FULL TEXTS

FT1- Evaluation of Lymphocyte Cell-Specific Protein-Tyrosine Kinase, G-Protein Signal Regulator 10 and DNA Methyltransferase 1 Gene Expressions in Patients with Ocular Active and Ocular Inactive Behçet's Disease

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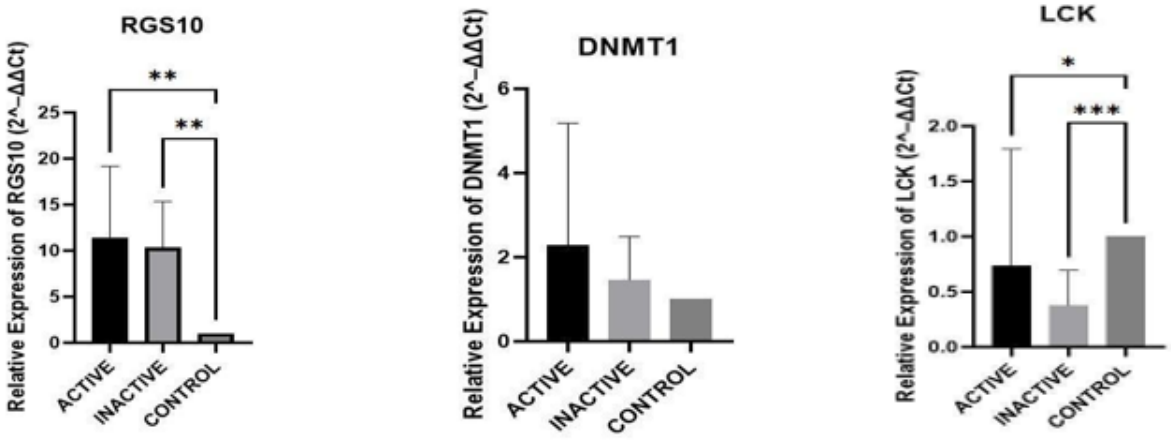
Introduction:
Behçet's disease is a multisystemic disorder with autoimmune and autoinflammatory features, observed more frequently in countries such as China, Japan, and Türkiye (Deng et al., 2022). Clinically, the disease manifests through recurrent oral and genital ulcers, cutaneous lesions, and ocular involvement, which is commonly seen in patients and may lead to vision loss (Guan et al., 2024). Due to the absence of a definitive diagnostic test, diagnosis relies on clinical findings, and genetic predisposition is particularly highlighted in carriers of the HLA-B51 allele (Lavalle et al., 2024). Additionally, environmental factors, infectious agents, and especially epigenetic mechanisms are believed to play a crucial role in disease pathogenesis (Zou et al., 2021; Emmi et al., 2024). One of the key mechanisms of epigenetic regulation is DNA methylation, primarily mediated by DNA methyltransferase-1 (DNMT1) (Zou et al., 2021). DNMT1 is known to influence disease progression by silencing pro-inflammatory genes or modulating anti-inflammatory responses (Caldiran & Cacan, 2022). Moreover, the genes Regulator of G Protein Signaling 10 (RGS10) and Lymphocyte Cell-Specific Protein-Tyrosine Kinase (LCK), which are regulated by epigenetic modifications, have significant roles in the control of immune responses and the pathogenesis of Behçet's disease (Caldiran & Cacan, 2022; Deng et al., 2022). This study aims to investigate the expression levels of DNMT1, RGS10, and LCK genes in patients with ocular involvement in Behçet's disease, thereby contributing to the understanding of immunological and epigenetic mechanisms in disease pathogenesis. Accordingly, it is aimed to provide a scientific basis for identifying disease-specific biomarkers and developing innovative therapeutic strategies.

Materials and Methods:
This study included a total of 45 individuals who were admitted to the Ophthalmology Department of Erciyes University and diagnosed with Behçet's disease (BD) according to international criteria. The participants were divided into three groups:

- BD patients with ocular involvement during the active phase (n = 15)
- BD patients with ocular involvement during the inactive phase (n = 15)
- Healthy control individuals (n = 15)

The control group consisted of systemically healthy individuals without any known ocular or chronic diseases. Informed consent was obtained from all participants. Total RNA was isolated from blood samples collected in EDTA tubes and cDNA synthesis was performed using the iScript cDNA Synthesis Kit. Real-time PCR was conducted using BIO-RAD SSoAdvanced Universal SYBR Green Supermix on a LightCycler 480 (Roche) device to measure mRNA expression levels of the LCK, RGS10, and DNMT1 genes. GAPDH was used as the housekeeping control gene. The project was supported by the Erciyes University Scientific Research Projects Unit with the project code TYL-2025-14428.

