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Serum IL-21, SFAS, and SFASL as Diagnostic and Prognostic Biomarkers of Psoriasis Severity

Zaid Mohammed Joodi Al-Janabi[1]*, Aeshah A. Ahmed[2], Mays Talib Abdallah[3], Mustafa H. Hussien[4]

[1]Department of Environment, College of Energy and Environmental Science, Alkarkh University of Science, Baghdad, 10081, Iraq
[2]College of Science, Alkarkh University of Science, Baghdad, 10081, Iraq
[3]Collage of Biotechnology, Al-Nahrain University, Baghdad, 10074, Iraq
[4]Department of Environmental Health, College of Energy and Environmental Science, Alkarkh University of Science, Baghdad, 10081, Iraq

Abstract

Psoriasis is an autoimmune condition with major immune and inflammatory reactions that cause epidermal changes. The blood molecules can show signs related to the progression or remission phase. Among those molecules are Interleukin-21 (IL-21), soluble FAS (SFAS), and soluble FAS ligand (SFASL), which are used separately to determine possible practical values. In our study, we found that these molecules are efficient for diagnosing patients with psoriasis. We used 50 patients with a plaque type of psoriasis in Iraq with a psoriasis severity level according to its Psoriasis Area and Skin Index (PASI), to which we added 50 healthy Iraqi subjects who matched the age and sex. We used blood molecules to test the values using an ELISA test to measure the values in blood molecules. We used non-parametric statistical methods to conduct our analysis. The methodology used included patients who underwent testing using PASI to which we added another category according to severity. We utilized these methods to test our data. We found that there are increased values for blood molecules (IL-21), (SFAS), (SFASL), which positively correlate with PASI values. As patients suffered more from PASI symptoms, values increased for (IL-21), (IL-21+sFas). We used an "Analysis" technique to test our values. We found that these values are completely sensitive for diagnosing patients. We identified "IL-21" to be dependent in terms of its values for describing patients' symptoms. We conclude that IL-21, SFAS, and SFASL, are related to patients' symptoms. These blood molecules are useful for diagnosing patients to whom we recommend future treatment.

Keywords: Psoriasis, IL-21, SFAS, SFASL, biomarkers, PASI

1. Introduction

Psoriasis is a chronic cutaneous disorder caused by the immune system and affects approximately 2-3% of the global population. The prevalence rate varies according to geographic region, ethnicity, and environmental factors [1,2]. In Iraq, the prevalence rates were reported to range between 0.7% and 2.3% [3]. Psoriasis typically appears as red, scaly patches on the skin but has been associated with arthritis and metabolic disorders, among other issues that make life more challenging [4]. Many cell types are implicated in its pathogenesis, including keratinocytes, dendritic cells, macrophages, and T lymphocytes. The IL-23/Th17 pathway acts primarily through the induction of cytokines, which promote the hyperproliferation of keratinocytes and disruption of the skin barrier [5,6].

Interleukin-21 (IL-21) is an important cytokine mainly produced by Th17 cells and follicular helper T cells. IL-21 exerts a biological influence by promoting proliferation in B and T lymphocytes, inducing stimulation in keratinocytes, and perpetuating the inflammatory process. Serum and skin lesions of patients with psoriasis also have high levels of IL-21, often correlating with the severity of the disease [7–9]. A study recently conducted by Han et al. confirmed that IL-21 and its receptor were strongly upregulated in psoriasis, correlating with erythema, angiogenesis, and enhanced expression of angiogenic mediators such as VEGF-A, ICAM-1, and MMP-9 [10].

