & Ohtsuki M, Risk factors for the development of psoriasis. *Int J of Mol Sci,* 20(18) (2019) 4347.

2 Grohmann T, Vivekanantham A, Coates LC, Pennington S, & FitzGerald O, Clinical, genetic and omics-based biomarkers that might support the identification of the development of psoriatic arthritis in individuals with psoriasis: a narrative review of the literature. *RMD open*, 10(4) (2024) e004176.

3 Patt YS, Watad A, Giovannini I, Abu-Obeida WH, Errichetti E, David P, De Marco G, & Zabotti A, Risk factors for psoriatic arthritis development in psoriasis patients: Myths, pitfalls, and pearls. *Clin Exp Rheumatol*, 42(2024) 1856.

4 Zabotti A, De Marco G, Gossec L, Baraliakos X, Aletaha D, Iagnocco A, Gisondi P, Balint PV, Bertheussen H, Boehncke HE, Namjanov NS, Wit M, Errichetti E, Marzo-Ortega H, Protopopov M, Puig L, Queiro R, Ruscitti P, Savage L, Schett G, Siebert S, Stamm TA, Studenic P, Tinazzi I, Van Den Bosch FE, Helm-van Mill A, Watad A, Slomen JS, & McGonagle DG, EULAR points to consider for the definition of clinical and imaging features suspicious for progression from psoriasis to psoriatic arthritis. *Annals of the Rheumatol Dis*, *82*(9) (2023)1162.

5 Zabotti A, Tinazzi I, Aydin SZ, & McGonagle D, From psoriasis to psoriatic arthritis: insights from imaging on the transition to psoriatic arthritis and implications for arthritis prevention. *Curr Rheumatol Rep*, 22(2020) 1.

6 Monaco ML, Bocchio RM, Natoli G, Giardina A, Cangemi I, Scibetta S, Argano C, & Corrao S, Critical importance of patient-reported outcomes for a comprehensive assessment of psoriatic arthritis patients. *Frontiers in Med*, 10(2024) 1332432.

7 Sbidian E, Chaimani A, Guelimi R, Garcia-Doval I, Hua C, Hughes C, Naldi L, Kinberger M, Afach S, & Le Cleach L, Systemic pharmacological treatments for chronic plaque psoriasis: a network metaanalysis. *Cochrane Database Syst Rev*, 7(2023) CD011535.

8 Schally J, Brandt HC, Brandt-Jürgens J, Burmester GR, Haibel H, Käding H, Karberg K, Lüders S, Muche B, Protopopov M, Rodriguez VR, Torgutalp M, Verba M, Zinke S, Poddubnny D, & Proft F Validation of the simplified disease activity index (SDAI) with a quick quantitative C-reactive protein assay (SDAI-Q) in patients with rheumatoid arthritis: a prospective multicenter cross-sectional study. *Therapy Adv in Musculoskeletal Dis*, 14 (2022) 1759720X221114107.

