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Research Article

Genetic Complexity of SLE: A Retrospective Analysis of Gene Mutations and Clinical Correlations

Metin Eser[1], Gulam Hekimoglu[2], Ozgur Kasapcopur[3], Sezgin Sahin[3], Nergis Akay[3], Betul Sozeri[4]

[1]University of Health Sciences, Umraniye Education and Research Hospital, Department of Medical Genetics, Istanbul, Türkiye
[2]University of Health Sciences, International Faculty of Medicine, Department of Histology and Embryology, Istanbul, Türkiye
[3]Istanbul University-Cerrahpaşa School of Medicine, Department of Pediatric Rheumatology, Istanbul, Türkiye.
[4]University of Health Sciences, Umraniye Education and Research Hospital, Department of Pediatric Rheumatology, Istanbul, Türkiye

Abstract

Aim: To investigate the genetic basis of systemic lupus erythematosus (SLE) by identifying pathogenic gene variants and examining their associations with distinct clinical and phenotypic manifestations, to improve understanding of disease heterogeneity and support the development of personalized therapeutic approaches.

Material and Methods: In this retrospective study, gene mutations in the peripheral blood of 19 SLE patients were analyzed using next-generation sequencing.

Results: The mutation rate and associated clinical symptoms for each gene mutation were observed. A mutation rate of 42% was discovered among the SLE patients. The study found that SLE is associated with multiple gene mutations, contributing to its complex clinical presentation. Specific gene mutations were associated with distinct clinical symptoms, such as glomerulonephritis and polyarthritis were linked to SOCS1 mutations. Scoliosis was associated with STAT1 mutations. A photosensitive malar rash was connected to complement mutations (C1qB, C1qC, and C3). An erythematous malar rash was related to PTPN22 mutations. Additionally, arthralgias were associated with TREX1 mutations.

Conclusion: SLE is a multifaceted, multisystem autoimmune disease with symptom variability from different gene mutations. The study advocates patient-specific gene therapy by predicting gene mutations based on clinical symptoms and confirming these mutations through molecular tests.

Keywords: Glomerulonephritis, Arthritis, SOCS1, STAT1, PTPN22, Complement mutations

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder marked by the production of autoantibodies and immune complexes, leading to diverse clinical phenotypes and tissue damage. It involves complex interactions among genetic, environmental, and hormonal factors. Autoantibodies in SLE contribute to disease by binding to self-antigens or inducing inflammation via antigen-antibody complexes (1). The immune system erroneously attacks the body's tissues, causing inflammation and damage across multiple organ systems, including glomerulonephritis, polyarthritis, and skin rashes.

SOCS1 (Suppressor of Cytokine Signaling 1) regulates cytokine signaling and immune response. Mutations in SOCS1 can disrupt cytokine signaling, leading to immune system hyperactivity, which is relevant in SLE (2). Additionally, STAT1 (Signal Transducer and Activator of Transcription 1) plays a crucial role in cytokine and growth factor signaling, regulating inflammation and immune defense. STAT1 gene mutations can cause abnormal immune responses, contributing to autoimmune diseases like SLE (3). Recent studies have shown that STAT1 mutations affect immune regulation, whether gain-of-function

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Corresponding Author: Gulam Hekimoglu, University of Health Sciences, International Faculty of Medicine, Department of Histology and Embryology, Istanbul, Türkiye
E-mail: gulam.hekimoglu@sbu.edu.tr

(GOF) or loss-of-function (LOF). GOF mutations are linked to heightened susceptibility to autoimmune diseases due to hyperactive immune responses, exacerbating SLE's inflammatory processes and clinical phenotypes (4). STAT1 mutations' impact on SLE can illuminate the disease's molecular mechanisms and identify therapeutic targets. Targeting abnormal STAT1 signaling may offer new treatments for SLE, particularly in patients with STAT1 mutations, and personalized medicine approaches could improve outcomes for these patients (5).