Problems in cell death also play a role; the Fas/FasL system regulates the apoptosis of immune cells, while soluble forms (sFas and sFasL) circulate in the blood and can alter this signal. Higher levels of these soluble markers have been reported in psoriasis, suggesting less apoptosis and more inflammation [11–17]. Biologic drugs that target IL-17, IL-23, and TNF-α are effective, but easy and reliable blood biomarkers are still limited. Studies on IL-21, sFas, and sFasL have yielded mixed results, often due to small sample sizes or differences in patient selection

Correspondence: Zaid Mohammed Joodi Al-Janabi, Department of Environment, College of Energy and Environmental Science, Alkarkh University of Science, Baghdad, 10081, Iraq, **e-mail:** zaid.joodi@kus.edu.iq, **Received:** October 9, 2025 **Accepted:** November 20, 2025

[18,19]. In the Middle East, including Iraq, data remain limited, although genetics and environment may affect biomarker levels [20–22].

This study was conducted to measure IL-21, sFas, and sFasL levels in Iraqi patients with psoriasis compared to healthy controls. Non-parametric tests and ROC analysis were used to test their value as simple serum markers of disease activity

2. Materials and Methods

2-1 Study population

Fifty patients with clinically confirmed psoriasis and fifty age- and sex-matched healthy controls were included in this case–control study. Recruitment was carried out at the Dermatology Unit, Baghdad Teaching Hospital, from January to December 2024. Psoriasis was diagnosed by dermatologists using clinical evaluation and standard criteria, and disease severity was assessed with the Psoriasis Area and Severity Index (PASI) [23]. Participants with autoimmune diseases, ongoing chronic infections, malignancies, or who had received systemic immunosuppressive therapy within the past three months were excluded.

2-2 Sample collection and processing

5 ml of venous blood was collected by venipuncture under aseptic conditions using plain vacutainer tubes. After clotting at room temperature, the samples were centrifuged at 3000 rpm for 10 min. Serum was then separated into aliquots and stored at –80 °C until testing. Repeated freeze–thaw cycles were avoided to ensure sample stability. During the first quarter of 2025, serum levels of IL-21, sFas, and sFasL were analyzed in the Central Research Laboratory at Baghdad Teaching Hospital. Measurements were performed using ELISA kits supplied by Elabscience Biotechnology Inc. (Houston, TX, USA; catalog numbers: E-EL-H6114 for IL-21, E-EL-H0956 for sFas, and E-EL-H6106 for sFasL). We used a BioTek ELx800 microplate reader (BioTek Instruments, Winooski, VT, USA) to measure optical density at 450 nm. We then used standard curves made according to the manufacturer's instructions to figure out the concentrations.

2-3 Ethical approval

The Institutional Review Board of Baghdad Teaching Hospital (Ref. No. PSO-2024-017) looked over and approved the study protocol. All procedures adhered to the ethical standards outlined in the Declaration of Helsinki (2013 revision). Before they could be part of the study, all participants had to give their written consent

2-4 Statistical analysis

In 2025, SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 9.0 (GraphPad Software, San Diego, CA, USA) were used to analyze the data. We used the Shapiro–Wilk test to check if the data were normal. Mean ± SD was used to show variables with a normal distribution, and median with Interquartile Range (IQR) was used to show skewed data. We used the Mann–Whitney U test for non-parametric data and the independent-samples t-test for parametric data to see if there were any differences between patients and controls. The Chi-square test was used to compare categorical variables. We used Spearman's rank correlation coefficient to investigate the relationships between biomarkers, PASI, and disease duration.

Receiver Operating Characteristic (ROC) curves were generated to evaluate diagnostic performance, and the Area Under the Curve (AUC) was reported with 95% confidence intervals. Multivariable associations with PASI were examined using multiple linear regression. A p-value < 0.05 was considered statistically significant.

3.Results

3-1 Baseline characteristics

Fifty patients with psoriasis and fifty healthy controls matched for age and sex were included. No high differences were observed between groups for age ($p = 0.69$) or sex ($p = 0.81$). Patients had a median disease duration of 7 years (IQR, 5–11 years) and a mean PASI score of 14.4 ± 4.5, indicating predominantly moderate to severe disease. Details are shown in Table 1.