Results:
Expression analysis of the RGS10, DNMT1, and LCK genes was performed using real-time PCR, with GAPDH as the reference gene. All group data were statistically analyzed using GraphPad Prism 9.0.0 software.
For the **RGS10 gene**, the Kruskal-Wallis nonparametric test was used due to the non-normal distribution of data across three groups. A statistically significant difference was found between each patient group and the control group ($p < 0.05$), while no significant difference was observed between the two patient groups. The expression of RGS10 was elevated in patient groups compared to the control group.
For the **DNMT1 gene**, data from all groups were normally distributed, and thus, the One-Way ANOVA parametric test was applied. No statistically significant difference was detected between the groups ($p > 0.05$). There was no notable change in DNMT1 expression levels between patient and control groups.
For the **LCK gene**, the Kruskal-Wallis nonparametric test was again used due to non-normal distribution across three groups. A significant difference was observed between each patient group and the control group ($p < 0.05$), but no significant difference was found between the patient groups. Notably, the expression difference in the inactive patient group was more pronounced compared to the active group. The expression level of LCK was decreased in patient groups relative to the control group.



Discussion:

In this study, the effect of ocular involvement associated with Behçet's disease (BD) on immune modulation and epigenetic regulatory mechanisms was investigated by examining the expression levels of the RGS10, DNMT1, and LCK genes. The obtained data suggest that these genes may exhibit significant expression changes in BD patients with ocular involvement.

The increased expression of the *RGS10* gene, especially in BD patients with ocular involvement during the active phase, suggests that this protein may function as a feedback regulator in controlling inflammation. *RGS10* can inhibit G protein signaling, thereby suppressing proinflammatory NF-κB activation and limiting the production of inflammatory cytokines (Ren et al., 2021; Lee et al., 2008). According to our findings, the expression of the *RGS10* gene was significantly elevated in patient groups compared to the control group, which is consistent with the literature. No significant difference in *RGS10* expression was observed between the active and inactive patient groups, suggesting that the expression level of this gene may not vary with the disease phase.

Recent studies have associated altered DNA methylation levels with various autoimmune diseases (Zou et al., 2021). Epigenetic regulatory enzymes such as *DNMT1* are believed to influence disease progression by suppressing the expression of proinflammatory genes or modulating anti-inflammatory responses (Alipour et al., 2017). However, in our study, no significant differences in *DNMT1* gene expression were observed among the groups.

Literature findings support the central role of T cell activation in BD patients with ocular involvement, with *LCK* contributing to increased intraocular inflammation by promoting T cell activation (Deng, 2022). In our study, a significant decrease in *LCK* gene expression was detected in the patient groups compared to the control group, supporting its potential role in BD pathogenesis. Moreover, expression levels were found to be lower in the inactive group than in the active group. This may suggest that *LCK* expression is not only associated with acute inflammation but may also play a role in chronic immune regulation. Accordingly, differential regulation of *LCK* at the peripheral and tissue levels could position it as a potential determinant of both systemic and tissue-specific immune responses.

In conclusion, these findings provide insight into the immunological and epigenetic roles of *RGS10*, *DNMT1*, and *LCK* in BD and may contribute to the identification of disease-specific biomarkers.

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FT2- Retrospective Analysis of Mutations Identified in the Beta-Globin Gene in Cases Studied for Beta-Thalassemia Genetics in the Department of Medical Genetics

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Introduction

Beta-thalassemia is a hereditary blood disease characterized by a decrease in erythrocyte and hemoglobin levels, which occurs as a result of mutations or deletions in the Beta-Globin (HBB) gene and is the most common disease worldwide and in our country (1,2). In epidemiologic studies conducted in Turkey, the average incidence of beta-thalassemia was found to be 2.1% and more than 200 mutations were reported (3,4). The most common beta-thalassemia mutations in Turkey include IVS-1-110, IVS-I-6, IVS-I-1, Codon 8, -30 and Codon 5 mutations. The spectrum of beta-thalassemia mutations varies according to regions (4,5). In the literature review, it was noticed that there were deficiencies in the conversion of routine study results into publications. In this study, we investigated the mutation data in the HBB gene in individuals whose beta-thalassemia genetics were studied in our center.

Method

The archival records of 782 individuals who underwent Sanger sequencing analysis for the Beta-Globin (HBB) gene in our center between 2010 and 2024 were retrospectively analyzed.