Moreover, C1qB, C1qC, and C3 are essential components of the complement system, which enhances the immune response by aiding antibodies and phagocytic cells in clearing pathogens and damaged cells. Mutations in these genes can impair complement function, increasing susceptibility to SLE. C1qB and C1qC encode subunits of the C1 complex, the first component of the classical complement pathway, crucial for clearing immune complexes and apoptotic cells. Deficiencies or mutations in C1q, involving C1qB and C1qC, result in defective clearance, leading to immune complex and apoptotic debris accumulation. This triggers autoimmunity and is strongly associated with SLE development (6). Patients with C1q deficiencies often exhibit severe, early-onset SLE with high disease activity (7). C3 is another critical complement protein involved in both the classical and alternative pathways, playing a key role in opsonization and membrane attack complex formation. Mutations in the C3 gene impair these processes, leading to insufficient clearance of pathogens and immune complexes (8). Though less common than C1q deficiencies, C3 deficiencies are significant in SLE pathogenesis, with patients showing a range of clinical phenotypes, including an increased risk of lupus nephritis (9). The role of C1qB, C1qC, and C3 mutations in SLE provides valuable insights into disease mechanisms and potential therapeutic targets. Enhancing complement activity or mimicking its function could benefit patients with these genetic mutations. Personalized medicine approaches that consider these genetic factors could improve disease management and outcomes for SLE patients (10).

Meanwhile, other genes, such as PTPN22 (Protein Tyrosine Phosphatase Non-Receptor Type 22), encode a phosphatase that regulates immune cell function by downregulating T-cell receptor signaling, maintaining immune balance. Mutations in PTPN22 increase susceptibility to autoimmune diseases, including SLE (11). LEMD3 (LEM Domain Containing 3) encodes a protein in the inner nuclear membrane, crucial for nuclear architecture and signal transduction. LEMD3 mutations are also linked to bone disorders and SLE, disrupting gene expression, cell proliferation, and differentiation (12). These mutations can cause aberrant activation of the TGF-β signaling pathway, essential for immune homeostasis, leading to inappropriate immune responses and SLE development (13). In addition, TREX1 (Three Prime Repair Exonuclease 1) is vital for repair and cytosolic DNA degradation. Mutations in TREX1 are associated with SLE, causing the accumulation of cytosolic DNA, which the immune system mistakenly identifies as foreign. They trigger innate immune responses, chronic inflammation, and autoimmunity (14). TREX1 mutations are linked to severe SLE manifestations, such as early-onset SLE and cerebral lupus (15). In this study, we aimed to elucidate the pathogenesis of SLE by correlating specific gene mutations with clinical findings.

MATERIALS AND METHODS

Patients

This is a retrospective analysis of a single-center cohort study. Between 2021 and 2024, patients who applied to our hospital's genetics department were involved in the present study. All participants provided written informed consent to be included in the study. The study protocol was approved by the local ethics committee of the Training and Research Hospital of the University, in accordance with the Helsinki Declaration of 1975.

DNA isolation

Genomic DNA was extracted from EDTA-anticoagulated peripheral blood using conventional methods and assessed for quantity and integrity before library construction. DNA isolation was performed with a semi-automated robotic system according to the manufacturer's instructions (Qiagen). The concentration and quality of the extracted DNA were assessed by UV spectrophotometry and fluorometric analysis (Qubit v3.0), with evaluation of purity based on 260/280 nm and 260/230 nm ratios. Libraries were prepared using protocols appropriate for the selected application, indexed for multiplexing, and assessed for fragment size and concentration.

Next-generation sequencing

Sequencing was performed on a high-throughput platform with run parameters selected to meet target coverage requirements. Primary data processing included basecalling, demultiplexing, and read quality assessment, followed by alignment to the reference genome and post-alignment refinement. Variant calling and annotation used validated bioinformatics workflows; results were filtered and interpreted according to established criteria, and clinically relevant findings were reported with assay limitations. Runs included positive and negative controls, and all experimental and analytical steps were documented for reproducibility and compliance. The Twist Human Core Exome v2 kit from Sophia Genetics is utilized for this. The sequencing reaction is carried out using the Illumina NextSeq® system and compatible reagent kits.