Table 1. Baseline characteristics of study participants

Variable	Patients (n=50)	Controls (n=50)	p-value
Age (years), mean ± SD	38.1 ± 10.6	37.2 ± 9.9	0.69
Sex (M/F)	29 / 21	27 / 23	0.81
Disease duration (years)	7 (IQR 5–11)	—	—
PASI score, mean ± SD	14.4 ± 4.5	—	—
Treatment status (naïve/treated)	31 / 19	—	—

3-2 Biomarker levels

Serum IL-21, sFas, and sFasL were highly higher in patients compared with controls ($p < 0.001$ for all). IL-21 levels were 241.8 pg/mL (IQR 197.5–288.6) in patients versus 93.7 pg/mL (IQR 72.1–119.3) in controls. Mean sFas and sFasL were also elevated (4.76 ± 1.09 and 1.94 ± 0.43 ng/mL in patients; 2.68 ± 0.92 and 1.15 ± 0.39 ng/mL in controls). Values are listed in Table 2 and shown in Figures 1A–C.

Table 2. Serum biomarker levels in patients and controls

Biomarker	Patients (n=50)	Controls (n=50)	p-value
IL-21 (pg/mL)	241.8 (197.5–288.6)	93.7 (72.1–119.3)	<0.001
sFas (ng/mL)	4.76 ± 1.09	2.68 ± 0.92	<0.001
sFasL (ng/mL)	1.94 ± 0.43	1.15 ± 0.39	<0.001

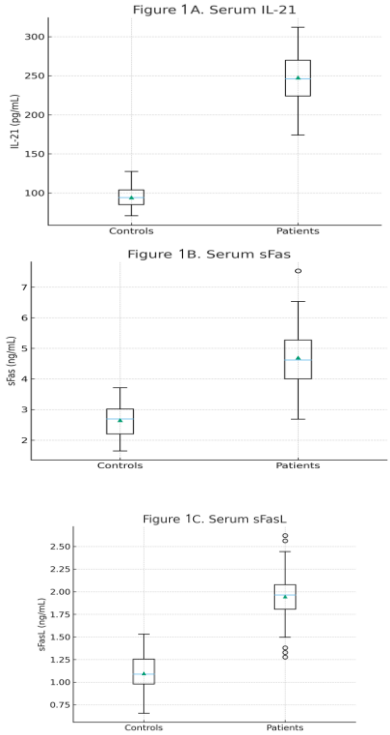

Figure1. Boxplots showing serum IL-21, sFas, and sFasL concentrations in patients versus controls

3-3 Correlations with disease severity

IL-21 correlated strongly with PASI ($\rho = 0.61$, $p < 0.001$). sFas ($\rho = 0.43$, $p = 0.003$) and sFasL ($\rho = 0.41$, $p = 0.004$) showed moderate correlations. Weaker associations were noted with disease duration (sFas: $\rho = 0.36$, $p = 0.01$; sFasL: $\rho = 0.33$, $p = 0.02$). Results are summarized in Table 3 and illustrated in Figures 2A–C.

Table 3. Correlations of serum biomarkers with PASI and disease duration

Biomarker	PASI ρ (95% CI)	p-value	Duration ρ	p-value	Partial ρ (adjusted)	p-value
IL-21	0.61 (0.42–0.75)	<0.001	0.29	0.04	0.58	<0.001
sFas	0.43 (0.21–0.61)	0.003	0.36	0.01	0.39	0.008
sFasL	0.41 (0.18–0.59)	0.004	0.33	0.02	0.36	0.012