Results

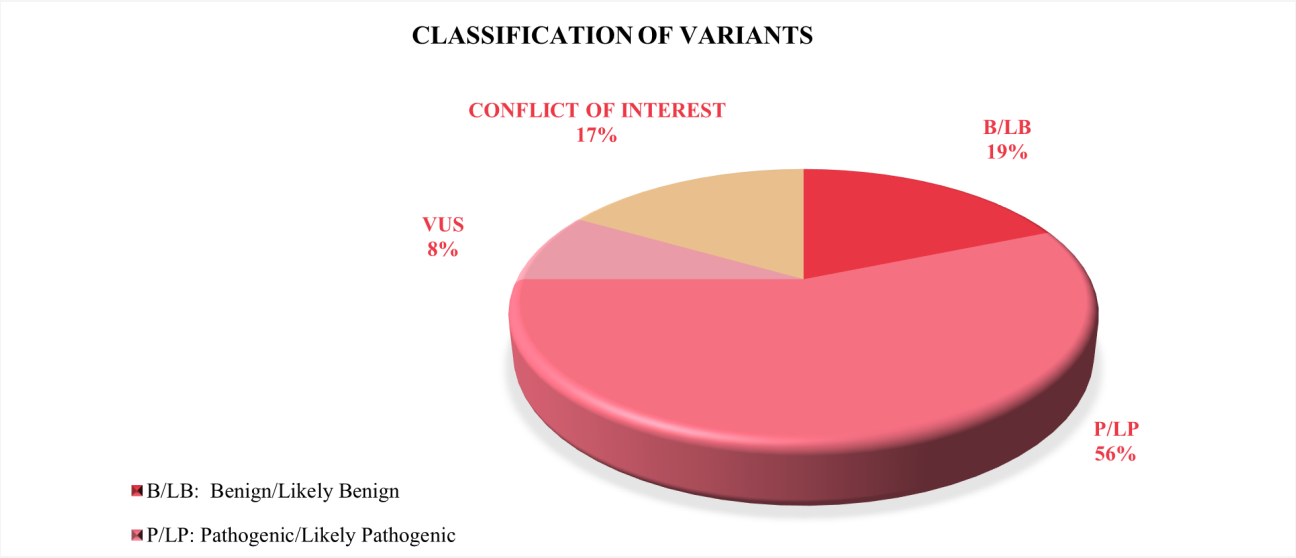
Within the scope of our study, a total of 782 individuals who underwent molecular genetic analysis were statistically evaluated with the SPSS 27.0.1.0 program and 53 different genetic mutations were detected in our center. When the gender distribution of the cases was analyzed, it was determined that 54% were female and 46% were male. According to the data obtained, it was determined that 56% of the mutations were pathogenic/probable pathogenic (P/LP), 53% of the mutations were homozygous and 47% were heterozygous genotypes. Demographic analysis revealed that the highest proportion (22.2%) of the age distribution of the applicants was in the 0-5 age group. When the distribution of previously reported variants in Turkey was analyzed in our center, it was found that the IVSI-110 G>A mutation was the most frequently observed variant with a rate of 22%.