Data analysis

Raw sequencing data were processed using the Sophia DDM® analysis platform. Alignment and variant calling were performed with Pepper®, a proprietary core algorithm developed by Sophia Genetics, based on the hg19 human genome reference. Variant annotation was subsequently conducted using MOKA® software (Sophia Genetics). For each detected variant, effects on the protein sequence (e.g., missense, nonsense), population frequencies (1000 Genomes, ESP, ExAC, gnomAD), and predictions from silico algorithms (SIFT, PolyPhen) were documented. Additional information regarding the potential deleterious impact of variants was also incorporated. The MUSKAT® software from Sophia Genetics was used to detect CNV. The databases developed by Maxwell et al. and the ClinVar database's expert research groups were used as references for variant classification (16-22). The standards set by Maxwell et al. were taken into consideration for additional variations that were not present in the databases. The American College of Medical Genetics and Genomics (ACMG) sequencing/sequence variations classification guidelines (23) were used as the basis for these criteria. The potential impact of missense variants on disease mechanisms was assessed by considering Pathogenic/Likely Pathogenic variants listed in the ClinVar database, which were used as supporting evidence for PP2 and BP1 at the gene level. A literature review was performed to determine whether loss of function represents the primary pathogenic mechanism, thereby supporting the application of PVS1. In addition, disease-specific literature was consulted to define allele frequency thresholds for BA1 and BS1 criteria. For PM2 evidence, an allele frequency cutoff of 0.0001 was applied (24).

Statistical analysis

The two-sample Pearson's chi-square test was used to assess the genetic mutation occurrence rates between male and female participants. Descriptive statistics were used to calculate the Mean ± SD of the age of the patients. The statistical analyses were performed using SPSS version 21 at a significance level of $p< 0.05$.

RESULTS

The mean age and standard deviation of the patients in our study were 18.21±12.04 years. Eight of them were females, and eleven of them were males. Mutation and phenotype comparisons were made between different genders and age groups, but no difference was observed ($p>0.05$). Therefore, the results are not presented. A total of 44 genes related to SLE were examined (see the Supplementary Materials). Among them, the rates of patients showing gene mutations in SOCS1, complement gene mutation, STAT1 gene mutation, PTPN22, LEMD3, and TREX1 were 5%, 16%, 5%, 5%, 5%, and 5%, respectively (Figure 1). The rate of patients who do not show gene mutation is 58%. There were no significant differences identified in genetic mutation occurrence rates between male and female participants.

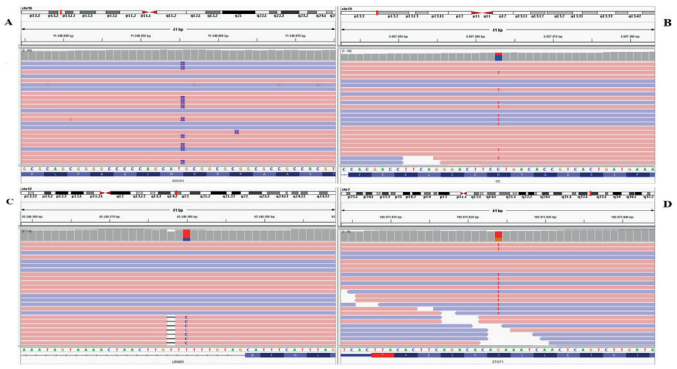

Figure 1. Representative Integrative Genomics Viewer (IGV) snapshots showing read alignments across selected genes. **A.** IGV view of the SOCS1 gene transcript (NM_003745.1). B. IGV view of the C3 gene transcript (NM_000064.4). **C.** IGV view of the LEMD3 gene transcript (NM_014319.5). **D.** IGV view of the STAT1 gene transcript (NM_007315.4). For each panel, aligned sequencing reads are displayed along the genomic coordinates, with colored bars indicating nucleotide mismatches relative to the reference genome.