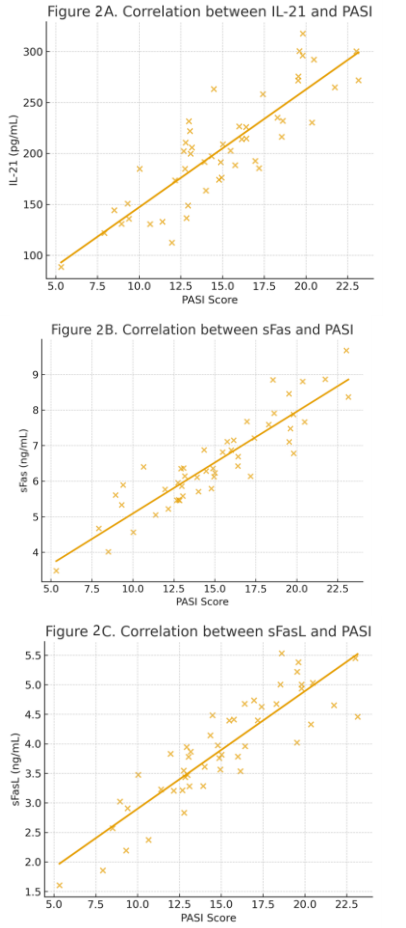

Figure 2. Scatter plots showing correlations of IL-21, sFas, and sFasL with PASI scores.

3-4 Diagnostic performance (ROC Analysis)

IL-21 demonstrated the best diagnostic performance, with an AUC of 0.89 (95% CI: 0.82–0.95, p < 0.001), a sensitivity of 86%, and a specificity of 82% at a threshold of 175 pg/mL. sFas and sFasL also performed well (AUC 0.84 and 0.81). The combined model of IL-21 and sFas reached an AUC of 0.92. The data are presented in Table 4 and Figure 3.

Table 4. ROC analysis of serum biomarkers in psoriasis patients and controls

Biomarker	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	Youden Index
IL-21	0.89 (0.82–0.95)	175 pg/mL	86	82	0.68
sFas	0.84 (0.76–0.91)	3.5 ng/mL	80	78	0.58
sFasL	0.81 (0.73–0.89)	1.5 ng/mL	77	74	0.51
IL-21 + sFas	0.92 (0.86–0.96)	–	–	–	–

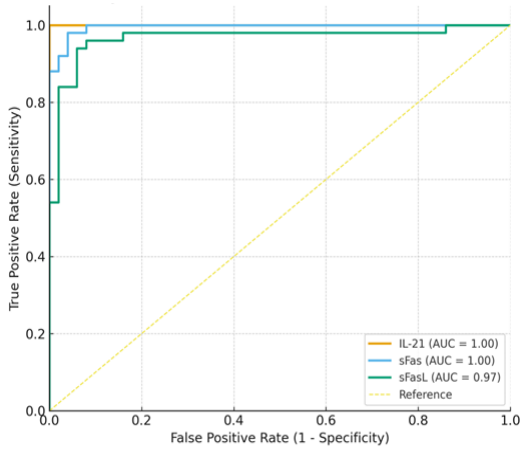

Figure 3. ROC curves for IL-21, sFas, and sFasL.

3-5 Stratified analyses by PASI Severity

Biomarker levels increased progressively from mild to severe subgroups. Significant differences were detected for IL-21 (p < 0.001), sFas (p = 0.002), and sFasL (p = 0.006). Post-hoc tests showed severe > moderate > mild for IL-21, and severe > mild for sFas and sFasL. Results are presented in Table 5.

Table 5. Serum biomarkers by PASI severity subgroup

Group (n)	IL-21 (pg/mL), median (IQR)	sFas (ng/mL), median (IQR)	sFasL (ng/mL), median (IQR)	Kruskal–Wallis p	Post-hoc (Dunn)
Mild (n=14)	198 (164–224)	4.12 (3.58–4.53)	1.72 (1.55–1.86)	–	–
Moderate (n=21)	238 (206–264)	4.78 (4.21–5.11)	1.93 (1.77–2.08)	–	–
Severe (n=15)	286 (254–311)	5.28 (4.69–5.81)	2.11 (1.95–2.26)	<0.001 / 0.002 / 0.006	IL-21: Sev>Mod>Mild; sFas, sFasL: Sev>Mild

3-6 Treatment Status (Naïve vs. Treated)

Naïve patients (n = 31) had higher IL-21 (median 252 pg/mL, IQR 209–296) than treated patients (227 pg/mL, IQR 188–268; p = 0.040). Differences in sFas and sFasL were not significant (p = 0.09 and p = 0.12). After adjusting for PASI, IL-21 remained significant (p = 0.030); the values are shown in Table 6.