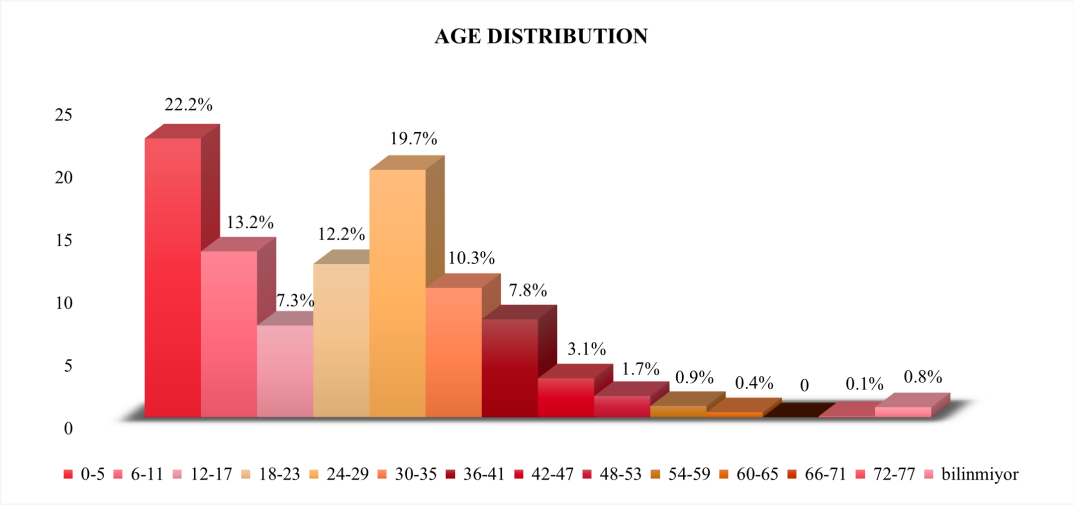
Conclusion

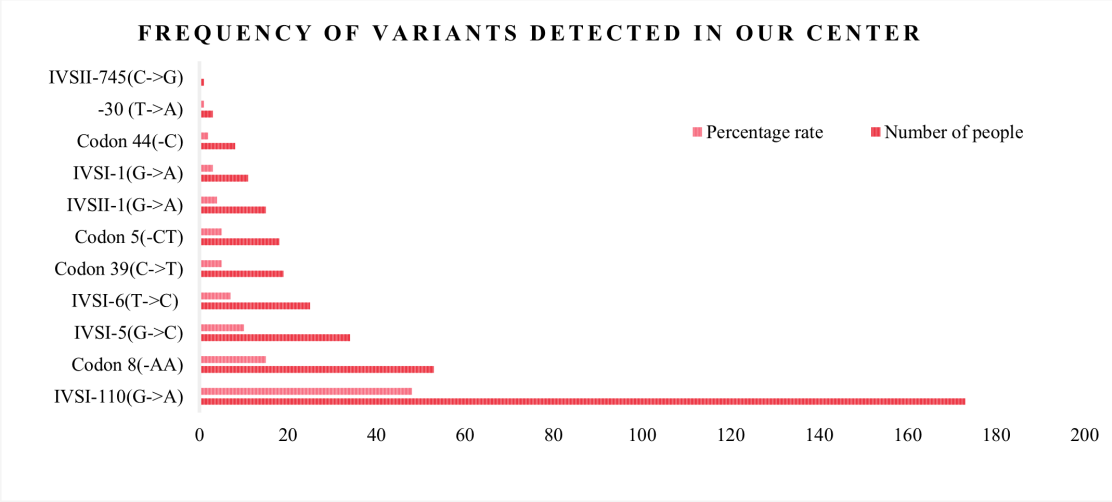
The data obtained in our study provide findings in terms of the clinical classification of genetic mutations, their distribution in the population and the demographic characteristics of the individuals admitted. When the distribution of rare abnormal hemoglobin variants in 37 individuals in our center is examined, the most common variant is Hb D-Los Angeles variant with a rate of 2.1%. Hb City of Hope (0.6%), Hb S (0.6%), Hb G-Coushatta (0.5%), Hb E-Saskatoon (0.3%), Hb Summer Hill (0.1%), Hb D-Iran (0.1%), Hb Volga (0.1%), Hb E (0.1%) variants followed by Hb D-Iran (0.1%). Our study contributes to the identification of new variants associated with Mediterranean anemia and updating genetic data.

Discussion

More than 200 mutations have been reported in the Turkish population. Mutation distributions vary by region due to geographical, ethnic and migration factors (1). In this study, a total of 53 different genetic mutations were identified, including 41 beta-thalassemia mutations and 12 hemoglobin variants. Mutations frequently observed in the Turkish population were also detected in our study (4-5). In line with the literature in Turkey, the most common mutation in our study was IVSI-110 (G>A) with 22%. This rate was reported as 20.65% in the study by Karaer et al. Although the findings were similar, the rate of this mutation was higher in our study (6). Unlike the study by Tadmouri, Codon 8 (-AA) was found to be the second most common mutation with a rate of 15% in our study. IVS I-5 (G>C) was the third most common mutation with a rate of 10%. IVS I-6 (T>C) mutation was identified in 7% of our study. This value is largely compatible with the rate of 7.2% reported by Tadmouri for our region and the rate of 10.33% reported by Karaer et al. This concordance suggests that the variant in question shows a stable distribution in terms of its prevalence in Turkey in general and especially in our region (6-8). The fact that the mutations detected in our center are mostly pathogenic indicates that clinically significant variants are common. Genotype distribution provides important information about the heterozygous (carrier) and disease status of individuals. In the study conducted in our center, a total of 37 individuals with rare hemoglobin variants were examined. It was determined







that 4.4% of these individuals had heterozygous (carrier) form of the variants, while 0.1% were homozygous. The most common Hb D-Los Angeles variant was observed in our center at a rate of 2.1%, which is higher than the rate reported by Güvenç et al. While the Hb E variant (0.1%) was found to be consistent with the literature, the Hb S variant (0.6%) was detected at a lower rate compared to the values reported in the literature (9). The fact that the proportion of individuals aged 0-5 who applied to our center was higher (22.2%) compared to other age groups suggests that awareness of early diagnosis is increasing in society. The findings of this study help address the lack of genetic data on the epidemiology of beta-thalassemia in our

center, clarify the mutation spectrum and support the identification of new variants. Updating genetic diagnostic algorithms will serve as a beneficial guide for the management and prevention strategies of thalassemia, as well as for the more effective planning of future national health policies.

This research was supported by Erciyes University Scientific Research Projects Coordinatorship as a Master's Thesis under the project code TYL-2025-14810.

Keywords: Beta- Thalassemia, Beta-Globin, Mutation, Retrospective, Genetics

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FT3- Identification of Key Genes Associated with Alzheimer's Disease through SVM-Based Classification of Cumulative Transcriptomic Data

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Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disease affecting more than 40 million people worldwide and one of the most common causes of dementia (1). In recent years, molecular substructure studies on Alzheimer's disease have increased significantly. Especially high-throughput transcriptomic techniques such as microarray and RNA-seq have allowed the identification of differentially expressed genes (DEGs) in diseased and healthy brain tissues. These genes are often linked to basic cellular processes such as neuroinflammation, synaptic communication, oxidative stress and mitochondrial dysfunction (2). However, most of these studies are limited to statistical approaches and cannot fully reflect the text of the ever-increasing pool of gene expression data. Machine learning (ML) is frequently used to identify complex patterns in high-dimensional datasets within complex biological datasets (3). Support Vector machines (SVM) have been used with very successful results for classification problems obtained with gene expression data (4). However, there are very few studies to date that have combined multiple dated microarray datasets against Alzheimer's disease cumulatively and analyzed them using ML algorithms. This creates opportunities for the discovery of potential biomarkers by combining old and new information. In this study, the microarray dataset of Alzheimer's disease, which was first published in 2004 and reanalyzed in 2010, was re-evaluated in detail with current machine learning techniques.