The patient with the SOCS1 gene mutation was found to have discoid lupus, glomerulonephritis, and polyarteritis. Photosensitive malar rash was observed in our patients showing complement gene C1qb, C1qc, and C3 mutations. A patient with a STAT1 mutation was found to have scoliosis. Subcutaneous connective tissue nevi, glomerulonephritis, and polyarthritis were found in the patient with a LEMD3 gene mutation. Erythematosus malar rash was found in a patient with a PTPN22 gene mutation. The patient with a TREX1 gene mutation was found to have a malar rash. Patients with no gene mutation were found to have ANA (+++), anti-dsDNA (+), arthralgias, and autoimmune hemolytic anemia. Genetic and non-genetic individuals have not shown any gender or age differences. Among our patients showing gene mutations, the rate of those with missense mutations was 62.5%, those with frameshift mutations were observed at a rate of 25%, and those with intronic mutations were observed at a rate of 12.5%. One patient showed homozygosity, and the others showed heterozygosity. Gene transcription, nucleotide, and ACMG classifications are shown in Tables 1, 2. Clinical symptoms of SLE patients are presented in Figure 2.

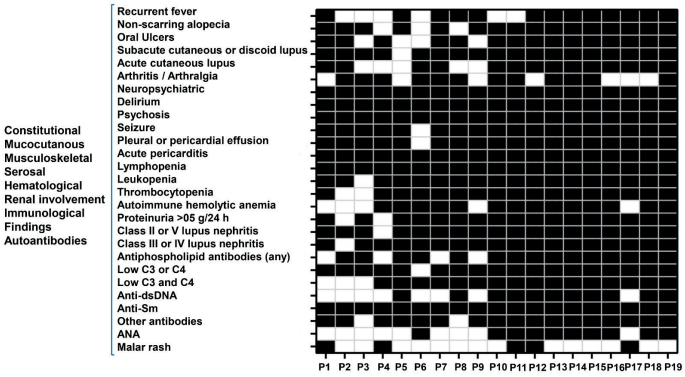

Figure 2. Clinical manifestations, laboratory findings, and immunological characteristics of patients. Heatmap representation of clinical manifestations, laboratory findings, and immunological characteristics of patients with systemic lupus erythematosus. Clinical features and laboratory parameters are grouped according to organ system involvement. Each column corresponds to one patient, and gray squares indicate the absence of the specified feature, while white squares indicate the presence.

Table 1. Genetic information of the SLE patients that indicated pathogenic/likely pathogenic variants

Patient No	Gene	GRCh37/hg19	Gene transcript	Nucleotide	rsID	Annotation/ Zygosity	ACMG classification
1	SOCS1	16:11348855	NM_003745.1	c.476_480dup p.(Met161Alafs* 46)	rs1470306246	Frameshift/ Heterozygous	Pathogenic (PVS, PM2, PP5)
10	C1qB	1:22660903	NM_001378156.1	c.278_297del p.(Met93ArgfsTer11)	-	Frameshift	Likely Pathogenic (PVS1, PM2)

Abbreviation: ACMG, American College of Medical Genetics and Genomics; PVS, Pathogenic very strong; PM, Pathogenic moderate; PP, Pathogenic supporting.

Table 2. Genetic information of the SLE patients that indicated VUS variants

Patient No	Gene	GRCh37/hg19	Gene transcript	Nucleotide	rsID	Annotation/ Zygosity	ACMG classification
2	C3	19:6697374	NM_000064.4	c.2777G>A p.(Arg926Lys)	-	Missense/ Heterozygous	VUS (PM2, BP4)
11	STAT1	2:191840550	NM_007315.4	c.2123C>A p.(Ser708Tyr)	-	Missense/ Heterozygous	VUS (PM2, PP3)
12	LEMD3	12:65637159	NM_014319.5	c.2306-9_2306-8delinsC	-	Missense/ Heterozygous	VUS (PVS1-M, PM2)
14	PTPN22	1:114380611	NM_001193431.2	c.1411T>A p.(Tyr471Asn)	rs200292847	Missense/ Heterozygous	VUS (PM2)
15	C1qC	1:22970643	NM_172369.5	c.127G>A p.(Gly43Arg)	rs759540631	Missense/ Heterozygous	VUS (PM2, PP3)
16	TREX1	3:48508047	NM_016381.5	c.158A>G p.(Tyr53Cys)	rs756787404	Missense/ Heterozygous	VUS (PM1, PM2, BP4)

Abbreviation: ACMG, American College of Medical Genetics and Genomics; BP, Benign supporting; PVS, Pathogenic very strong; PM, Pathogenic moderate; PP, Pathogenic supporting.