9 Erpek E, Solmaz D, Bülbül H, Kozacı LD, Karaca N, & Akar S, Evaluation of the relationship between serum irisin levels

and disease activity in ankylosing spondylitis patients. *Evaluation*, 16(1) (2024) 1.
10 Ghoreschi K, Balato A, Enerbäck C, & Sabat R, Therapeutics targeting the IL-23 and IL-17 pathway in psoriasis. *The Lancet*, 397(10275) (2021) 754.
11 Jin JQ, Wu D, Spencer R, Elhage KG, Liu, J, Davis M, & Liao W, Biologic insights from single-cell studies of psoriasis and psoriatic arthritis. *Exp Opinion on Biol Therapy*, 22(12) (2022) 1449.
12 Robert M, Miossec P, IL-17 in Rheumatoid Arthritis and Precision Medicine: From Synovitis Expression to Circulating Bioactive Levels. *Front Med*, 14(2019) 364.
13 Xu H, Agalioti T, Zhao J, Steglich B, Wahib R, Vesely MCA, & Gagliani N, The induction and function of the anti-inflammatory fate of TH17 cells. *Nat Commun*, 11(1) (2020).
14 Kong B, & Lai Y, IL-17 family cytokines in inflammatory or autoimmune skin diseases. *Adv in Immu*, 163(2024) 21.
15 Gotesman RD, Vender R, Bimekizumab for Moderate-to-Severe Plaque Psoriasis. *Skin Therapy Lett*, 26(2021) 1.
16 Puig L, Bakulev AL, Kokhan MM, Samtsov AV, Khairutdinov VR, Morozova MA, Zolkin NA, Kuryshev IV, Petrov AN, Artemeva AV, Zinkina-Orikhan AV, Efficacy and Safety of Netakimab, A Novel Anti-IL-17 Monoclonal Antibody, in Patients with Moderate to Severe Plaque Psoriasis. Results of A 54-Week Randomized Double-Blind Placebo-Controlled PLANETA. *Clin Trial Dermatol Ther*, 11(2021) 1319.
17 Liu J, Zeng L, Huang X, Liu L, Guo N, Zhang J, & Zhang G. The case-control study on relationship between the serum concentration of IL-7 and the pathogenesis of psoriasis: ampere systematic review and meta-Analysis. *Eur J of Inflamm*, 21(2023).
18 Zalesak M, Danisovic L, & Harsanyi S, Psoriasis and Psoriatic Arthritis—Associated Genes, Cytokines, and Human Leukocyte Antigens. *Medicina*, 60(5) (2024) 815.
19 Cabral-Pacheco GA, Garza-Veloz I, Castruita-De la Rosa C, Ramirez-Acuña JM, Perez-Romero BA, Guerrero-Rodriguez JF, & Martinez-Fierro ML, The roles of matrix metalloproteinases and their inhibitors in human diseases. *Annals of the Rheumatol Dis*, 21(24) (2020) 9739.
20 Johansen MB, Nielsen SH, Port H, Todberg T, Løvendorf MB, & Skov L, Biomarkers of Extracellular Matrix Fragments in Patients with Psoriasis. *Int J of Mol Sci*, 26(1) (2024) 261.
21 Chandran V, Liao W, & de Vlam K, Biomarkers in psoriasis and psoriatic arthritis: where are we now? *The J of Rheuma*, 51(2) (2024) 74.
22 Michalak-Stoma A, Bartosińska J, Raczkiewicz D, Kowal M, Krasowska D, & Chodorowska G, Assessment of Selected Matrix Metalloproteinases [MMPs] and Correlation with Cytokines in Psoriatic Patients. *Mediators Inflamm*, 2021(2021) 9913798.
23 Wirth T, Balandraud N, Boyer L, Lafforgue P, & Pham T, Biomarkers in psoriatic arthritis: A meta-analysis and systematic review. *Frontiers in Immunology*, 13(2022) 1054539.
24 Chen Z, Hu Y, Gong Y, Zhang X, Cui L, Chen R, Yu Y, Yu Q, Chen Y, Diao H, Chen J, Wang Y, & Shi Y, Interleukin-33 alleviates psoriatic inflammation by suppressing the T helper type 17 immune response. *Immunology*, 160 (2020) 382.
25 Zhou Z, Yan F, & Liu O, Interleukin (IL)-33: an orchestrator of immunity from host defence to tissue homeostasis. *Clin & Transl Immuno*, 9(6) (2020) e1146.
26 De Martinis M, Ginaldi L, Sirufo MM, Bassino EM, De Pietro F, Pioggia G, & Gangemi S, IL-33/Vitamin D Crosstalk in Psoriasis-Associated Osteoporosis. *Front Immunol*, 11(2021) 604055.
27 Zhou X, Hu Y, Liu L, Liu L, Chen H, Huang D, & Zhang J, IL-33-mediated activation of mast cells is involved in the progression of imiquimod-induced psoriasis-like dermatitis. *Cell Commun and Sig*, 21(1) (2023) 52.
28 Yuan C, IL-33 in autoimmunity; possible therapeutic target. *Int immunopharmaco,* 108(2022) 108887.
29 Campanati A, Marani A, Martina E, Diotallevi F, Radi G, & Offidani A, Psoriasis as an immune-mediated and inflammatory systemic disease: from pathophysiology to novel therapeutic approaches. *Biomed*, 9(11) (2021) 1511.
30 Dong Y, Hu H, Fu D, Zheng S, Wang Q, Keshav KC, & Tian Z, Serum expression of IL-33 and ST2 in patients with psoriasis vulgaris. *Arch of Iranian Med*, 24(9) (2021) 689.
31 Duan Y, Dong Y, Hu H, Wang Q, Guo S, Fu D, Song X, & Kalvakolanu DV, Tian Z IL-33 contributes to disease severity in Psoriasis-like models of mouse. *Cytokine*, 119(2019) 159.
32 Cannavò SP, Bertino L, Di Salvo E, Papaianni V, Ventura-Spagnolo E, & Gangemi S, Possible Roles of IL-33 in the Innate-Adaptive Immune Crosstalk of Psoriasis Pathogenesis. *Med of inflamm*, 2019(1) (2019) 7158014.
33 AbdelWahed MA, Elmogy MH, Abdelsalam M, & Zohdy M, Serum interleukin-33 level may serve as a new marker for psoriasis diagnosis. *Egyptian J of Dermatol and Venerology*, 41(2) (2021) 109.
34 Tsuda H, Tominaga SI, Ohtsuki M, & Komine M. Nuclear IL-33 regulates cytokinesis and cell motility in normal human epidermal keratinocytes. *J of Dermatol Sci*, 105(2) (2022) 113.
35 Guo J, Zhang H, Lin W, Lu L, Su J, & Chen X, Signaling pathways and targeted therapies for psoriasis. *Sig Trans and Tar Therapy*, 8(1) (2023) 437.
36 Chan BC, Lam CW, Tam LS, & Wong CK, IL33: roles in allergic inflammation and therapeutic perspectives. *Frontiers in immunology*, 10(2019) 364.
37 Bodoor K, Al-Qarqaz F, Heis LA, Alfaqih MA, Oweis AO, Almomani R, & Obeidat MA, IL-33/13 Axis and IL-4/31 Axis Play Distinct Roles in Inflammatory Process and Itch in Psoriasis and Atopic Dermatitis. *Clin Cosmet Inves Dermatol*, 13(2020) 419.
38 Patt YS, Watad A, Giovannini I, Abu-Obeida WH, Errichetti E, David P, De Marco G, McGonagle D, & Zabotti A, Risk factors for psoriatic arthritis development in psoriasis patients: Myths, pitfalls, and pearls. *Clin Exp Rheumatol*, 42(2024) 1856.
39 Khalid W, Al-Tae FM, Ahmed AA, & Al-Chalabi QS, Assessment of serum level of IL-6 and IL-37 cytokines in patients with psoriasis. *Romanian J of Med Pract*, 19(4) (2024) 100.
40 Kc K, Hu H, Mahatara T, Koirala S, Shrestha S, Sharma SK, Song X, Tian Z, The Correlation between Interleukin 33 and Psoriasis: *A Sys Rev and Meta-Anal Dermato*, 3(2023) 13-24.
41 Kiełbowski K, Bakinowska E, Ostrowski P, Pala B, Gromowska E, Gurazda K, Dec P, Modrzejewski A & Pawlik A, The role of adipokines in the pathogenesis of psoriasis. *Intl J of Mol Sci,* 24(7) (2023) 6390.