Methods

Gene expression datasets related to Alzheimer's disease were sourced from two studies (5,6). These datasets were used to create a SVM model for classifying Alzheimer's patients and healthy individuals. The model's performance was enhanced through Monte Carlo cross-validation.

Feature selection identified the most significant genes based on Information Gain Ratio and ANOVA tests, resulting in a final set of 50 genes. To assess these genes as potential biomarkers, we conducted a thorough literature review to examine their associations with Alzheimer's disease, drawing on published studies and evaluating their quality. The validation of the model and the biomarkers depends on their identification in at least 50 relevant studies.

Results

The trained model performs well in differentiating Alzheimer's patients from healthy controls, as evidenced by its classification accuracy (0.968), F1 score (0.968), sensitivity (0.968), specificity (0.971), Matthews correlation coefficient (0.927), and area under the curve (0.995) values. Based on gene expression data, these findings show that the developed SVM model performs a robust and dependable classification.

As a result of a literature review conducted on the 50 most sig-

nificant genes identified through analyses, it was determined that 15 of these genes were directly and significantly associated with AD. ATP6V1D (7), PLCB1 (8) and KIAA0368 (9) genes were identified as hub genes with significant effects on synaptic transmission and neuronal health. MRPL15 (10), ACO2 (11) and DNM1L (12) genes were associated with mitochondrial dysfunction and energy metabolism disorders. KPNA2 (13) and WDFY3 (14) genes contribute to neuronal cell protection by participating in nuclear transport and autophagy mechanisms, respectively. RFK (15) and USP19 (16) genes have been implicated in the regulation of neuroinflammation and ferroptosis processes. While the QPCT (17) gene plays a critical role in the formation of toxic pGlu-Aβ forms, the FGF20 (18) gene shows a protective effect against Alzheimer's pathology by supporting cognitive endurance. The CNR1 (19), C3orf14 (20) and NRXN1 (21) genes have been linked to synaptic function and neuronal communication.

Conclusion

This study aims to develop a reliable machine learning model that can differentiate healthy individuals from patients with Alzheimer's disease using cumulative microarray gene expression data. After preprocessing the data, selecting relevant features, and applying SVM-based classification, 15 key genes were identified, consistent with findings from previous experimental studies. These genes have the potential to contribute to early diagnosis and the development of biomarkers.

Keywords: Alzheimer's disease, support vector machine, gene expression, biomarker

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FT4- Unraveling Post-Transcriptional Regulation in Ataxia-Telangiectasia: A Systems Biology Perspective on microRNA-Target Networks

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Introduction

Ataxia-telangiectasia (AT) is a rare genetic condition related with ATM gene mutations, which control the two cellular processes: DNA double-stranded break repair and cell cycle control (1). The wide range of AT clinical presentations including cerebellar degeneration together with immune deficiency along with cancer predisposition requires moving past traditional genetic explanations since patients exhibit variable treatment outcomes (2). This study examines post-transcriptional gene regulation, with a particular emphasis on microRNAs (miRNAs) (3). These short, non-coding RNAs play a critical role in the precise regulation of mRNA translation, which presents opportunities for the modulation of disease pathways in populations affected by ataxia telangiectasia (AT) (4). Given the complexity and phenotypic variability of AT, this study aims to systematically explore the post-transcriptional regulatory landscape mediated by miRNAs. By integrating RNA-seq and non-coding RNA-seq data, we investigate the interactions between differentially expressed miRNAs and their mRNA targets, perform functional enrichment analyses, and identify critical signaling pathways potentially contributing to AT pathogenesis. The goal is to uncover regulatory hubs and candidate biomarkers that may provide mechanistic insights into the variable clinical outcomes observed in AT and guide future therapeutic strategies.

Methods

RNA-seq and non-coding RNA-seq data related to Ataxia telangiectasia were collectively analyzed to identify significant hub genes and potential biomarkers. To achieve this, we downloaded the RNA-seq data with the GEO number GSE175776 (2) and the non-coding RNA-seq data with the GEO number GSE266411(4). The analysis focused on microRNA-mRNA interactions.

In the data analysis process, differential expression analysis was conducted using the DESEQ2(5) and limma (6) packages in R software. The results of these analyses were filtered based on log2 fold change (log2FC) values less than -2 or greater than 2, and a p-value threshold of less than 0.1 was used to determine statistical significance. The identified genes were categorized as up-regulated or down-regulated, along with related miRNAs.

Targets and network interactions of upregulated and downregulated miRNAs were created using TargetScan (7) and MiRTarBase (8). Experimentally validated strong and weak interactions were sourced from MiRTarBase, and the resulting miRNA networks were designed to include at least three interactions. We compared the expression pattern of miRNAs and mRNAs in Ataxia patients with that of control groups using tidyR and dplyR in RStudio software.