DISCUSSION

Our studies have identified mutations in the SOCS1gene among SLE patients. These mutations can lead to an impaired ability to control cytokine signaling, resulting in excessive inflammatory responses. Specifically, our research found that SOCS1 mutations are associated with glomerulonephritis and arthritis in SLE patients. Glomerulonephritis and arthritis are both common and severe manifestations of SLE. The association between SOCS1 gene mutations and these conditions suggests that altered cytokine signaling due to these genetic changes may contribute to the inflammatory processes underlying these symptoms. Our study results are consistent with the other studies that the SOCS1 gene mutation is associated with both glomerulonephritis (25) and arthritis (26). Understanding the role of SOCS1 mutations in SLE can provide insights into the molecular mechanisms driving the disease and highlight potential targets for therapeutic intervention. Targeted therapies that can correct or compensate for the defective SOCS1 function might help in managing the inflammatory symptoms of SLE more effectively.

In the present study, we observed that scoliosis, a condition characterized by abnormal lateral curvature of the spine, was associated with STAT1 mutations in SLE patients. This finding suggests a potential link between STAT1 mutations and musculoskeletal abnormalities in SLE. The precise mechanisms by which STAT1 mutations contribute to scoliosis in SLE are not fully understood but altered immune signaling and chronic inflammation likely play a role (27). We identified mutations in C1qB, C1qC, and C3 genes among SLE patients, with specific clinical phenotypes associated with these mutations. For example, photosensitive malar rash was linked to mutations in C1qB and C3, indicating that defective complement activity might contribute to skin manifestations in SLE. The precise mechanism likely involves impaired clearance of apoptotic cells in the skin, leading to localized immune responses and inflammation upon UV exposure (28). We also found in our study that mutations in the PTPN22 gene were associated with erythematous malar rash, a hallmark of SLE characterized by a red, butterfly-shaped rash across the cheeks and nose. The link between PTPN22 mutations and skin manifestations in SLE suggests that the altered immune regulation due to this mutation contributes to the localized inflammatory responses observed in the skin (29). The identification of PTPN22 mutations in SLE patients has significant therapeutic implications. Understanding the role of this genetic variant in disease pathogenesis can guide the development of targeted therapies aimed at modulating T-cell activity (30).

Additionally, our study has shown that mutations in the LEMD3 gene are associated with certain clinical phenotypes of SLE, such as cutaneous involvement and musculoskeletal abnormalities. These findings suggest that the disruption of nuclear architecture and altered signal transduction caused

by LEMD3 mutations may contribute to the diverse clinical features observed in SLE patients (3). Targeting the pathways affected by these mutations, such as the TGF-β signaling pathway, could provide new avenues for treatment. Therapies aimed at correcting or compensating for the disrupted nuclear functions may help manage the symptoms and progression of SLE in patients with LEMD3 mutations (31). In our study, mutations in the TREX1 gene were associated with arthralgias, which are common in SLE patients. The link between TREX1 mutations and joint manifestations may be due to the chronic inflammatory state induced by the accumulation of undegraded DNA, leading to immune-mediated joint damage (32). Targeting the pathways activated by cytosolic DNA, such as the STING (Stimulator of Interferon Genes) pathway, could offer new therapeutic strategies for managing SLE, particularly in patients with TREX1 mutations. Inhibitors of the STING pathway or other components of the innate immune response could potentially mitigate the excessive inflammation seen in these patients (33). Interestingly, some SLE patients show no gene mutations but are present with high ANA (+++), anti-ds DNA (+), autoimmune hemolytic anemia, and pericardial effusion. This suggests that non-genetic factors also play a crucial role in SLE development and manifestations, indicating the complexity and multifactorial nature of the disease (34).