Table 6. Serum biomarkers by treatment status at sampling

Biomarker	Naïve (n=31)	Treated (n=19)	p-value	Adjusted p (for PASI)
IL-21 (pg/mL), median (IQR)	252 (209–296)	227 (188–268)	0.040	0.030
sFas (ng/mL), mean ± SD	4.92 ± 1.05	4.51 ± 1.12	0.090	0.081
sFasL (ng/mL), mean ± SD	2.01 ± 0.44	1.84 ± 0.41	0.120	0.110

3-7 Multivariable models predicting PASI

Regression analysis explained 52% of the variance in PASI (R^2 = 0.52). IL-21 was the strongest independent predictor (β = 0.51, p < 0.001), followed by sFas (β = 0.19, p = 0.045), while other factors were not significant. Estimates are provided in Table 7.

Table 7. Multivariable linear regression predicting PASI

Predictor	Std. β	SE	t	p-value	95% CI (β)
IL-21 (pg/mL)	0.51	0.09	5.7	<0.001	0.33 – 0.69
sFas (ng/mL)	0.19	0.09	2.0	0.045	0.00 – 0.38
sFasL (ng/mL)	0.11	0.08	1.4	0.18	−0.05 – 0.27
Age (years)	0.04	0.08	0.4	0.67	−0.12 – 0.19
Sex (M=1)	−0.03	0.08	−0.3	0.74	−0.18 – 0.12
Disease duration (years)	0.16	0.08	1.9	0.06	−0.01 – 0.33
Treatment (naïve=1)	0.08	0.08	1.0	0.31	−0.08 – 0.24

3-8 Sensitivity analyses

Excluding treated patients (n = 31) produced similar results: IL-21 ρ = 0.58 ($p < 0.001$), sFas ρ = 0.41 ($p = 0.022$), sFasL ρ = 0.38 ($p = 0.031$). ROC values were comparable (IL-21 AUC = 0.88, sFas AUC = 0.83, and sFasL AUC = 0.80). Non-parametric tests were confirmed appropriate (Shapiro–Wilk $p < 0.05$ for IL-21 and sFasL).

Discussion

This study demonstrated remarkably higher serum concentrations of IL-21, sFas, and sFasL in patients with psoriasis compared with matched healthy controls (Tables 1–2; Figures 1A–C). The most notable increase was observed for IL-21, which demonstrated a strong correlation with PASI scores (ρ = 0.61, $p < 0.001$) and remained very high in multivariable analysis (Table 7). ROC analysis was used to validate further the most powerful diagnostic biomarker, IL-21 (AUC = 0.89). Accuracy rose when combined with sFas (AUC = 0.92) (Table 4; Figure 3). In stratified analysis, all three biomarkers increased stepwise, with IL-21 exhibiting the most pronounced increase (Table 5), which demonstrates its dual role as both an activity and severity marker.

Our results are consistent with previous reports indicating higher IL-21 levels in psoriatic patients [15, 16]. The same relationship between Th17-related inflammation and IL-21 expression was reported by Caruso et al. [7]. The level of increased sFas and sFasL agrees with previous reports of enhanced Fas/FasL signaling in chronic inflammatory disorders [17]. Results reported by Han et al. are consistent with diagnostic performance of IL-21 observed in our study [10] and support its possible clinical relevance. Recent reviews also underlined that soluble FasL might fail to induce apoptosis but may drive inflammatory pathways, which supports the idea that high levels of sFas/sFasL in psoriasis reflect ongoing immune activation [19]. Minor differences in absolute values might be due to differences in the length of the disease, population differences, or laboratory technique.

IL-21 promotes Th17 differentiation, keratinocyte proliferation, and the release of pro-inflammatory cytokines [15,16]. These mechanisms, crucial in the pathophysiology of the disease, explain the strong association of psoriasis with PASI that we found. Dysregulation of the Fas/FasL pathway leads to prolonged immune activation and defective lymphocyte apoptosis [17]. The high serum levels of sFas and sFasL detected in our patients, and the association of these proteins with PASI (Table 3; Figures 2A–C), provide a basis for considering disordered apoptosis as a key mechanism for the chronicity of the disease.