The resulting interactions between hub miRNAs and mRNAs were analyzed using KEGG (9), REACTOME (10), WIKIPATHWAYS (11), and Gene ONTOLOGY(12) analyses to determine the pathways in which they are involved. A reference p-value of less than 0.1 was set for this analysis. The KEGG, REACTOME, and WIKIPATHWAYS analyses were conducted using iDEP 2.0 (13) and MIENTURNET (14). The results of the analysis were visualized with ggplot.

Results

Based on the results of the differential expression analysis, 37 miRNAs were found to be downregulated, while 11 miRNAs were upregulated in patients. Additionally, among individuals with ataxia, 775 mRNAs were upregulated, and only 74 mRNAs were downregulated. The study that analyzed this binary data revealed a significant hub network comprising approximately 150 interactions between downregulated miRNAs and upregulated mRNAs. Within this network, a total of 24 miRNAs were identified as targeting the remaining mRNAs (Figure 1).

Integrative pathway enrichment analysis based on microRNA-target gene associations has identified several signaling pathways that are targeted by microRNAs through at least ten different genes. These pathways represent key regulatory centers that may have significant biological relevance to complex disease mechanisms.

Notably, multiple pathways associated with neurodegenerative diseases emerged as some of the most extensively targeted. Specifically, twelve genes (ATXN1, BCL2, BDNF, CACNA1C, CHRM3, GNAQ, GRM5, KRAS, LRP6, PLCG1, PPP3R1, UBE2G1) are regulated by hsa-miR-30a-5p. This indicates a potential role for this microRNA in synaptic signaling, immune response pathways, and neurodegenerative processes (15).

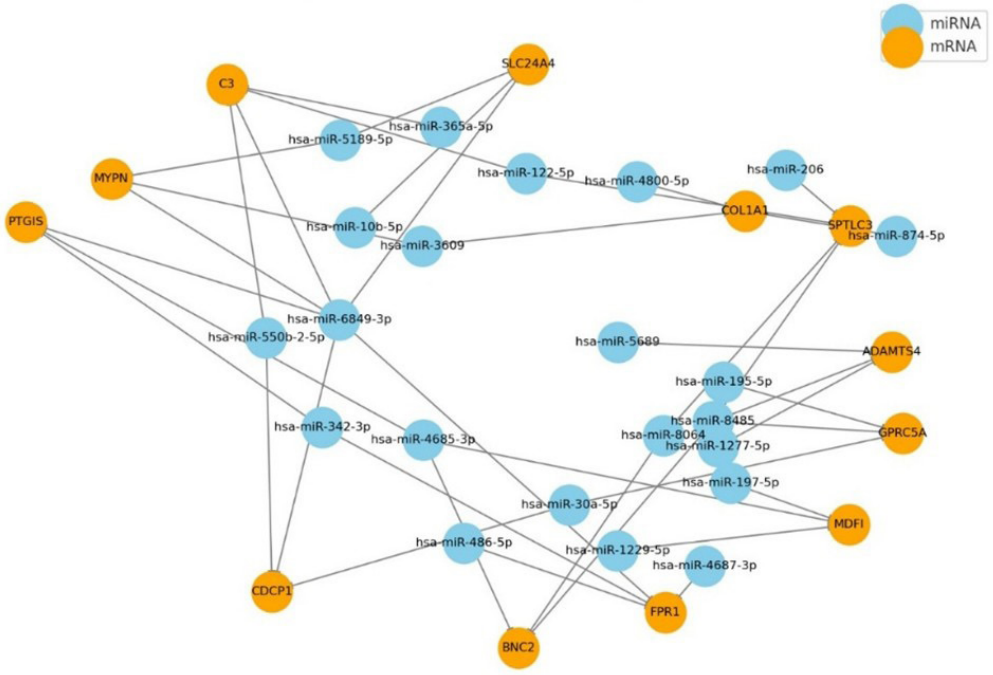

Figure 1. Network analysis determination of miRNAs and mRNAs that have an effect on the development of ataxia telangiectasia disease. According to differential expression analysis, orange nodes represent upregulated genes, while blue nodes represent downregulated miRNAs.

The cellular senescence pathway, which is associated with twelve genes (E2FC, FOXO3, HIPK2, KRAS, NFATC2, NFATC3, PPP3R1, SERPINE1, SMAD2, TSC1, ZFP36L1, ZFP36L2), was also found to be regulated by hsa-miR-30a-5p. This suggests that this microRNA may play a role in cellular metabolism, aging, and proliferation mechanisms (15).

Additionally, the calcium signaling pathway, targeted by seven genes (ATP2B2, CHRM3, EDNRA, FGF9, GNAQ, NFATC2, NFATC3) under the regulation of hsa-miR-195-5p, further emphasizes the importance of miRNA-mediated regulation in calcium-dependent signal transduction and transcriptional control (16).