Our study has several limitations. First, its retrospective design limits the ability to establish causal relationships between identified gene mutations and specific clinical phenotypes. Second, the small sample size reduces the statistical power of the analysis and limits the generalizability of the results to the broader SLE population. Third, the single-center nature of the study may introduce selection bias. Therefore, the biological significance of the mutations and their direct contribution to disease mechanisms remain to be confirmed in future, larger, prospective, and multicenter studies.

CONCLUSION

STAT1 mutations significantly contribute to SLE pathogenesis, particularly through clinical phenotypes like scoliosis, highlighting the role of genetics in the disease's heterogeneity. Similarly, mutations in C1qB, C1qC, and C3 genes disrupt the complement system, causing persistent inflammation in SLE. The PTPN22 mutation poses a genetic risk for SLE, linked to immune dysregulation and symptoms like erythematous malar rash. LEMD3 mutations disrupt nuclear integrity and TGF-β signaling, while TREX1 mutations lead to cytosolic DNA accumulation, both contributing to SLE pathogenesis and diverse symptoms.

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Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: This study was approved by the Ethical Committee of Umraniye Training and Research Hospital (Ethics No: B.10.1.TKH.4.34.H.GP.0.01/169, 13/06/2024), School of Medicine, University of Health Sciences, Istanbul, Turkey.

Supplementary Material

A total of 44 genes related to SLE were examined. Those are ACP5, ADA2, C1qA, C1qB, C1qC, C1S, C2, C3, C4A, C8A, CASP10, CFTR, CTLA4, CYBA, CYBB, DDX41, DNASE1, DNASE1L3, FAS, FASLG, FCGR2A, FCGR2B, IGHG2, IGKC, IRAK1, LEMD3, MASP2, NCF1, NCF2, PEPD, PNP, PRKCD, PTPN22, RASGRP1, SAMHD1, SEMA6B, SERPING1, SMPD1, SOCS1, SPP1, STAT4, TNFAIP3, TPP2, and TREX1 genes.

REFERENCES

1. Ahmad YA, Bruce IN. Genetic epidemiology: systemic lupus erythematosus. Arthritis Res. 2001;3:331-6.
2. Yoshimura A, Naka T, Kubo M. SOCS proteins, cytokine signaling and immune regulation. Nat Rev Immunol. 2007;7:454-65.
3. Couto AR, Bruges-Armas J, Peach CA, et al. A novel LEMD3 mutation common to patients with osteopoikilosis with and without melorheostosis. Calcif Tissue Int. 2007;81:81-4.
4. Ott N, Faletti L, Heeg M, Andreani V, Grimbacher B. JAKs and STATs from a Clinical Perspective: Loss-of-Function Mutations, Gain-of-Function Mutations, and Their Multidimensional Consequences. J Clin Immunol. 2023;43:1326-59.
5. Rauch I, Müller M, Decker T. The regulation of inflammation by interferons and their STATs. JAKSTAT. 2013;2:e23820.
6. Botto M, Kirschfink M, Macor P, et al. Complement in human diseases: Lessons from complement deficiencies. Mol Immunol. 2009;46:2774-83.
7. Pickering MC, Walport MJ. Links between complement abnormalities and systemic lupus erythematosus. Rheumatology (Oxford). 2000;39:133-41.
8. Walport MJ. Complement and systemic lupus erythematosus. Arthritis Res. 2002;4 Suppl 3:S279-S93.
9. Liu T, Yang M, Xia Y, et al. Microarray-based analysis of renal complement components reveals a therapeutic target for lupus nephritis. Arthritis Res Ther. 2021;23:223.
10. Truedsson L, Bengtsson AA, Sturfelt G. Complement deficiencies and systemic lupus erythematosus. Autoimmunity. 2007;40:560-6.
11. Namjou B, Kim-Howard X, Sun C, et al. PTPN22 association in systemic lupus erythematosus (SLE) with respect to individual ancestry and clinical sub-phenotypes. PLoS One. 2013;8:e69404.