This study, therefore, by thoroughly investigating IL-21, sFas, and sFasL and applying multivariable modeling and ROC analysis, shows good diagnostic performance, one of its many strong points. It adds regionally to the literature, as it is one of the early systematic studies assessing these biomarkers in an Iraqi population. Limitations are represented by the moderate sample size and case-control, cross-sectional design that lacks the possibility of causal inference. Heterogeneity in treatments may have affected biomarker levels; however, this was mitigated by stratified and adjusted analyses (Tables 6–7).

These findings together suggest that IL-21, particularly in combination with sFas, may be a promising biomarker panel for assessing disease activity and providing diagnostic support in psoriasis. The stepwise relationship of PASI severity with biomarker levels (Table 5) suggests that they may be useful to monitor patients. Future studies should investigate the mechanistic basis of IL-21/Fas interactions in psoriasis and validate these findings in

larger, longitudinal cohorts.

Conclusions

This study showed that patients with psoriasis have higher serum IL-21, sFas, and sFasL compared with healthy controls. IL-21 showed the strongest correlation with disease severity. Correlation tests showed that IL-21 is correlated with PASI levels, while sFas and sFasL provide additional information about disease duration. According to ROC results, IL-21 was the best single diagnostic marker. Accuracy increased when IL-21 was combined with sFas. Stepwise increases across mild, moderate, and severe groups also supported the contribution of these biomarkers to showing disease activity. Besides, differences between untreated and treated patients suggest that IL-21 may also help track treatment response. Regression analysis showed IL-21 as the main predictor of PASI. In conclusion, IL-21, especially in combination with sFas, could be used as a simple blood-based marker set for diagnosing and monitoring psoriasis. Larger studies should be conducted in order to confirm these results, establish unequivocal cut-off values, and address how these markers can be combined with genetic or molecular tools to advance personalized care in further aspects.

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References

1.Michalek IM, Loring B, John SM. Global report on psoriasis. Geneva: World Health Organization; 2016. Available from: https://www.who.int/publications/i/item/global-report-on-psoriasis

2.Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020;369:m1590. doi:10.1136/bmj.m1590

3.Al Samarai AG. Prevalence of skin diseases in Iraq: a community-based study. Int J Dermatol. 2009;48(6):648–9. doi:10.1111/j.1365-4632.2009. 03812.x

4.Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk factors for the development of psoriasis. Int J Mol Sci. 2019;20(18):4347. doi:10.3390/ijms20184347

5.Wang Z, Zheng H, Zhou H, Huang N, Wei X, Liu X, Li J. Systematic screening and identification of novel psoriasis-specific genes from the transcriptome of psoriasis-like keratinocytes. Mol Med Rep. 2019;19(1):529–42. doi:10.3892/mmr.2018.9667

6.Janyga S, Kajdaniuk D, Czuba Z, Ogrodowczyk-Bobik M, Urbanek A, Kos-Kudła B, Marek B. Interleukin (IL)-23, IL-31, and IL-33 play a role in the course of autoimmune endocrine diseases. Endocr Metab Immune Disord Drug Targets. 2024;24(5):585–95. doi:10.2174/1871530324666240118123456

7.Caruso R, Botti E, Sarra M, Esposito M, Stolfi C, Diluvio L, Monteleone G. Involvement of interleukin-21 in the epidermal hyperplasia of psoriasis. Nat Med. 2009;15(9):1013–5. doi:10.1038/nm.1970

8.Oliveira PSS, Cardoso PR, Lima EV, Pereira MC, Duarte ALBP, Pitta IDR, Pitta MGR. IL-17A, IL-22, IL-6, and IL-21 serum levels in plaque-type psoriasis in Brazilian patients. Mediators Inflamm. 2015; 2015:819149. doi:10.1155/2015/819149