Conclusion

Expertise in detecting ataxia AT in cerebellar tissue, together with the presence of chromosomal instability and immune dysfunction, suggests that the identified microRNAs may critically impact important disease markers (4,17). Among these miRNAs, hsa-miR-195-5p is particularly noteworthy because it affects DNA damage responses and neuronal survival in AT by targeting pathways related to neurodegeneration and various components of calcium signaling pathways. Additionally, hsa-miR-30a-5p's involvement in metabolic and cardiac signaling may impact the systemic symptoms associated with the condition. Experimental evidence shows that the dysregulation of miRNAs in AT not only relates to variations in outcomes from ATM mutations but also plays a direct role in the variability of clinical presentations. The established networks linking miRNAs, pathways, and genes hold potential as targets for future therapeutic interventions and research validation in the treatment of AT.

Keywords: Ataxia–telangiectasia, miRNA-mRNA interaction, pathway analysis, system biology

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FT5- Retrotransposon Profiling at CNV Breakpoints in Obese Patients: Insights from a Single-Center Study

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Introduction Copy number variations (CNVs) are genomic structural variations that play a role in the pathogenesis of various genetic traits and diseases.1,2 Transposable elements are DNA sequences that can move within the genome. Initially they were considered as junk DNA, but in recent years they have been recognised as playing active roles in genome evolution and gene regulation.3 Approximately 45% of the human genome is derived from transposable elements. These are DNA transposons and retrotransposons.4 Retrotransposons can be classified into two groups: Long terminal repeats (LTR) and non-LTR. Long interspersed nuclear element (LINE) and short interspersed nuclear element (SINE) families are prominent in non-LTR retrotransposons. Retrotransposons such as LINE, SINE, and LTR are mobile elements that can cause genomic instability by inducing structural rearrangements through RNA-mediated retrotransposition.5-7 Many studies have shown that retrotransposons are associated with breakpoints of CNVs.8 Obesity is a global health problem and a complex disease associated with multiple genetic and environmental factors. Obesity emerges as a result of genetic predispositions interacting with environmental factors. This interaction has increased the interest in epigenetic regulation. This may contribute to the understanding of the disease at the molecular level.9 Findings suggest that the methylation level of retrotransposons, such as LINE-1, may be associated with various phenotypes of obesity and metabolic syndrome.10 The main aim of this study is to identify the retrotransposon profile at the breakpoints of CNVs detected through analyses in a single-centre cohort of obese patients. Based on these data, this study aims to gain insight into the possible mechanisms underlying the structural genomic variations associated with obesity.

Methodology In this study, SNP microarray analysis (Illumina BeadChip Microarray, Infinium HTS, >700K probes) was performed on genomic DNA samples from 47 individuals diagnosed with obesity. The data were analysed using GenomeStudio v2.0.5. During the evaluation of structural variations, only CNVs ranging in size from 50 kilobases (kb) to 5 megabases (Mb) were included in the analysis. These thresholds were set to ensure both the selection of clinically significant variations and technically more reliable results. CNVs suspected to have a mosaic structure or low signal intensity were excluded from the study to minimise possible analysis errors.

Results A total of 126 CNVs that met the criteria determined as a result of CNV analyses were included. The genomic coordinates of the CNVs were determined, and their start and end points (breakpoints) were thoroughly evaluated using the RepeatMasker track in the UCSC Genome Browser to assess the presence, type, and distribution of retrotransposons within these regions. Within the scope of this assessment, regions where repetitive elements of the same class and family were present at both ends of the CNVs were considered potential breakpoints. Analysis of the retrotransposon profiles at the breakpoints of the CNVs included in the obese patient cohort

revealed that 40 CNVs (31.7%) contained the same type of retrotransposon at their breakpoints. It was determined that 35 (87.5%) of these CNVs were associated with the LINE-1 (L1) family, 3 (7.5%) with LINE-2 (L2), and 2 (5%) with the Mammalian-wide Interspersed Repeats (MIR) family. The majority of the CNVs were associated with LINE families, particularly L1.

Discussion

Obesity is a complex disease caused by the interaction of genetic and environmental factors. Epigenetic mechanisms, such as DNA methylation, histone modifications, and non-coding RNAs, are major contributors to interindividual variation, and can influence the risk of obesity.11 Epigenetic changes may even mediate the long-term effects of environmental factors, a phenomenon known as "metabolic memory." 12 Genome-wide association studies have shown single nucleotide polymorphisms associated with obesity. However, these variants are insufficient to fully explain the genetic basis of obesity; therefore, structural variations, particularly CNVs, have gained increasing attention. CNVs are known to cause changes in gene copy number, thereby altering DNA dosage. Some large CNVs may be relatively common in certain populations and appear benign, but when combined with other genomic alterations, they can contribute to disease phenotypes such as obesity.13,14 Our study identified retrotransposons belonging to the same class and family at CNV breakpoints, suggesting that these elements may contribute to genomic instability and the formation of CNVs. Retrotransposons, which constitute the majority of transposable elements, are mobile sequences capable of integrating into various regions of the genome via reverse transcription. The high sequence homology between elements belonging to the same class and family increases the potential for recombination in these regions, thereby predisposing the genome to instability. In particular, the facilitation of non-allelic homologous recombination between non-allelic regions makes this mechanism a major factor in CNV formation.15,16 The prominent presence of LINE elements, particularly those belonging to the L1 family, in our study suggests that these retrotransposons are located in genomic regions that are more prone to structural rearrangements and may have the potential to contribute to CNV formation. The human genome is known to be prone to LINE–LINE recombination events, which contribute to genomic instability and can lead to unbalanced structural variants.17 L1 elements, the most abundant transposons in the human genome, are widely distributed due to their high retrotransposition activity and play a key role in CNV formation.5