12. Mumm S, Wenkert D, Zhang X, McAlister WH, Mier RJ, Whyte MP. Deactivating germline mutations in LEMD3 cause osteopoikilosis and Buschke-Ollendorff syndrome, but not sporadic melorheostosis. J Bone Miner Res. 2007;22:243-50.
13. Hellemans J, Preobrazhenska O, Willaert A, et al. Loss-of-function mutations in LEMD3 result in osteopoikilosis, Buschke-Ollendorff syndrome, and melorheostosis. Nat Genet. 2004;36:1213-18.
14. Crow YJ, Hayward BE, Parmar R, et al. Mutations in the gene encoding the 3'-5' DNA exonuclease TREX1 cause Aicardi-Goutières syndrome at the AGS1 locus. Nat Genet. 2006;38:917-20.
15. Rice GI, Bond J, Asipu A, et al. Mutations involved in Aicardi-Goutières syndrome implicate SAMHD1 as a regulator of the innate immune response. Nat Genet. 2009;41:829-32.
16. Ensembl VEP pick options. https://www.ensembl.org/info/docs/tools/vep/script/vep_other.html#pick_options
17. Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA), ncbi.nlm.nih.gov/clinvar/submitters/505954/
18. Evidence-based Network for the Interpretation of Germline Mutant Alleles (ENIGMA), ncbi.nlm.nih.gov/clinvar/submitters/504863/
19. Pharmacogenomics Knowledge Base,Stanford University (PharmGKB), ncbi.nlm.nih.gov/clinvar/submitters/500295/
20. The Clinical and Functional TRanslation of CFTR (CFTR2), ncbi.nlm.nih.gov/clinvar/submitters/500092/
21. ClinGen RASopathy Expert Panel (CIINGEN-RAS), ncbi.nlm.nih.gov/clinvar/submitters/506439/
22. ClinGen Inherited Cardiomyopathy Expert Panel (CMP-EP), ncbi.nlm.nih.gov/clinvar/submitters/506161/
23. Maxwell KN, Hart SN, Vijai J, et al. Evaluation of ACMG-Guideline-Based Variant Classification of Cancer Susceptibility and Non-Cancer-Associated Genes in Families Affected by Breast Cancer. Am J Hum Genet. 2016;98:801-17.
24. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17:405-24.
25. Fujimoto M, Tsutsui H, Xinshou O, et al. Inadequate induction of suppressor of cytokine signaling-1 causes systemic autoimmune diseases. Int Immunol. 2004;16:303-14.
26. Egan PJ, Lawlor KE, Alexander WS, Wicks IP. Suppressor of cytokine signaling-1 regulates acute inflammatory arthritis and T cell activation. J Clin Invest. 2003;111:915-24.
27. Shumilova A, Vital EM. Musculoskeletal manifestations of systemic lupus erythematosus. Best Pract Res Clin Rheumatol. 2023;37:101859.
28. Graham RR, Cotsapas C, Davies L, et al. Genetic variants near TNFAIP3 on 6q23 are associated with systemic lupus erythematosus. Nat Genet. 2008;40:1059-61.
29. Gregersen PK, Olsson LM. Recent advances in the genetics of autoimmune disease. Annu Rev Immunol. 2009;27:363-91.
30. Bottini N, Peterson EJ. Tyrosine phosphatase PTPN22: multifunctional regulator of immune signaling, development, and disease. Annu Rev Immunol. 2014;32:83-119.
31. Wordsworth P, Chan M. Melorheostosis and Osteopoikilosis: A Review of Clinical Features and Pathogenesis. Calcif Tissue Int. 2019;104:530-43.
32. Lee-Kirsch MA, Chowdhury D, Harvey S, et al. A mutation in TREX1 that impairs susceptibility to granzyme A-mediated cell death underlies familial chilblain lupus. J Mol Med (Berl). 2007;85:531-7.
33. Lee-Kirsch MA, Günther C, Roers A. Nucleic acid-mediated autoinflammation and autoimmunity-type I interferonopathies. J Mol Med (Berl). 2016;94:1081-4.
34. Parks CG, de Souza Espindola Santos A, Barbhaiya M, Costenbader KH. Understanding the role of environmental factors in the development of systemic lupus erythematosus. Best Pract Res Clin Rheumatol. 2017;31:306-20.