9.Wang Y, Wang LL, Yang HY, Wang FF, Zhang XX, Bai YP. Interleukin-21 is associated with the severity of psoriasis vulgaris through promoting $CD4^+$ T cells to differentiate into Th17 cells. Am J Transl Res. 2016;8(7):3188–96. PMID:27508040; PMCID: PMC4969456

10.Han D, Li F, Zhao Y, Wang B, Wang J, Liu B, Mou K, Meng L, Zheng Y, Lu S, Zhu W, Zhou Y. IL-21 promoting angiogenesis contributes to the development of psoriasis. FASEB J. 2024;38(1):e23375. doi: 10.1096/fj.202201709RRRRC

11.Rich RR, Fleisher TA, Shearer WT, Frew AJ, Schroeder HW Jr, Weyand CM. Clinical immunology: principles and practice. 4th ed. Philadelphia: Elsevier; 2013. ISBN:9780723436911. Available from: https://books.google.iq/books?id=MRTa5qwTc7AC

12.Skoumal M, Woodward KB, Zhao H, Wang F, Yolcu ES, Pearson RM, Shirwan H. Localized immune tolerance from FasL-functionalized PLG scaffolds. Biomaterials. 2019; 192:271–81. doi: 10.1016/j.biomaterials.2018.11.029
13.Muraki M. Sensitization to cell death induced by soluble Fas ligand and agonistic antibodies with exogenous agents: a review. AIMS Med Sci. 2020;7(3):122–203. doi:10.3934/medsci.2020.3.122
14.Gilhar A, Yaniv R, Assy B, Serafimovich S, Ullmann Y, Kalish RS. Fas pulls the trigger on psoriasis. Am J Pathol. 2006;168(1):170–5. doi:10.2353/ajpath.2006.050612
15.Myśliwiec H, Baran A, Myśliwiec P, Górska M, Flisiak I. Upregulation of the sFas/sFasL system in psoriatic patients. Adv Med Sci. 2015;60(1):164–8. doi: 10.1016/j.advms.2014.09.004
16.Duran G, Kasap M, Gunesacar R, Dogramaci A, Denli Y. Investigation of the relation between FAS, FASLG polymorphisms and serum Fas, FASL levels in patients with psoriasis. Rev Rom Med Lab. 2018;26(8):112–28. doi:10.2478/rrlm-2018-0027
17.Gregory-Ksander M, Marshak-Rothstein A. The FasLane to ocular pathology: Metalloproteinase cleavage of membrane-bound FasL determines FasL function. J Leukoc Biol. 2021;110(5):965–77. doi:10.1002/JLB.4MR0521-718R
18.Borska L, Andrys C, Krejsek J, Hamakova K, Kremlacek J, Palicka V, Fiala Z. Genotoxic and apoptotic effects of Goeckerman therapy for psoriasis. Int J Dermatol. 2010;49(3):289–94. doi:10.1111/j.1365-4632.2009.04285.x
19.Kurma K, Boizard-Moracchini A, Galli G, Jean M, Vacher P, Blanco P, Legembre P. Soluble CD95L in cancers and chronic inflammatory disorders: a new therapeutic target? Biochim Biophys Acta Rev Cancer. 2021;1876(2):188596. doi: 10.1016/j.bbcan.2021.188596
20.Xu J, Yin Z. An unusual presentation of psoriasis. BMJ. 2020;371:m3345. doi:10.1136/bmj.m3345
21.Alkhaliq GQ. Immunological study for a sample of Iraqi psoriatic patients [MSc thesis]. Baghdad: College of Science, University of Baghdad; 2020.
22.Al-Janabi RHK. Cytological and some immunological factors in psoriatic patients treated with Etanercept [PhD thesis]. Baghdad: College of Science, University of Baghdad; 2018.
23.Crowther JR. The ELISA guidebook. 2nd ed. Totowa, NJ: Humana Press; 2009. Methods Mol Biol. 2009;516. doi:10.1007/978-1-60327-254-4