L1 elements are known to have significant effects on the structure and genetic diversity of the human genome. Through genetic and epigenetic mechanisms, they can contribute to mutations, structural variations, and a wide range of human diseases.4 One study showed that lower L1 methylation levels in the visceral adipose tissue of severely obese individuals were associated with higher fasting glucose and diastolic blood pressure levels, as well as an increased risk of metabolic syndrome.10 Although not directly identified in our study, Alu elements, an important retrotransposon family, are also associated with structural and epigenetic genomic changes.18 In one study, Alu elements in the intron 2 region of the POMC gene were associated with a hypermethylation variant observed in obese children that increases the risk of obesity by decreasing POMC expression.19 These studies indicate how retrotransposons may contribute to disease risk by influencing the epigenetic regulation of nearby genes.

In conclusion, our study demonstrates that retrotransposons, particularly L1, play a prominent role at CNV breakpoints in individuals with obesity. This finding is in line with the growing evidence that retrotransposons not only predispose the genome to structural alterations, but may also contribute to the development of obesity and related metabolic complications through their methylation status and epigenetic effects on nearby genes. Future studies should investigate retrotransposon-associated structural variations and their epigenetic status in larger cohorts from different populations, as well as in various tissues, particularly in metabolically active tissues and in cell types relevant to obesity. Functional studies are needed to validate the underlying mechanisms, and integrated analyses of genetic and epigenetic data should be conducted.

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FT6- The Importance Of Polymorphism And Alleles Of The NPY Gene In Metabolic Syndrome And It Is Components

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Introduction

Metabolic syndrome (MetS) is a systemic metabolic disorder and represents one of the most pressing issues in modern medicine. The main components of MetS include: abdominal obesity, insulin resistance, arterial hypertension, and dyslipidemia (1). The neuropeptide Y (NPY) gene plays an important role in the regulation of energy balance, appetite and metabolism (2). The NPY gene encodes a 36-amino acid neuropeptide that is involved in various physiological and homeostatic processes both in the central and peripheral nervous systems (3,4). Some of its polymorphisms are associated with an increased risk of developing MetS including obesity, insulin resistance, and lipid metabolism disorders. An association has been confirmed between the NPY gene allele and impaired glucose tolerance as well as the development of insulin resistance (5,6).

Methods

A cross-sectional descriptive study was conducted involving 190 patients. All participants underwent assessment of anthropometric parameters (waist circumference ≥94 cm in men and ≥80 cm in women), blood pressure measurement (systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg) and evaluation of blood triglycerides, glucose and lipid levels (triglycerides ≥1.7 mmol/L, HDL cholesterol <1.03 mmol/L in men and <1.29 mmol/L in women and fasting glucose ≥5.6 mmol/L). MetS was diagnosed according to the IDF (2005) criteria. All patients underwent genotyping to identify a single nucleotide polymorphism (SNP) of the NPY gene using the PCR-RFLP method. Patients with incomplete examination or genotyping data were excluded from the statistical analysis (6 patients). The remaining participants were divided into two groups: those with MetS (n=120) and those without MetS (n=70). Statistical analysis was performed using the SPSS 25 program. The study was approved by the Ethical Committee of the International Kazakh-Turkish University named after H.A. Yasavi (protocol No. 30 dated 30.05.2024).

Results

The prevalence of genotypes and alleles of the NPY gene polymorphism was studied. The mean age of the participants was 49.78±11.1 years. According to the results of the genetic analysis the distribution of NPY gene genotypes and alleles was as follows: CC genotype – 17.9%, TC genotype – 56.8%, TT genotype – 22.1%. The frequency of the C allele was 48.6%, and the T allele – 51.4%. A statistically significant positive association was found between the T allele and the component of MetS represented by fasting hyperglycemia (χ^2=4.04, p=0.032). No statistically significant associations were found for the other components of MetS.

Conclusion

Thus, the association of the NPY gene polymorphism may play a significant role in predisposition to the components of metabolic syndrome. In our study, the T allele was more frequently observed in patients with fasting hyperglycemia. The NPY gene carrying the T allele may contribute to a more adaptive stress response by reducing cortisol release, thereby preventing an increase in blood glucose levels — this is particularly important in individuals predisposed to diabetes and MetS. Genetic testing for these polymorphisms could serve as a useful tool for assessing the risk of developing MetS and has clinical relevance for the prevention and treatment of metabolism-related diseases.

Keywords
NPY gene polymorphism, metabolic syndrome, metabolic components, impaired glucose

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